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Gynecology & Obstetrics

Preoperative HADS-Scores

Circulating Progesterone Levels

Highlights

Carcinome Papillaire Mammaire

Choriocarcinoma of the Fallopian

Discovering Thoughts, Inventing Future

VOLUME 17 ISSUE 1 VERSION 1.0

Global Journal of Medical Research: E
Gynecology and Obstetrics

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Preoperative HADS-Scores and Quality of Life One Year after Surgery for Breast Cancer

By Korell Matthias, Funkel Vanessa, Heck Esther & Stollwerck Peter

Abstract- Purpose: The use of HADS-score is worldwide accepted as a screening tool to identify cancer patients with additional need for psychooncological support. Elevated values for anxiety respectively depression are correlating with higher complaints like e.g. postoperative pain. We tried to investigate patient's situation at least one year following surgery for breast cancer.

Methods: In April 2016, 91 patients with breast cancer, operated before April 2015, were asked to participate at a survey regarding different parameters of their quality of life. The questionnaire included the feeling of attractiveness, satisfaction with postoperative pain and scar formation as well as the overall satisfaction using a visual analogue scale (VAS; 0 – 10). These results were correlated with the preoperatively applied HADS-scores. For statistical analysis SPSS was used (Student's paired t test).

Results: 69 women (75,8 %) responded the questionnaire. Of these 8 (11,6 %) respectively 15 (21,7 %) has had an elevated score for depression respectively anxiety and 9 women (13 %) had refused to fill out the HADS-form at the time of surgery.

Keywords: HADS-score, breast cancer, quality of life.

GJMR-E Classification: NLMC Code: WP 840

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Preoperative HADS-Scores and Quality of Life One Year after Surgery for Breast Cancer

Korell Matthias [α], Funkel Vanessa [σ], Heck Esther [ρ] & Stollwerck Peter [ω]

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Results: 69 women (75,8 %) responded the questionnaire. Of these 8 (11,6 %) respectively 15 (21,7 %) has had an elevated score for depression respectively anxiety and 9 women (13 %) had refused to fill out the HADS-form at the time of surgery.

There was no significant difference regarding age, tumor stage, type of surgery and postoperative systemic therapy in the different groups. The statistical analysis showed that there was significantly more satisfaction with the postoperative pain level in patients with HADS-D > 7 vs. HADS-D < 7 (9,5 vs. 7,6; $p<0,05$). In contrast, patients who refused the HADS-screening showed less satisfaction with the postoperative pain level (6,4 vs. 7,9 with HADS-screening; $p<0,05$). In these patients, the reduction of post- versus preoperative attractiveness was significantly higher, too (- 2,0 vs. – 0,1 with HADS-screening; $p<0,05$).

Conclusion: One year following surgery for breast cancer, patients with preoperative elevated HADS-score (anxiety and depression) showed even better results in respect to satisfaction with postoperative pain, which could be a result of the additional psychooncological support given to these. Women who refused to participate in the HADS-screening showed worse outcome in quality of life parameters one year following surgery. This should be taken into account in our oncological practice and must be further investigated in appropriate studies. Maybe patients not participating in HADS-screening need more psychooncological support than themselves respectively physicians are expecting.

Keywords: HADS-score, breast cancer, quality of life.

I. Introduction

The diagnosis "cancer" provokes tremendous reactions of fear and uncertainty in every person (1). The HADS-score is a worldwide accepted tool to identify patients with significant anxiety respectively depression, which is found in about 20-30% of patients primarily diagnosed with breast cancer. (2;3). The severity of psychological symptoms is influenced by the type of surgery but the quality of life is often impaired even after breast conserving operation (4).

The psychological morbidity can influence patient´s outcome in many aspects. E.g. the preoperative score for depression predicts higher levels of acute postoperative pain following breast surgery (5). Patients with elevated anxiety in HADS-A-score are experiencing significant more postoperative pain, too (6)

The level of anxiety respectively depression is decreasing over time, but about one third of patients suffers from psychological morbidity even more than 1 year following breast surgery (7, 8).

We want to follow up the patients after one year following primary surgery regarding parameters of quality of life (QoL).

II. Patients and Methods

In April 2016, 91 patients with primary breast cancer following surgery in our unit earlier than April 2015, were contacted. Preoperatively, 73 women had filled in the routinely used HADS-form, whereas 18 patients (19,8%) refused to. The patient´s age was 62,9 years in average (33 – 83 min-max). The HADS results were positive for depression in 11 cases (> 7; 15,1%) and for anxiety in 17 cases (> 10; 18,7%).

Patients with elevated scores for anxiety or depression were offered intensified psychooncological support.

For statistical analysis SPSS was used (Student's paired t test after check for normality).
A p-value <0,05 was regarded as significant.

III. Results

69 patients (75,8%) responded and sent back the questionnaire. Table 1 displays the distribution of the preoperative HADS-findings in the group of responders.

The mean age was 63,3 years (33-83 years). 46 patients (66,7%) received breast conserving surgery, while 15 (21,7%) respectively 8 (11,6%) were operated

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by mastectomy without respectively with implant reconstruction.

There was no significant difference regarding age, tumor stage, type of surgery (breast conserving versus mastectomy versus implant reconstruction) and postoperative systemic therapy in the different HADS-groups. (Table 2).

The satisfaction with the postoperative pain level was 7,7 in average (VAS „0“ – completely unsatisfied; „10“ – completely satisfied) (table 3). It was significantly higher in patients with preoperative elevated scores for depression (HADS-D>7 9,5 versus 7,6 HADS-D<8, p<0,05). There was a trend in favour of patients with higher level of anxiety (HADS-A>10 8,7 versus 7,6 HADS-A<8, p<0,1).

In contrast, patients who refused the HADS-screening were significant less satisfied with postoperative pain levels (HADS refused 6,4 versus 7,9 HADS accepted, p<0,05).

The satisfaction with actual scar formation was 6,6 in average and showed no significant differences in the different HADS groups (VAS „0“ – completely unsatisfied; „10“ – completely satisfied) (table 4)

The results of self-estimated quality of life are displayed in table 5. It was 7,1 in average with no detectable significant differences (VAS„0“ – worse; „10“ – excellent).

The self-rated attractivity (VAS „0“ – completely unalluring; „10“ – absolutely attractive) before and after surgery for breast cancer was not significant different (6 versus 5,6) and showed no influence of preoperative HADS-scores. (table 6).

In patients who refused HADS screening, the reduction of attractivity before and after breast cancer was significantly higher (6,9 before and 4,9 after breast cancer versus 5,9 and 5,8 in HADS accepted – p<0,05).

IV. Discussion

Women with breast cancer have the highest incidence of symptomatic depression and/or anxiety compared with other cancer patients (9). Although the prognosis of breast cancer is better in general than e.g. cancer of esophagus, the breast cancer patients suffer significant more often under symptomatic depression (28,1% vs. 15,6%) respectively anxiety (32,0% vs. 8,0%) (9).

The hospital anxiety and depression score (HADS) is well established and worldwide used in different diseases to identify patients with risk for psychological morbidity (10; 11).

In patients with breast cancer the HADS screening identify a high rate of patients with significant anxiety respectively depression which can significantly impair quality of life (QoL) (3). There are several different known risk factors like e.g. young age, which leads to significantly more impairment of QoL by menopausal symptoms, loss of fertility respectively attractivity, weight gain, physical in activity etc.(12).

In contrary, married women showed better results than singles (13).

The advantage of breast conserving surgery versus mastectomy in respect to QoL is still significant even 5 years after the primary diagnosis (14).

In case of depressive comorbidity in breast cancer patients, the use of short-term psychodynamic psychotherapy is effective in increasing QoL (15). In the treatment group 44% were HADS-D negative versus only 23% in the control arm. Therefore, every patient with a pathological HADS result is offered an intensified psychooncological support, because an intervention with psychotherapy is effective in reducing the severity of symptoms (16).

Nevertheless, sixty-three percent of cancer patients reported one or more unmet needs (17).

Pathological HADS findings are not only problematic for the patients but also for their partners. E.g. high anxiety levels lead to severe psychosocial and psychosexual problems like premature ejaculation (18). Like cancer patients, partners are reporting requirements which are often not fulfilled, too (19; 20).

Overall, the HADS screening represents an useful screening tool to adjust the psychooncological support to the individual needs. One year after the surgery for breast cancer our patients with primarily elevated scores for anxiety respectively depression didn´t show worse results in satisfaction with postoperative pain or scar formation. There was no significant decrease in self estimated attractivity compared before and after the breast cancer surgery.

It is unknown, whether the good results of patients with pathological HADS scores are success of the intensified psychooncological support. But, there are no hints for a need to change our clinical routine.

In contrary, patients who refused to participate in HADS screening at the time of surgery showed significantly worse outcome in satisfaction with postoperative pain and attractivity one year after treatment. We do not know the reason for some patientsrefusing the HADS screening. Some commented„ I don´t need support – I am fine “and others announced„ I will fill it inlater“, but without returning it.

Due to the small number of patients in our study one cannot draw definite conclusions. But, these results should motivate to further investigate why patients refuse to fill in our routine HADS screening chart. Possiblythey need more psychooncological support than themselves respectively physicians are expecting. We will further try to follow up all patients with breast cancer and will look more closely at women who refuse participation in HADS screening.

Compliance with ethical standards

All authors state no conflicts of interests Informedconsent was obtainedfrom all individual participantsincluded in thestudy.

There was no external financial founding

Author`s contribution:

M Korell: Protocol development, Data analysis, Manuscript writing
V Funkel: Data collection, Data analysis
E Heck: Protocol development, Data collection
P Stollwerck: Protocol development, Manuscript editing

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Tables

Table 1: Distribution of HADS-results

	n	(%)
all	69	100
HADS-D 0-7	52	75,4
HADS-D > 7	8	11,6
HADS-A 0-7	33	47,8
HADS-A 8-10	12	17,4
HADS-A >10	15	21,8
HADS refused	9	13
HADS accepted	60	87

Table 2: Age distribution and type of surgery (BCS – breast conserving surgery; mastectomy; reconstruction with implant)

	n	yrs (average)	BCS	mastectomy	implant
all	69	63,3	46 (66,7%)	15 (21,7 %)	8 (11,6 %)
HADS-D 0-7	52	61,7	36 (69,2%)	8 (15,4%)	8 (15,4 %)
HADS-D > 7	8	64,9	5 (62,5%)	3 (37,5%)	0 (0 %)
HADS-A 0-7	33	62,3	22 (68,7%)	6 (18,7%)	5 (15,6%)
HADS-A 8-10	12	61,1	11 (91,7%)	0 (0 %)	1 (8,3%)
HADS-A >10	15	63,1	8 (53,3%)	5 (33,3%)	2 (13,3)
HADS refused	9	69,9	5 (55,6%)	4 (44,4%)	0 (0%)
HADS accepted	60	62,3	41 (68,4%)	11 (18,3%)	8 (13,3%)

No significance

Table 3: Satisfaction with postoperative pain level (visual analogue scale – VAS)

	VAS (SD)		
all	7,7 (2,7)		
HADS-D 0-7	7,6 (2,5)		
HADS-D > 7	**9,5 (0,9)**	**p<0,05**	**vs. HADS_D 0-7**
HADS-A 0-7	7,6 (2,6)		
HADS-A 8-10	7,3 (2,6)		
HADS-A >10	**8,7 (1,4)**	**p<0,1**	**vs. HADS_A<7**
HADS refused	**6,4 (3,9)**	**p<0,05**	**vs. HADS accepted**
HADS accepted	7,9 (2,1)		

(„0“ – completely unsatisfied; „10“ – completely satisfied)

SD – standard deviation, no significance beside stated

Table 4: Satisfaction with actual scar formation (visual analogue scale – VAS).

	VAS (SD)
all	6,6 (2,9)
HADS-D 0-7	6,5 (2,9)
HADS-D > 7	8 (2,8)
HADS-A 0-7	6,8 (2,8)
HADS-A 8-10	4,8 (3,4)
HADS-A >10	7,9 (2,3)
HADS refused	6 (2,6)
HADS accepted	6,7 (2,9)

(„0“ – completely unsatisfied; „10“ – completely satisfied)

SD – standard deviation, no significance

Table 5: Self estimated quality of life (visual analogue scale – VAS).

	VAS (SD)
all	7,1 (2,2)
HADS-D 0-7	7,2 (2,4)
HADS-D > 7	7,7 (1,4)
HADS-A 0-7	7,3 (2,6)
HADS-A 8-10	7,2 (1,6)
HADS-A >10	7,1 (2,4)
HADS refused	6,4 (1,7)
HADS accepted	7,2 (2,3)

(„0“ – worse; „10“ – excellent)

SD – standard deviation, no significance

Table 6: Self estimation of „feeling attractive “before and after surgery of breast cancer (BC) (visual analogue scale – VAS).

	before BC	after BC	difference		
	VAS (SD)	VAS (SD)	(SD)		
all	6 (2,3)	5,6 (2,4)	- 0,4 (2,4)		
HADS-D 0-7	6 (2,4)	5,8 (2,5)	- 0,2 (2,4)		
HADS-D > 7	5,5 (3,2)	5,5 (1,4)	0 (2,8)		
HADS-A 0-7	6,1 (2,4)	6 (2,6)	- 0,1 (2,5)		
HADS-A 8-10	5 (2,5)	5 (2,0)	0 (1,9)		
HADS-A >10	6,3 (2,7)	5,6 (2,2)	- 0,7 (2,7)		
HADS refused	6,9 (1,1)	4,9 (2,5)	**- 2 (2,2)***	**p<0,05**	**vs. HADS accepted**
HADS accepted	5,9 (2,5)	5,8 (2,4)	- 0,1 (2,4)		

(„0“ – completely unalluring; „10“ – absolutely attractive)

SD – standard deviation, no significance beside stated

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Early Contralateral Intramammary Lymph Node Metastasis Presented Soon after Mastectomy in Nigeria: Case Report

By Wilson IB Onuigbo & Hyacinth E Onah

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Abstract- Mastectomy is an event that needs follow up. In this community, a report concerned recurrence in the mastectomy scar itself. Therefore, the present paper deals with metastasis beyond the midline itself, namely, spread across to an intramammary lymph node. It is considered here that interest in this location has long been delayed although its very existence was known as far back as 1892.

Keywords: *breast, cancer, mastectomy, metastasis, intramammary node, contralateral, spread, 1892 history.*

GJMR-E Classification: *NLMC Code: QZ 202*

Strictly as per the compliance and regulations of:

Early Contralateral Intramammary Lymph Node Metastasis Presented Soon after Mastectomy in Nigeria: Case Report

Wilson IB Onuigbo [α] & Hyacinth E Onah [σ]

Abstract- **Mastectomy is an event that needs follow up. In this community, a report concerned recurrence in the mastectomy scar itself. Therefore, the present paper deals with metastasis beyond the midline itself, namely, spread across to an intramammary lymph node. It is considered here that interest in this location has long been delayed although its very existence was known as far back as 1892.**

Keywords: breast, cancer, mastectomy, metastasis, intramammary node, contralateral, spread, 1892 history.

I. Introduction

Breast cancer is a subject of consuming interest worldwide from several angles (1,2). The senior author's interest was first aroused in this area with the epidemiology of breast masses among the local adolescents (3). Historical aspects also followed (4,5). In terms of malignancy, the importance of follow up after mastectomy was appreciated (6). Little wonder that our interest flowered with regard to the present case.

II. Case Report

NEG, 36-year-old, Para 4 woman consulted the junior author (HEO) at the University of Nigeria Teaching Hospital, Enugu. She complained of ulcerative lesion in the *left* breast of 8 months' duration. Therefore, she underwent mastectomy. At follow up, after 4 months, there was a nodule in the *right* breast. After the usual investigations, it was biopsied.

When the specimen was received by the senior author (WIBO), it was a 3 cm ovoid, smooth surfaced mass. On section, it exhibited pale and darker areas. After routine processing, the lesion turned out to be a lymph node which proved to be the seat of metastatic cancer cells that formed glands typically. The Figure shows that both early subcapsular and deeper parenchymal deposits were picturesque. Therefore, metastatic poorly differentiated adenocarcinoma was diagnosed therefore.

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III. Discussion

The question of the presence of lymph nodes within the breast itself has long been debated (7,8). Elsewhere, this was fully traced locally with reference to tuberculous lymphadenopathy within the breast (9).

Incidentally, a massive work was presented during the Meeting of the Edinburgh Medico-Chirurgical Society, as far back as 6th January, 1892. It concerned the careful observations made by Harold Stiles (10), assistant to the Professor of Surgery, University of Edinburgh, on the presence of lymph nodes in the breast. Consequently, it is well that modern literature now has this long neglected evidence!

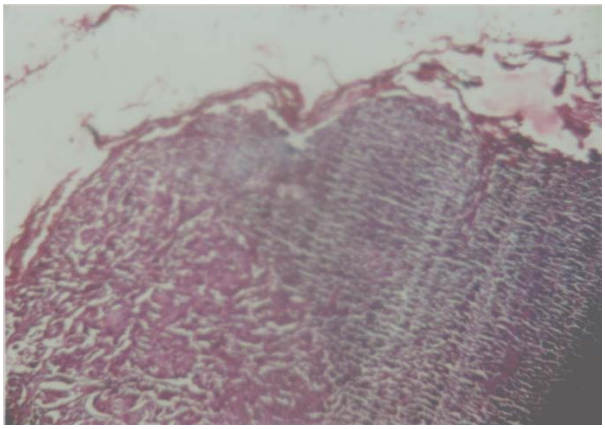

Figure 1: Lymph node showing sub-capsular and deeper deposits of poorly differentiated adenocarcinoma.

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Circulating Progesterone Levels and Ongoing Pregnancy Rates in Controlled Ovarian Stimulation Cycles in Assisted Reproduction Techniques

By Verma Shailja & Pratap Kumar
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Abstract- How can we prevent premature leutinization in our IVF cycles? To help find the solution a study designed with specific exclusion criteria in an assisted reproductive centre of a tertiary care hospital was designed. In a period of 2 years 100 patients were followed up prospectively. GnRH antagonist protocol was implemented for all recruits because of shorter duration of treatment and as it prevented hyperstimulation. Specific criteria was chosen for GnRH anatagonist initiation. Serum Progesterone measurements were used to predict premature leutinization. Electro-chemiluminiscence Immunoassay using COBAS 6000 used for the measurements. Three different groups analysed in above cohort and we concluded that despite of progesterone rise pregnancy outcome was unaffected. Why is the question answered in discussion.

Keywords: *GnRH (gonadotropin releasing hormone), progesterone, IVF, leutinization.*

GJMR-E Classification: *NLMC Code: WJ 190*

Strictly as per the compliance and regulations of:

Circulating Progesterone Levels and Ongoing Pregnancy Rates in Controlled Ovarian Stimulation Cycles in Assisted Reproduction Techniques

Verma Shailja [α] & Pratap Kumar [σ]

Abstract- How can we prevent premature leutinization in our IVF cycles? To help find the solution a study designed with specific exclusion criteria in an assisted reproductive centre of a tertiary care hospital was designed. In a period of 2 years 100 patients were followed up prospectively. GnRH antagonist protocol was implemented for all recruits because of shorter duration of treatment and as it prevented hyperstimulation. Specific criteria was chosen for GnRH anatagonist initiation. Serum Progesterone measurements were used to predict premature leutinization. Electro-chemiluminiscence Immunoassay using COBAS 6000 used for the measurements. Three different groups analysed in above cohort and we concluded that despite of progesterone rise pregnancy outcome was unaffected. Why is the question answered in discussion.

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I. Introduction

One of the essential components of a successful *in vitro* fertilization/embryo transfer (IVF – ET) cycles is the procurement of mature oocytes that will develop into good embryos with good implantation potential. There are a variety of ovulation induction protocols being utilized to achieve this goal but the markers of optimal maturity remain controversial.

The progesterone increase at, or just before, the onset of LH surge, was thought to be the response of granulosa cells to increased pituitary LH pulses. On the other hand, progesterone can also augment the positive feedback of estradiol on the LH surge[1]. During controlled ovarian stimulation (COS) cycle, progesterone levels rapidly increase following Human Chorionic Gonadotropin (hCG) administration given to induce final oocyte maturation[2]. However, we have also noticed premature LH (Leutinizing hormone) surge caused by the modulatory action of estradiol (E2) levels induced by gonadotropins which have led to premature luteinization and further more cancellation of treatment cycles in patients who are undergoing *in vitro* fertilization (IVF). We can now suppress the release of endogenous gonadotropins from pituitary by introduction of Gonadotropin releasing hormone (GnRH) agonists and antagonists which can decrease incidence of premature LH surge[2]. Despite use of GnRH analogues, subtle increase in serum progesterone levels (beyond an arbitrary threshold value) have been observed at the end of follicular phase in stimulation cycles for IVF and ICSI – ET[3].

This pre-hCG progesterone increase is referred as 'premature luteinization'[4], the term though is misleading as the increasing levels of serum progesterone occurs with GnRH analogues, i.e. it is taking place under low serum LH concentration.

Rather than the excessive amount of progesterone being produced by granulosa cells as a part of early luteinization, it is more likely that excess number of follicles are responsible for elevated progesterone levels as each one may be producing a normal amount of progesterone, consistent with late follicular phase[5]. Whether the presence of increased levels of progesterone on the day of hCG will affect ongoing pregnancy rate is the subject of debate.

Hence, we have investigated association between serum progesterone levels on the day of human Chorionic Gonadotropin (hCG) administration and the probability of ongoing pregnancy in woman undergoing Controlled Ovarian Stimulation for IVF (*in vitro* fertilization)/ICSI-ET (Intracytoplasmic sperm injection with Embryo transfer) in our this study.

II. Methodology

This prospective single center study was done under the ethical guidelines of our institution. A total of 100 patients were included meeting the above criteria and received GnRH antagonist protocol for pituitary down regulation. Study period was of 2 years. Cases of endometriosis and women with above 35 years of age were excluded. The initial dose of gonadotropins was individualized for each patient according to age, BMI, basal FSH levels, antral follicle count and previous response to controlled ovarian stimulation. Dose adjustments performed according to ovarian response, monitored by TVS & serum E2 levels. As a part of routine

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clinical practice, determination of serum progesterone levels were performed on the day of hCG administration.

a) Progesterone measurement

Laboratory measurement of serum progesterone was done using electro-chemiluminiscence Immunoassay "ELISA" using COBAS 6000. Results are determined via a calibration curve which is instrument – specifically generated by 2-point calibration & a master curve provided via the reagent barcode. Quality control using Elecsys Preci Control Universal 1 and 2 are done at least once in 24 hours when test is in use, once per reagent kit, and after every calibration. Measuring range is 0.030 – 60.00 ng/ml. For purpose of statistical analysis serum progesterone was divided into 3 categories as follows: a) <1 ng/ml b)1-1.5 ng/ml c) >1.5 ng/ml.

b) Statistical analysis

The analysis was performed using SPSS version 16 software. The statistical analysis of the data was performed using Pearson Chi – square test or Fischer Exact test. *p* – value of < 0.05 was considered significant.

c) Results

Three groups were formed as described above. The results were compared with the levels of progesterone on the day of hCG administration in stimulation cycle with various outcomes as described below. Baseline characteristics of 100 cases were comparable in all the three groups. Outcomes were measured in terms of total number of mature eggs; quality of embryos; pregnancy outcomes.

Out of 93 women who had less than 1 ng/ml serum progesterone on day of menses, 64.5 % remained less than 1 ng/ml on the day of hCG, 21.5 % it was raised to 1-1.5 ng/ml and in 14 % to >1.5 ng/ml. Three women who had 1-1.5 ng/ml had equal proportion on the day of hCG whereas those who had more than 1.5 ng/ml of progesterone on day 2 of cycle (n = 4) had equal proportion in 1-1.5 ng/ml & more than 1.5 ng/ml. This shows that most of the women show a rise in levels of progesterone on the day of hCG (0.022).

Out of 61 women 59% had estradiol levels less than 3000 pg/ml, 32.8 % had estradiol levels in 3000-6000 pg/ml & 8.2 % had estradiol levels >6000 pg/ml, whereas in group with 1-1.5 ng/ml and more than 1.5 ng/ml progesterone only 4.3 % & 6.2 % women had estradiol more than 6000 pg/ml. Though there is a positive correlation between rising estradiol levels and progesterone levels, this was not seen in this study (Table 1). We saw good endometrial thickness in all three groups irrespective of serum progesterone levels.

Table 1: Comparing serum progesterone levels on the day of hCG with serum Estradiol level.

Serum progesterone on the day of hCG	Estradiol values (pg/ml) on day of hCG						Total (n=100)
	<3000		3000-6000		>6000		
	n	%	n	%	n	%	
<1 ng/ml (n = 61)	36	59	20	32.8	5	8.2	61
1-1.5 ng/ml (n = 23)	16	69.6	6	26.1	1	4.3	23
>1.5 ng/ml (n = 16)	11	68.8	4	25	1	6.2	16
Total (n = 100)	63	63	30	30	7	7	100

(P value is 0.92 by applying Fischer's Exact Test, hence not statistically significant)

In terms of retrieving good mature eggs also we see that out of 61 women with serum progesterone less than 1 ng/ml 78.7% had up to 8 mature eggs, 18% had 9-16 mature eggs whereas 3.3% had more than 16 mature eggs. In women with 1-1.5 ng/ml progesterone (n = 23) 56.5% had less than 8 mature eggs & rest 43.5% had 9-16 mature eggs, whereas out of 16 women with more than 1.5 ng/ml progesterone, 62.5% had up to 8 mature eggs whereas 31.5% had 9-16 mature eggs & 6.2% had more than 16 mature eggs.

Hence we see that good numbers of mature eggs were retrieved in equal proportion in all the three categories (Table 2).

Table 2: Comparing serum progesterone on the day of hCG and number of mature eggs retrieved

Serum progesterone on the day of hCG	Number of mature eggs retreived						Total (n=100)
	Up to 8		9 - 16		More than 16		
	n	%	n	%	n	%	
<1 ng/ml (n = 61)	48	78.7	11	18	2	3.3	61
1-1.5 ng/ml (n = 23)	13	56.5	10	43.5	0	0	23
>1.5 ng/ml (n = 16)	10	62.5	5	31.2	1	6.2	16
Total (n = 100)	71	71	26	26	3	3	100

(P value is 0.10 by applying Fischer's Exact Test, hence not statistically significant)

Sixty one women had progesterone levels less than 1 ng/ml, out of them 26.2% had no best grade embryos retrieved 39.3% had up to 2 & 34.4% had more than 3 best grade embryos. In comparison, group with 1-1.5 ng/ml progesterone 17.4% had no embryos, 39.1% had up to 2 & 43.5% had more than 3 best grade embryos.

Finally, out of 16 women with more than 1.5 ng/ml progesterone 25% had no best embryos, 43.8% had up to 2 and 31.2% had more than 3 best embryos. Hence, best grade embryos were retrieved in equal proportion in all groups (Table 3).

Table 3: Comparing serum progesterone on the day of hCG and best embryos retrieved

Serum progesterone on the day of hCG	Best embryos retreived						Total (n=100)
	Nil		Upto 2		More than 3		
	n	%	n	%	n	%	
<1 ng/ml (n = 61)	16	26.2	24	39.3	21	34.4	61
1-1.5 ng/ml (n = 23)	4	17.4	9	39.1	10	43.5	23
>1.5 ng/ml (n = 16)	4	25	7	43.8	5	31.2	16
Total (n = 100)	24	24	40	40	36	36	100

(P value is 0.89 by applying Pearson Chi-Square test, hence not statistically significant)

Ninety one cases came for follow up beta hCG testing to us out of them 41.8% were pregnant. We further followed these pregnant cases, 71% of these pregnant women had their first antenatal scan done with us showing cardiac activity present.

Three cases were chemical pregnancy whereas other 3 cases had ectopic pregnancies (Table 4).

Table 4: Comparing serum progesterone on the day of hCG and pregnancy

Serum progesterone on the day of hCG	Pregnant		Non pregnant		Total (n = 91)
	n	%	n	%	
<1 ng/ml (n = 56)	26	46.4	30	53.6	56
1-1.5 ng/ml (n = 20)	6	30	14	70	20
>1.5 ng/ml (n = 15)	6	40	9	60	15
Total (n = 91)	38	41.8	53	58.2	91

(P value is 0.47 by applying Pearson Chi-Square test, hence not statistically significant)

In the group with progesterone levels > 1.5 ng/ml 40% patient became pregnant & 60% patients were non pregnant, though statistically not significant we followed up these cases & compared their serum progesterone levels with their pregnancy outcome by the first trimester scan for presence of cardiac activity, excluding chemical pregnancy.

Progesterone estradiol ratio >1 as the definition of premature luteinization was proposed to be associated with low ovarian reserve as well as poor pregnancy outcomes in some studies[6].

Hence we found that though pregnancy outcome is higher in groups with ratio <1 but this difference was not statistically significant (Table 5).

Table 5: Comparing serum progesterone estrogen ratios on the day of hCG with pregnancy outcome

Progesterone estrogen ratio on the day of hCG	Pregnant		Non pregnant		Total (n = 91)
	n	%	n	%	
<1 (n = 84)	37	44	47	56	84
>1 (n = 7)	1	14.3	6	85.7	7
Total (n = 91)	38	41.8	53	58.2	91

(P value is 0.23 by applying Fischer's Exact test, hence not statistically significant)

III. Discussion

Several mechanisms have been proposed to explain subtle elevation of progesterone on the day of hCG administration. It has been suggested that excessive luteinization of the follicles occurs either due to late administration of hCG or exposure of granulosa cells to high concentration of LH forms, exogenous gonadotropin treatment[7, 8]. Both of them seem unlikely in our set up as GnRH antagonist protocol was used and

no premature LH surge or decline in estradiol was seen post hCG administration. Also, good fertilization rates are contradictory to excessive luteinization explanation. Another explanation is that follicle maturation may occur at a lower follicle diameter than expected, resulting in post-mature oocytes. However, hCG administration decision was not based solely on ultrasound findings; furthermore, no adverse effect was reported on the maturation phase of the oocytes, or fertilization or cleavage rates of embryos in the group with higher progesterone levels on the day of hCG administration[9].

However, treatment with GnRH antagonists has been reported to suppress both immuno-active and bioactive LH but not the subtle rise in progesterone on day of hCG administration[10.] Small elevation in progesterone levels on the day of hCG is not caused by elevation of LH because of higher pituitary output or external stimulation rather it may likely because of a local increase from the ovaries and an increase in receptivity of LH at the level of granulosa cells. There are also other intra-ovarian regulators which can be involved in the regulation of ovarian steroidogenesis[11], and also there is somatomedin-C which is found to augment significantly FSH induced progesterone biosynthesis in the rat *in vitro* culture[12].

Our results have shown no difference in serum estradiol levels on the day of hCG, irrespective of higher or lower progesterone levels; none of our cases had significant premature LH surge; the number of oocytes recruited and their fertilization & cleavage rates did not differ between the three groups that we took in this study.

The possibility that small changes in the progesterone levels, on the day of hCG, may primarily effect the endometrium rather than on the ovary has already been proposed. An abnormal rise of progesterone prior to LH surge was reported to affect the uterine endometrium and it results in asynchronization between embryonic development and the endometrial environment[12].

The hormonal receptors present in the endometrium may be affected and may influence other factors responsible for implantation, like platelet activating factor (PAF), one of the factors reported to be involved in the process of implantation[13].

In a study of 115 cases, IVF/ET cycle outcomes were retrospectively correlated with progesterone levels on the day of hCG, as findings demonstrated that even modest increase in progesterone was associated with reduced pregnancy rates. So they recommended to cryopreserve all embryos rather than having a fresh embryo transfer[14]. Other changes in clinical practice may include administrating hCG at a smaller follicle size if progesterone levels start rising.

We require more studies to define the optimal markers of follicle maturation facilitating better timing of hCG administration[15].

In a study on one thousand twelve women undergoing 1,189 IVF-ET cycles, Fanchin et al demonstrated that when there is an adequately required response to controlled ovarian stimulation, an elevated P levels are not associated with lower pregnancy outcomes. This indicates that good embryo quality may compensate for the adverse endometrial effects of progesterone but when there is a weak response to controlled ovarian stimulation (poor responders), premature elevation can lead to lower pregnancy rates[16].

The cause of increase in serum progesterone levels is poorly understood. It may just reflect the mature granulosa cell response to high FSH exposure. It can be a possibility that the gonadotropin used in the stimulation regimen and the amount of LH suppression may play a role in the phenomenon, as both FSH & LH activity may differ in both quality & quantity between products and batches seperately.

Ubaldi et al showed some results indicating that there may be an association between the circulating FSH concentration an late follicular phase progesterone concentrations. This observation can lead to an alternate hypothesis for the increased progesterone secretion in the cycles which are treated with purified FSH[17]. It is also possible that reduced LH stimulation reduces the degree of catabolism of progesterone to androgens & estrogens, as reported above, which leads to excess progesterone secretion into the circulation.

Fleming in his study also raised the issue of methodology used for measuring progesterone in the studies, retained in meta – analysis, which were neither conceived nor validated for measuring low levels of progesterone in the follicular phase[18]. His own data showed that assay precision was varying depending on whether petrol – ether extraction step was used or not sufficiently supports this methodology concern. Also he provided with the evidence supporting the possibility that progesterone measurements at the end of controlled ovarian treatments could be flawed by patient specific matrix effects [18]. The method used in our study had a strict inclusion and exclusion criteria for case selection and the method used for progesterone measurement had a good precision hence unlikely that results are affected by above raised issue.

In Bosch et al study, the strength of association observed might be attenuated by the method used to group patients according to progesterone levels because their assay had sensitivity of 0.2 ng/ml, whereas assay used in this study has sensitivity of 0.030 ng/ml[19].

At present we have no consensus on whether the elevation of progesterone on day of hCG is associated with achieving of a pregnancy. Several studies have denied such association[4, 19, 20, 21], whereas other studies have concluded possibility of a negative association that is probability of pregnancy decreasing significantly when progesterone levels on the day of

hCG for final oocyte maturation, rises above a threshold [7, 16, 22]. In this study we noted that there is no association between elevation of progesterone on the day of hCG administration and pregnancy rate. It should be noted that if negative association between progesterone elevation on day of hCG and the chances of pregnancy do exists, it might be worth exploring the possibility of cryopreserving the resulting embryos and they can be transferred in a subsequent frozen – thawed cycle[23, 14] or another alternative is administrating hCG early in the follicular phase prior to progesterone elevation[18].

Different detrimental levels of serum progesterone on day of hCG in terms of pregnancy outcome has been proposed by above mentioned studies but in this study no such level could be indentified as in all cases we had good response to controlled ovarian stimulation protocol.

Limitation of this study was less sample size hence results were not statistically significant and larger studies size is required.

We found that though there is a rise in serum progesterone seen during controlled ovarian stimulation cycles on the day of hCG in GnRH antagonist cycle but this rise has no significant effect on endometrium thickness, number & quality of oocytes retrieved, number & quality of embryos retrieved and finally pregnancy outcome.

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Choriocarcinoma of the Fallopian Tube: A Case Review

By N. Abounouh, FZ. Belkouchi, MA. Benyahia & S. Bargach

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Abstract- Chorioarcinoma of the Fallopian tube is a rare genital malignancy tumor. The diagnosis is difficult. Treatment is managed by chemotherapy following surgery. A 37 years-old patient, was admitted to the emergency room, accusing lower abdominal pain, accompanied by vaginal bleeding without amenorrhea. A tubal ectopic pregnancy was suspected, the patient underwent laparotomy. Histological examination revealed a choriocarcinoma of the fallopian tube.

Our aim reporting this case is to show the importance of performing histopathological exam of the tubal specimen in the patients with ectopic pregnancy. Since this pathology is extremely rare, highly aggressive, but still curable.

Keywords: *choriocarcinoma, fallopian tube, ectopic pregnancy, chemotherapy.*

GJMR-E Classification: *NLMC Code: WJ 190*

Choriocarcinoma of the Fallopian Tube: A Case Review

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Keywords: choriocarcinoma, fallopian tube, ectopic pregnancy, chemotherapy.

I. Introduction

Choriocarcinoma is extremely rare and aggressive form of gestational trophoblastic disease. It occurs due to neoplastic changes in the chorionic villi epithelium. The most common site of origin is the uterus; the incidence of choriocarcinoma in the fallopian tube is very low [1]. We report a case of choriocarcinoma of the Fallopian tube treated successfully with surgery and chemotherapy.

II. Case Report

The patient is a 37 years-old woman, admitted to emergency room vaginal bleeding and lower abdominal pain without amenorrhea. Her menstrual cycles was regular; she had 2 vaginal deliveries and no previous gynecologic operations.

On admission, her temperature was 37°C pulse rate 90pulse/min, and blood pressure 125/70 mm Hg. Vaginal examination revealed moderate vaginal bleeding and a normal ante flexed uterus, with no adnexal palpable tumor. Her blood test results were: Hemoglobin 12, 7 g/l00 ml of; platelets 500.000/mm3; her blood group A+. The patient underwent transvaginal ultrasonography which showed a normal uterine cavity with no signs of intrauterine gestational sac or embryo. But an ectopic mass of 49x36 mm was visualized in the right adnexal region, vascularized with Doppler flow, and there was images of free fluid limited to the pelvis. A level of 15943 mIU/ml β-Hcg was detected.

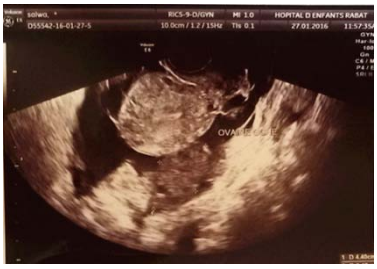

Figure 1: Transvaginal ultrasonography showing normal uterine cavity, and Left ovary measuring 44x22 mm

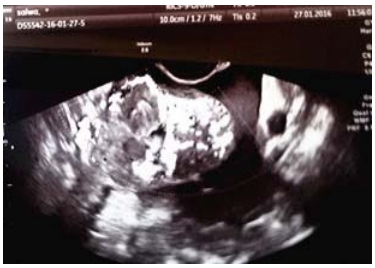

Figure 2: Transvaginal ultrasonography showing normal uterine cavity, and right adnexal mass measuring 49x36 mm

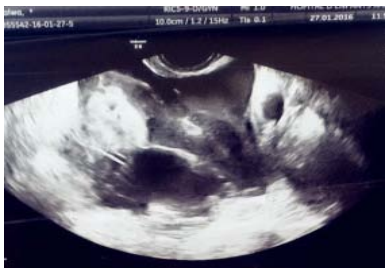

Figure 3: Ultrasonography showing free pelvic fluid. MRI was realized showing an ectopic pregnancy

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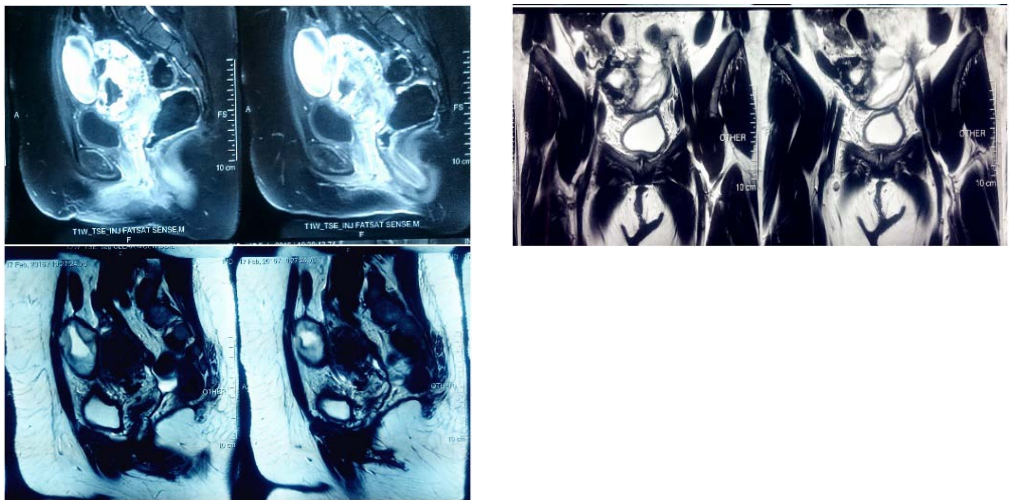

Figure 4: MRI showing a right adnexal tumor corresponding to an ectopic pregnancy.

An emergency laparotomy was made. On exploration, was noted an abundant haemoperitoneum with 700 cc of blood that was evacuated, on the right fallopian tube as well was an actively bleeding ectopic mass invading the right lateral side of the uterus; ovaries weren't affected, interadnexial subtotal hysterectomy was performed. The postoperative course was uneventful.

Histological examination of the specimen revealed an invasion of the fallopian tube with signs of rupture. No villous formations were found, the uterus was partially invaded. A diagnosis of choriocarcinoma of Fallopian tube was made.

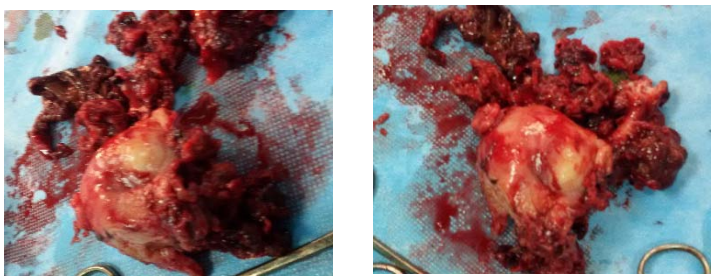

Figure 5: Post-operative macroscopic view of the uterus and right tumor specimen.

The patient underwent complement of radiologic and laboratory examinations. Computed tomography scans of the abdomen and thorax were realized showing Pulmonarmetastasis. The patient workup indicated that the FIGO score was 6. Chemotherapy was planned, she was administered monochemotherapy using methotrexate 1 mg/kg intravenously on days 1, 3, 5 and 7 alternating with folinic acid 0.1 mg/kg intramuscularly on days 2, 4, 6 and 8 of the cycle.

Treatment response was monitored weekly by checking serum β-Hcg measurements that gradually decreased and became negative after 2 months and then monthly measurements were made. The patient responded well to the chemotherapy and no side effects were observed. The patient was followed up for 1 year and was disease free till that period.

III. Discussion

Choriocarcinoma is a malignant type of the gestational trophoblastic disease which usually originates from uterine cavity. On rare occasions they may occur in the tube, cervix [2] horn of the uterus, vagina or other pelvic organs [3]. The incidence is 0.8% of all the gestational trophoblastic disease [4]. It is generally very aggressive [5]; and otherwise can simulate other gynecologic diseases such as ovarian cyst, tubo-ovarian abscess and ectopic pregnancy [4], with clinical similar symptoms as amenorrhea, vaginal bleeding and vascular instability along with increased B hCG titer.

MRI, endovaginal ultrasound and colourflow Doppler play an important role in the diagnosis of intrauterine choriocarcinoma [6]. However, no specific

imaging findings have been defined for extra-uterine choriocarcinoma; in our case, the ultrasonography suspected malignant adnexal tumor but it wasn't visible with MRI.

Histological examination of a surgically resected specimen is essential for the confirmation and diagnosis of choriocarcinoma. In our case, a tubal pregnancy was suspected, but the examination of the specimen affirmed the diagnosis of choriocarcinoma.

Choriocarcinoma, produces up to hundred times the amount of β- Hcg .β-Hcg level measured in our case was up to15943 mIU/ml β-Hcg. Therefore, the measurement of β- Hcg concentrations are very useful to assess the response to treatment and detect any recurrences.

The treatment of tubal choriocarcinoma is as of the uterine type, surgery with chemotherapy [7]. In tubal choriocarcinoma conservative treatment for younger women can be established. Salpingectomy or adnexectomy without removal of the uterus Is done, followed by chemotherapy [8]. For older women with no child desire, a bilateral adnexectomy or hysterectomy can be preconized [9]. Our Patient underwent hysterectomy.

Choriocarcinoma can metastasize into the lungs, brain, liver, and even very rarely into the fetus [5]. Because of this highly metastatic potential , monochemotherapy using méthotrexate and l'actinomycine D ; or multiple drugs chemotherapy using méthotrexate, d'actinomycine D, d'étoposide, cisplatine, cyclophosphamide, vincristine and bléomycine [8] is essential and proves to be very effective in trophoblastic tumors. The literature shows that patient with choriocarcinoma even with metastasis can achieve complete remission [10].

The women who are treated for extra-uterine choriocarcinoma should receive effective contraception for 1 to 2 years after the completion of their treatment, with B-hcgmonitoring.

IV. Conclusion

The tubal choriocarcinoma is a rare disease with bad prognosis if not treated. This study reminds us the importance of the histological examination of any ectopic pregnancy. The tubal choriocarcinoma diagnosis can be made while suspecting an ectopic pregnancy with a high level of βHCG, a salpingectomy must be carried, and chemotherapy must be followed to improve the prognostic and surviving rate.

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Wernicke's Encephalopathy Associated with Hyperemesis Gravidarum: A Case Report

By Soraya Saleh Gargari, Maasoumeh Saleh, Fereshteh Bagherifard & Maasoumeh Alizadeh

Shahid Beheshti University of Medical Science

Abstract- We report the case of a 30 year-old woman, at 16 weeks of gestational age, with hyperemesis gravidarum. She presented with blurred vision and ophthalmoplagia, VI nerve palsy, distraction and gazing were detected in physical examination. The resonance magnetic imaging was repoeted normal. Her pregnancy was terminated with suspected preeclampsia, but she had gradually decline in GCS and heparin was started with suspected sinus venosus thrombosis. Unfortunately, she died and then in review of brain imaging in the mortality conference, she had typical changes of Wernicke's encephalopathy. WE is a potentially reversible condition if treated early. We would like to emphasize the importance of prompt thiamine supplementation in pregnant women with prolonged vomiting in pregnancy, especially before starting intravenous or parentral nutrition. Early thiamine replacement will reduce maternal morbidity and fetal loss rate. It was a missed management WE in another center, so we have decided to report it to think of this diagnosis in cases of hyperemesis garavidarum with neurologic symptoms. This report is according to documents.

Keywords: *hyperemesis gravidarum, wernicke encephalopathy, thiamin.*

GJMR-E Classification: *NLMC Code: WJ 190*

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Wernicke's Encephalopathy Associated with Hyperemesis Gravidarum: A Case Report

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I. Introduction

HG is characterised by severe, protracted nausea and vomiting associated with weight loss of more than 5% of pre-pregnancy weight, dehydration and electrolyte imbalances (1). Wernicke's encephalopathy (WE) and Korsakoffs psychosis are severe manifestations of thiamine deficiency. WE is commonly associated with alcoholism, probably because chronic alcohol ingestion results in increased thiamin utilization, reduced GI uptake and impaired phosphorylation of thiamin. WE has also been reported in an increasing array of conditions that affect nutrition, however, including prolonged intravenous feeding, gastrointestinal procedures and diseases, malignancies, infections, starvation and hyperemesis gravidarum. WE has classic triad of oculo-motor abnormalities, cerebellar dysfunction, and altered mental state, which might manifest as disorientation, confusion or even coma. The majority of patients with WE do not have all three triad signs, only 10% of patients exhibit all three features (2). Untreated WE is fatal. Mortality rate is 10% to 20% among treated patients (3). In patients suspected of WE, thiamine treatment should be started immediately (4). Blood should be immediately taken to test for thiamine, other vitamins and minerals levels. Following this an immediate intravenous or intramuscular dose of thiamine (50-100 mg) should be administered (5) two or three times daily. Thiamine administration is usually continued until clinical improvement ceases. Concomitant liver failure, infection or delirium tremens often makes the cause of death unclear (6).

If glucose is given, such as in hypoglycaemic alcoholics, thiamine must be given concurrently. If this is not done, the glucose will rapidly consume the remaining thiamine reserves, exacerbating this condition (4).

Other nutritional abnormalities should also be looked for, as they may be exacerbating the disease (7, 8). In particular, magnesium, a cofactor of transketolase which may induce or aggravate the disease (4).

II. Case Presentation

A 30 years old woman, gravidity 2, parity 1, with history of a vaginal delivery 13 years ago, with gestational age of 16 weeks, admitted in another center with chief complaint of blurred vision. She had gestational diabetes on diet and obsessive compulsive disorders (OCD) who discontinued her medications in early pregnancy. She had 20kg weight loss during pregnancy due to anorexia and vomiting and had two admissions in gestational age of 10 weeks and 12 weeks with diagnosis of hyperemesis gravidarum. In this admission, physical examination showed: Blood pressure fluctuation from 120 to 160 mmHg systolic and from 80 to 100 mmHg diastolic, Pulse rate: 120 beats per minute, Temprature: 370C. Also she had ophthalmoplagia, VI nerve palsy, distraction and gazing. In lab tests, elevated liver enzymes, elevated ESR, hypokalemia, proteinuria (1+) and ketonuria (1+) was detected. Methylprednisolon was started for the patient by internist due to increased ESR and elevated liver enzymes and CNS symptoms. Blood pressure was controlled with atenolol and Mg-SO4 started with diagnosis of preeclampsia. Brain MRI and MRV requested by neurologist due to CNS symptoms and suspected sinus venosus thrombosis, and were reported normal by radiologist. In examination by ophthalmologist, no abnormal findings were detected. Lumbar punctuation was done and her intracranial

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pressure was normal. With diagnosis of preeclampsia, pregnancy was terminated 10 days after admission with vaginal misoprostol. After pregnancy termination, her CNS symptoms were continued, so ANA and antiphoshpholipid antibodies were requested by neurologist that were normal. One day after pregnancy termination, she had gradually decline in GCS. During 24 hours, GCS decline to 3/15 and with suspected sinus venosus thrombosis, heparin was started for her, but unfortunately she died 18 days after termination. In mortality conference, the management of case was evaluated respectively and her brain imaging was reviewed. Brain MRI had typical changes of WE (image 1). This patient was a missed diagnosis WE.

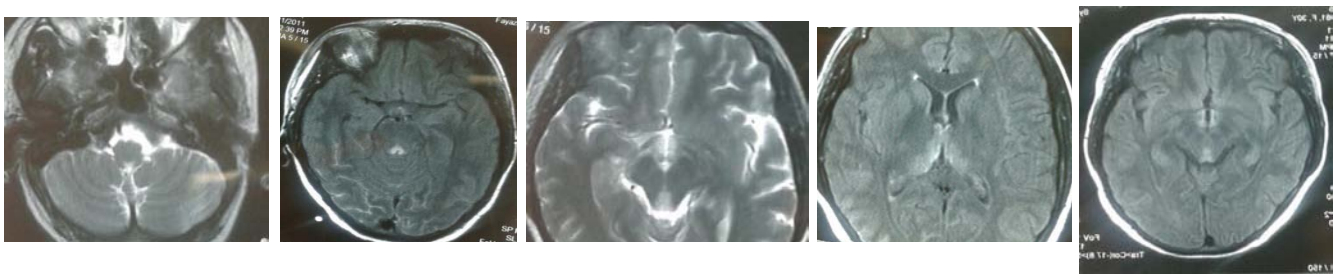

Image 1: On the T2 and FLAIR images, increased signal intensity is present at periaqueductal gray matter and both mammillary bodies, highly suggestive of WE. Periaqueductal gray matter involvement is suggestive of two diagnoses: 1. Leigh disease, 2. WE. For differentiation between them: involvement of mammillary bodies is infavor of WE and is against diagnosis of Leigh disease.

III. Discussion

WE is a potentially reversible yet serious neurological manifestation caused by vitamin B1 (thiamine) deficiency (9). If the cells with high metabolic requirements have inadequate stores of thiamine, energy production drops, and neuronal damage ensues (10). Time to deplet the body's store of thiamine is about 3 weeks (11). The daily requirement of thiamine is around 1.1 mg/day for females, and it increases to 1.5 mg/day, particularly during pregnancy and lactation (12).The prevalence of WE in a non-alcoholic patient varies from 0.04% to 0.13% (13). Many cases of WE in pregnancy with hyperemesis gravidarum (HG), were first reported in 1914 (14). Most patients present with the triad of ocular signs, ataxia and confusion (9). MRI is the imaging modality of choice because it is highly specific (93%) and comparatively safer than computed tomography (CT) scan (9). On imaging, it is commonly seen on MRI as areas of symmetrical increased T2/FLAIR signal involving the mammillary bodies, dorso-medial thalami, tecatl plate, periaqueductal area, and around the third ventricle. Lab assessment of blood transketolase activity and thiamine pyrophosphate (TPP) are not very reliable (9). Almost 80% cases remain undiagnosed, as the majority are diagnosed on autopsy (15). Guidelines by the European Federation of Neurological Societies (EFNS) recommend that thiamine should be given 200 mg thrice daily via intravenous route, started before any carbohydrate, and continued until there is no further improvement in signs and symptoms (16). WE is precipitated by administration of glucose-containing fluids before thiamine supplementation (9). If the condition is not recognized and treated early, patients can have permanent brain injury, manifested by impairment of recent and remote memory, apathy, and confabulation, along with persistent manifestations of WE, including ataxia and varying degrees of ohthalmoparesis. The main factors triggering death are thought to be infections and liver dysfunctions (6). After acute recovery, patients should undergo detailed neurocognitive evaluation to document residual deficits. Cognitive deficits are the last to recover and they may not recover completely. Patients should be followed periodically to ensure they do not relapse and continue to be adherent to dietary supplementation with a multivitamin and thiamine. Our case shows highly clinical suspicion is needed for diagnosis of WE in cases of hyperemesis gravidarum and early treatment is essential for prevention of complications and death.

IV. Conclusion

Patients at high risk for developing thiamine deficiency may benefit from supplementary thiamine intake either parenterally or orally depending on clinical circumstances. All patients suspected of having WE after stabilization of their cardiovascular and respiratory systems should be treated with parenteral thiamine to avoid permanent brain injury, including the development later of Korsakoff's psychosis and death.

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Carcinome Papillaire Mammaire Intra Kystique: A Propos De Deux Cas

By N. Abounouh, FZ. Belkouchi, F. Zidane, M. Yousfi, S. Amrani & S. Bargach

University Faculty of Medicine Rabat

Résumé- Le carcinome papillaire intra kystique (CPIK) du sein est une variante de carcinome intracanalaire, il s'agit d'une lésion papillaire localisée dans un canal galactophore dilaté ou kystique. Ces lésions peuvent être de deux types : soit une lésion centrale unique, désigné sous le nom de carcinome papillaire intrakystique soit des lésions multifocales prenant naissance dans les lobules, connues comme variante papillaire du carcinome canalaire in situ. Le CPIK est rare et représente 0,5 à 1% des carcinomes mammaires[1,2]. Il est caractérisé par une croissance lente avec un bon pronostic. Cependant, l'attitude thérapeutique n'est pas bien codifiée, d'où le risque de traiter abusivement une telle lésion. A l'occasion de ces deux observations, nous rappelons les aspects diagnostiques, thérapeutiques et évolutifs de cette tumeur rare.

Mots clés: *carcinome papillaire intra kystique, diagnostic, traitement.*

GJMR-E Classification: *NLMC Code: WJ 190, WQ 400*

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Mots clés: carcinome papillaire intra kystique, diagnostic, traitement.

I. Introduction

Le carcinome papillaire intra kystique (CPIK) du sein constitue une tumeur rare, dont l'incidence est de l'ordre de 0,5% à 1% des cancer du sein[1,2]. Son aspect anatomopathologique est caractéristique, il doit être différencié du carcinome canalaire in situ ou du carcinome invasif, qui lui sont parfois associés. Le pronostic du CPIK semble excellent dans sa forme isolé, mais la prise en charge thérapeutique n'est pas clairement établie.

II. Observations

Cas N° 1:

Il s'agit d'une patiente âgée de 70ans, hypertendue depuis 5ans sous traitement, 12ème geste 9ème pare (7 enfants vivants), ménopausée depuis plus de 10 ans , sans notion de prise de traitement hormonal substitutif, qui consulte pour un nodule du sein gauche de découverte fortuite à l'autopalpation sans signes inflammatoires en regard ni écoulement mamelonnaire.

A l'examen on note la présence d'un nodule sus aréolaire à cheval entre les deux quadrants supérieurs du sein gauche, bien limité, dur, mobile par rapport aux plansprofond et superficiel, de 2cm de diamètresans anomalies cutanées ou mamelonnaires associées.

Une mammographie bilatérale réalisée, met en évidence des seins de densité glandulo-graisseuse classée ACR2.Puis en rétroaréolaire du sein gauche on note la présence d'une opacité dense, arrondie, de contours irréguliers, avec un aspect de "queue de comète", et présence de microcalcifications pléomorphe, éparses bilatérales sans regroupement suspect, sans distorsion architecturale ni épaississement cutané (figure1).

L'échographie mammaire retrouve cette formation tissulaire au niveau de la jonction des deux quadrants supérieurs, à 10mm du mamelon et 4mm du plan cutané, hypoéchogène, hétérogène, de contours irréguliers, contenant des foyers kystiques, sans atténuation postérieure et mesurant 17mm/ 16mm (figure2).

Une extemporanée, montre macroscopiquement un foyer d'allure kystique mesurant 1,6 ×1.3 ×1cm à contenu plein charnu, de couleur blanc grisâtre et à paroi épaisse. Ce foyer est situé à ras de la limite d'exérèse la plus proche. L'examen anatomopathologique montre une prolifération carcinomateuse délimitée par une capsule fibreuse épaisse. Cette prolifération est faite de massifs solides comportant des axes fibreux et composés de cellules assez monomorphes aux noyaux aux atypies faibles et hyperchromatiques, avec des figures de mitoses estimées à environ 7mitoses/10 champs au grossissement 40. Il n'a pas été vu de composante intracanalaire ni embole vasculaire péritumoral. Cette lésion est située à ras de l'une des limites de résection chirurgicales (figure3, figure4).

Une étude immuno-histochimique réalisée montre:

-Anticorps anti-P63 (clone 4A4, Cell Marque): Négatif.
-Anticorps anti-CK14 (Clone L.L002, Cell Marque): Négatif.

Ces aspects sont ceux d'un carcinome papillaire de bas grade dans sa forme solide encapsulé.

Vue l'âge de la patiente, l'absence d'imagerie par résonance magnétique renseignant sur la présence d'éventuels foyers de carcinome in situ ou carcinome micro-invasif, ainsi que des limites de résection chirurgicale marginale, la patiente a bénéficié dans un deuxième temps d'une mastectomie avec curage ganglionnaire.

L'examen anatomopathologique de la pièce chirurgicale a révélé la présence d'un micro foyer de carcinome intracanalaire de haut grade avec nécrose, sans éléments invasifs ni embolesvasculaires, avec absence d'atteinte ganglionnaire.

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L'évaluation immuno-histochimique des récepteurs hormonaux a montré:

Des récepteurs oestrogénique: positifs
Des récepteurs progestéroniques: positifs

Un Hercept test: négatif.

Par ailleurs la patiente a bénéficié d'un traitement adjuvant à base d'hormonothérapie (tamoxifène).

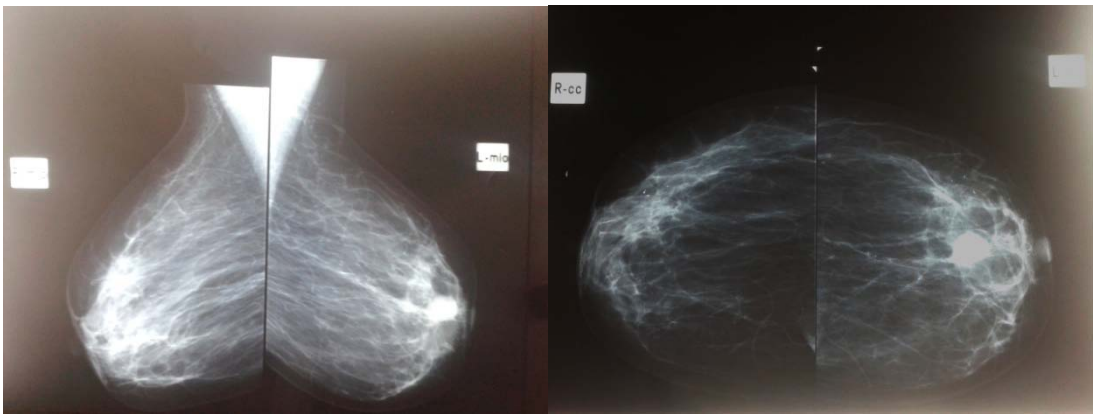

Figure 1: Mammographie cliché de profil et de facedu sein gauche montrant une opacité dense arrondie rétroaréolaire du sein gauche

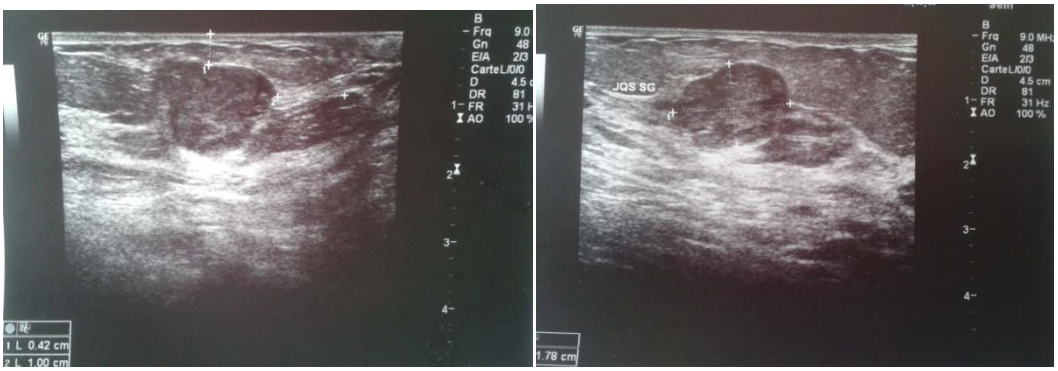

Figure 2: Image échographique d'une formation hétérogène à double composante Tissulaire et kystique

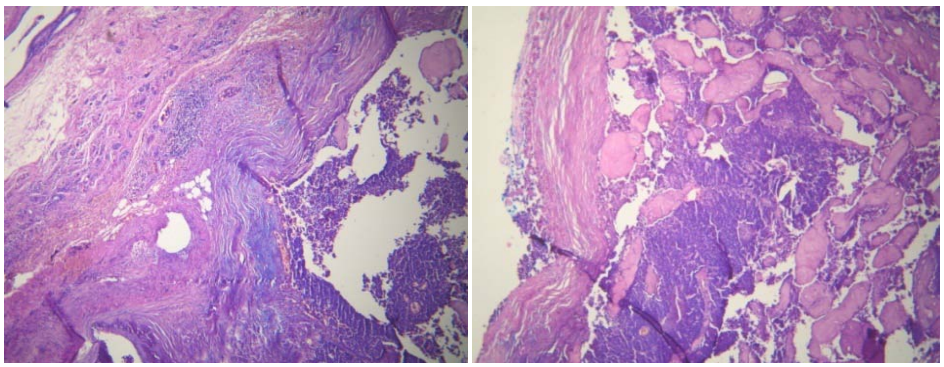

Figure 3: (Gx10)Img 0127, 0129, 0146 :Prolifération tumorale Carcinomateuselimitée par une capsule épaisse fibreuse

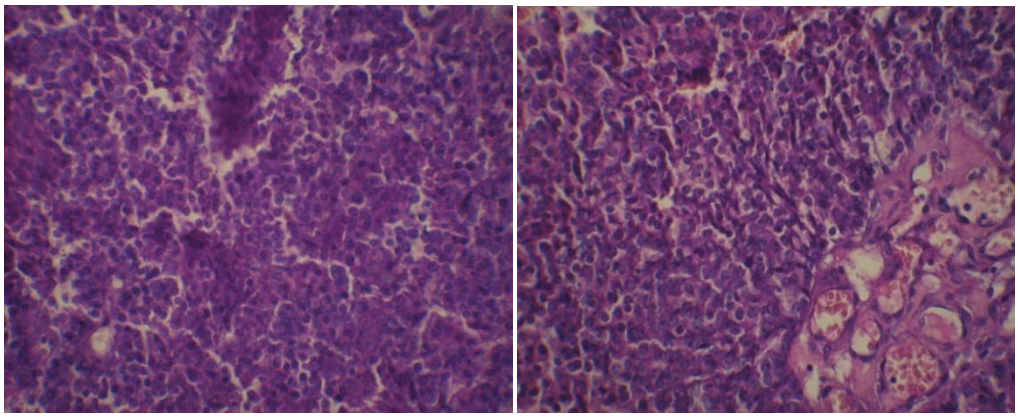

Figure 4: (Gx40)Img 0139, 0153:Population cellulaire monomorphe peu atypique autour d'un axe fibreux et vasculaire

Cas N° 2:

Il s'agit de Mme B.Y âgée de 56ans, hypertendue depuis 1an sous traitement, nulligeste nullipare , veuve, toujours réglée, consultant pour un nodule du sein droit apparu dans les suite d'un traumatisme direct, sans signes inflammatoires en regard ni écoulement mamelonnaire.

A l'examen clinique, on note la présence d'un nodule au niveau de la jonction des deux quadrants externes du sein droit, se prolongeant en rétroaréolaire, de 3cm×1.5cm de diamètre, dur, mobile par rapport aux plans profond et superficiel, sans signes inflammatoire en regard ni rétraction cutanée, ou écoulement mamelonnaire. Les aires ganglionnaires sont libres.

Une mammographie bilatérale met en évidence la présence en rétro-mamelonnaire et quadrant inféro-externe du sein droit, d'une opacité flous, spiculée d'environ 3cm de diamètre. Sans distorsion architecturale ni épaississement cutané (figure 5).

L'échographie révèle la présence en rétroaréolaire et quadrant inféro-externe du sein droit, d'un nodule tissulaire, hétérogène mal limité de 32mm de diamètre. Sans adénopathies visibles (figure 6).

La patiente a été opérée. Une extemporanée réalisée est revenu en faveur d'un processus malin, et complétée par une mastectomie avec curage ganglionnaire.

L'examen histologique a montré une prolifération tumorale correspondant à une prolifération carcinomateuse papillaire encapsulée dans sa variante solide de grade intermédiaire, faite de cellules assez monomorphe aux noyaux avec atypies hyperchromatiques, nettement anisocaryotiques, et nucléolées avec des figures de mitose s'agençant en massifs cribriformes ou compacts. Une capsule fibreuse et épaisse délimite cette prolifération et s'invagine profondément dans celle-ci. On y observe par ailleurs quelques rares foyers de carcinome micro-invasifs et extra-capsulaires avec présence de foyers de carcinome in situ minime de grade intermédiaire , sans nécrose et sans embole vasculaire péri tumoral évident. Aucun des ganglions du curage axillaire n'est métastatique.

La patiente a reçu une radiothérapie adjuvante avec une bonne tolérance clinique.

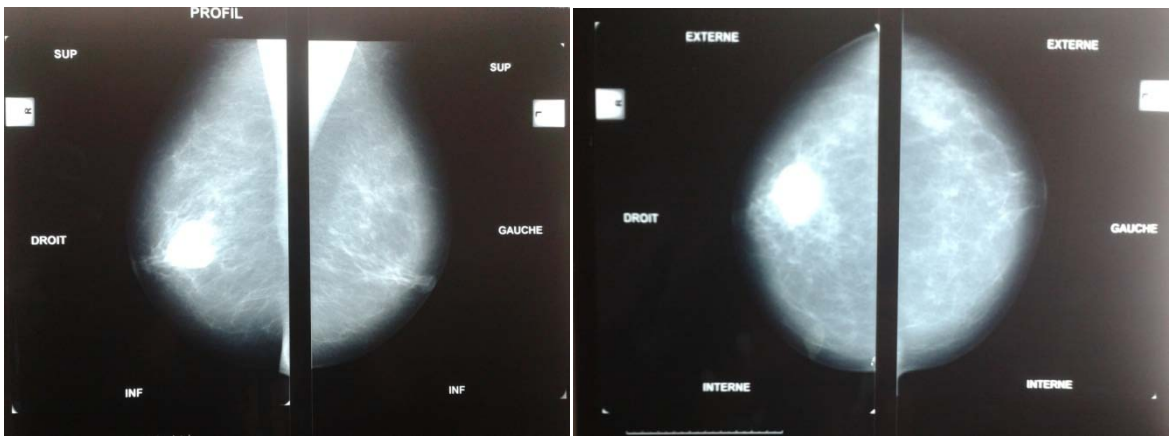

Figure 5: Mammographie cliché de profil et de face montrant une opacité floue, arrondie spiculéerétroaréolaire du sein droit

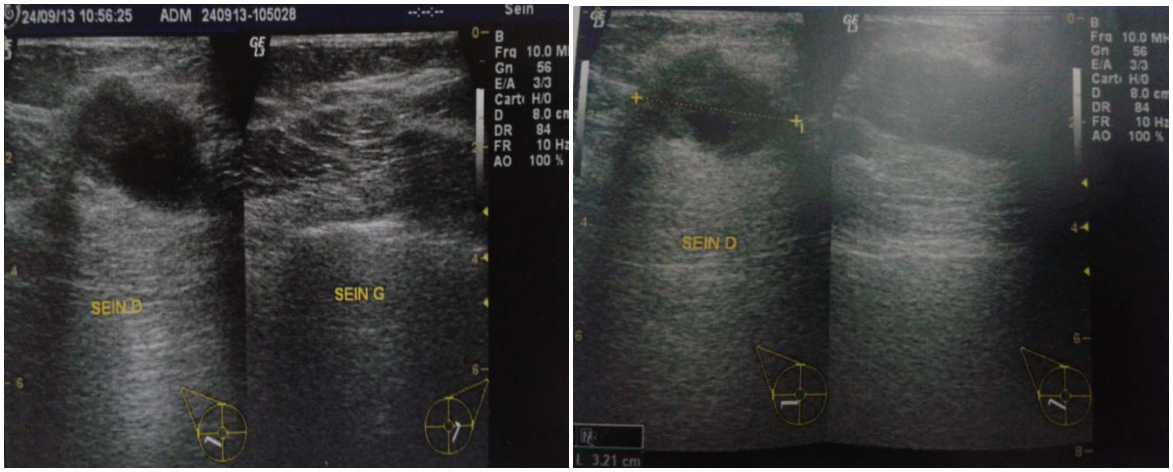

Figure 6: Aspect échographique d'un nodule tissulaire, hétérogène, rétroaréolaire du sein droit.

III. Discussion

Le carcinome papillaire intra kystique (CPIK) est une entité particulière du cancer du sein. C'est une tumeur canalaire maligne rare qui représente 0,5 à 1% de l'ensemble des carcinomes mammaires[1,2]. Il peut apparaitre isolé ou associé en périphérie à un carcinome canalaire in situ ou carcinome invasif [1]. L'âge moyen de découverte varie de 55 ans à 67ans selon les auteurs[2,3]. Il est caractérisé généralement par une croissance lente avec un bon pronostic[3].

Cliniquement la tumeur se révèle par une masse centrale, plus précisément dans la région rétroaréolaire, comme c'est le cas pour nos deux patientes. La taille tumorale varie de 1 à 14cm. La tumeur peut aussi se manifester par un écoulement mamelonnaire sanglant, et dans certains cas, elle peut rester asymptomatique et se révèle lors d'une mammographie systématique. Dans notre deuxième observation la masse s'est révélée suite à un traumatisme. L'atteinte ganglionnaire est rare[2,4].

A la mammographie le CPIK apparait généralement comme une opacité ronde, ovalaire ou lobulaire. Les contours sont généralement nets, bien circonscrits mais peuvent être cachées ou indistincts par endroits, observés sur la mammographie de notre patiente. les contours spiculés sont rares[5,6].

L'échographie mammaire révèle la présence d'une masse kystique complexe avec une composante solide nodulaire, avec des échos postérieurs traduisant des hémorragies spontanées. Le mode doppler met en évidence une vascularisation riche, centrale avec de nombreux vaisseaux intra-muraux traversant la portion solide de la masse[2,6,7,8,].

L'imagerie par résonance magnétique est sensible, elle permet d'orienter le diagnostic en montrant le cloisonnement et les nodules muraux, mais reste non spécifique dans le diagnostic des tumeurs papillaire[2,6].

La biopsie de la lésion intéressant la portion solide est généralement informative. L'examen macroscopique retrouve une formation arrondie, ou polylobé, friable et hémorragique limitée par une capsule fibreuse et épaisse[3,7].

En microscopie l'architecture tumorale est papillaire, la lésion est habituellement localisée dans un canal kystique, elle est caractérisée par une arborescence fibro-vasculaire grêle dépourvue d'une couche de cellules myoépithéliales, et une prolifération épithéliale néoplasique présentant les caractéristiques morphologiques d'un carcinome canalaire in situ(CCIS) de bas grade nucléaire[9,10]. Plus rarement, comme dans notre 2ème cas clinique, le contingent épithélial présente des caractéristiques d'un CCIS de grade intermédiaire ou de haut grade. On peut également retrouver un CCIS dans le tissu mammaire adjacent. En périphérie des carcinomes papillaires intrakystiques, on note fréquemment un entrappement des structures épithéliales dans la paroi fibro-hyaline à l'origine des aspects pseudo infiltrants. On parle de carcinome infiltrant associé à un carcinome papillaire intrakystique lorsqu'il existe une infiltration du tissu mammaire à l'extérieur de la paroi du carcinome papillaire intrakystique[9,10].

La stratégie thérapeutiquereste variable vue la rareté de ce type de carcinome mammaire. En générale le pronostic du CPIK dans sa forme isolée apparait excellent quel que soit le type de l'intervention. La chirurgie mammaire conservatrice reste la plus utilisée. Carter et al.[11] à partir d'une série de 7 cas de CPI isolés, ayant été traitéspar une tumorectomie, n'ont pas observé de récidive locale après un suivi de 7ans. L'absence de métastases ganglionnaires axillaires dans l'étude de Baron et al. [12] et celle de Harris et al. [13]combiné à l'absence de récidive, suggèrent que le traitement de choix d'un CPI isolé est une tumorectomie élargie. Néanmoins, dans certains cas, la mastectomie peut être proposée (les grosses tumeurs, insuffisance des marges, la récidive et les préférences de la

patiente)[2,14] ce qui est le cas pour nos deux patientes ayant bénéficié d'un Patey. Aucune association entre le taux de récidive locale et le type de chirurgie n'a été démontré[2]. Les métastases ganglionnaires restent exceptionnelles.

La biopsie du ganglion sentinelle peut présenter une excellente alternative pour l'évaluation ganglionnaire en cas de carcinome invasif associé[1].

Le rôle du traitement adjuvent reste controversé. Cependant de nombreuses études recommandent la radiothérapie chez les jeunes femmes de moins de 50ans, et dans les formes associées à un carcinome canalaire in situ [15] ce qui est le cas pour notre deuxième patiente.

La chimiothérapie n'est pas obligatoire. L'hormonothérapie est principalement prescrite pour réduire le risque de récidive locale en cas de récepteurs hormonaux positifs, nous avons mis notre patiente sous tamoxifène. En dépit de ces principes généraux, le traitement optimal du CPIK reste controversé[16].

IV. Conclusion

Le carcinome papillaire intra kystique est une entité particulière et rare du cancer du sein. Son pronostic est excellent dans ca forme isolé. Le diagnostic est évoqué à l'échographie puis confirmé par l'examen histopathologique et immuno-histochimique. La prise en charge thérapeutiques reste variable, néanmoins le traitement reste conservateur en l'absence de composante infiltrante.

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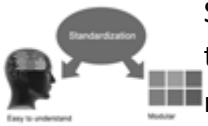

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To avoid postal delays, all transaction is preferred by e-mail. A finished manuscript submission is confirmed by e-mail immediately and your paper enters the editorial process with no postal delays. When a conclusion is made about the publication of your paper by our Editorial Board, revisions can be submitted online with the same procedure, with an occasion to view and respond to all comments.

Complete support for both authors and co-author is provided.

4. MANUSCRIPT'S CATEGORY

Based on potential and nature, the manuscript can be categorized under the following heads:

Original research paper: Such papers are reports of high-level significant original research work.

Review papers: These are concise, significant but helpful and decisive topics for young researchers.

Research articles: These are handled with small investigation and applications

Research letters: The letters are small and concise comments on previously published matters.

5.STRUCTURE AND FORMAT OF MANUSCRIPT

The recommended size of original research paper is less than seven thousand words, review papers fewer than seven thousands words also.Preparation of research paper or how to write research paper, are major hurdle, while writing manuscript. The research articles and research letters should be fewer than three thousand words, the structure original research paper; sometime review paper should be as follows:

Papers: These are reports of significant research (typically less than 7000 words equivalent, including tables, figures, references), and comprise:

(a)Title should be relevant and commensurate with the theme of the paper.

(b) A brief Summary, "Abstract" (less than 150 words) containing the major results and conclusions.

(c) Up to ten keywords, that precisely identifies the paper's subject, purpose, and focus.

(d) An Introduction, giving necessary background excluding subheadings; objectives must be clearly declared.

(e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition; sources of information must be given and numerical methods must be specified by reference, unless non-standard.

(f) Results should be presented concisely, by well-designed tables and/or figures; the same data may not be used in both; suitable statistical data should be given. All data must be obtained with attention to numerical detail in the planning stage. As reproduced design has been recognized to be important to experiments for a considerable time, the Editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned un-refereed;

(g) Discussion should cover the implications and consequences, not just recapitulating the results; conclusions should be summarizing.

(h) Brief Acknowledgements.

(i) References in the proper form.

Authors should very cautiously consider the preparation of papers to ensure that they communicate efficiently. Papers are much more likely to be accepted, if they are cautiously designed and laid out, contain few or no errors, are summarizing, and be conventional to the approach and instructions. They will in addition, be published with much less delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and to make suggestions to improve briefness.

It is vital, that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

Format

Language: The language of publication is UK English. Authors, for whom English is a second language, must have their manuscript efficiently edited by an English-speaking person before submission to make sure that, the English is of high excellence. It is preferable, that manuscripts should be professionally edited.

Standard Usage, Abbreviations, and Units: Spelling and hyphenation should be conventional to The Concise Oxford English Dictionary. Statistics and measurements should at all times be given in figures, e.g. 16 min, except for when the number begins a sentence. When the number does not refer to a unit of measurement it should be spelt in full unless, it is 160 or greater.

Abbreviations supposed to be used carefully. The abbreviated name or expression is supposed to be cited in full at first usage, followed by the conventional abbreviation in parentheses.

Metric SI units are supposed to generally be used excluding where they conflict with current practice or are confusing. For illustration, 1.4 l rather than 1.4 × 10-3 m3, or 4 mm somewhat than 4 × 10-3 m. Chemical formula and solutions must identify the form used, e.g. anhydrous or hydrated, and the concentration must be in clearly defined units. Common species names should be followed by underlines at the first mention. For following use the generic name should be constricted to a single letter, if it is clear.

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Abstract, used in Original Papers and Reviews:

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Key Words

A major linchpin in research work for the writing research paper is the keyword search, which one will employ to find both library and Internet resources.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy and planning a list of possible keywords and phrases to try.

Search engines for most searches, use Boolean searching, which is somewhat different from Internet searches. The Boolean search uses "operators," words (and, or, not, and near) that enable you to expand or narrow your affords. Tips for research paper while preparing research paper are very helpful guideline of research paper.

Choice of key words is first tool of tips to write research paper. Research paper writing is an art.A few tips for deciding as strategically as possible about keyword search:

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- It may take the discovery of only one relevant paper to let steer in the right keyword direction because in most databases, the keywords under which a research paper is abstracted are listed with the paper.
- One should avoid outdated words.

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Acknowledgements: Please make these as concise as possible.

References

References follow the Harvard scheme of referencing. References in the text should cite the authors' names followed by the time of their publication, unless there are three or more authors when simply the first author's name is quoted followed by et al. unpublished work has to only be cited where necessary, and only in the text. Copies of references in press in other journals have to be supplied with submitted typescripts. It is necessary that all citations and references be carefully checked before submission, as mistakes or omissions will cause delays.

References to information on the World Wide Web can be given, but only if the information is available without charge to readers on an official site. Wikipedia and Similar websites are not allowed where anyone can change the information. Authors will be asked to make available electronic copies of the cited information for inclusion on the Global Journals Inc. (US) homepage at the judgment of the Editorial Board.

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TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

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3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

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11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

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18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

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20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

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33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

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Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

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· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

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Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

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The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

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- Fundamental goal
- To the point depiction of the research
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- Significant conclusions or questions that track from the research(es)

Approach:

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The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

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- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
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Approach:

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- Explain materials individually only if the study is so complex that it saves liberty this way.
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- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

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- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

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- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

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- Resources and methods are not a set of information.
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- Leave out information that is immaterial to a third party.

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The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
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- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

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- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
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- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

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The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
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Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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