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Gastrointestinal Stromal Tumors: Response Evaluation Criteria of CHOI through Computed Tomography

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Materials and Methods: A retrospective study from January 2009 to January 2014 in patients with a confirmed diagnosis with access to CT scan; a response to the treatment was observed according to CHOI criteria.

Results: A total of 31 patients were enrolled in this study, 61% received targeted therapy with Imatinib and 38% received second-line Imatinib and Sunitinib treatment, with a minimum follow up of 6 months and a maximum of one year. According to CHOI criteria, 45.2% of the patients reached CR, 19.4% had SD, 19.4% reached PR, and 16.1% had PD.

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Conclusions: Tumor response assessment according to CHOI criteria was useful for the evaluation of molecular targeted therapy in patients with GIST tumor.

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I. Introduction

Treatment responses for the assesment of tumors performed with CT scans were initially assesed only according to RECIST criteria; however, it was not useful for the evaluation of gastrointestinal stroma tumors because the size of the tumor was not the only characteristic.

The biggest correlation in response is based on a reduction in density measured in Housfield units. This measurement is correlated with the tumoral necrosis and cistic or myxoid deterioration. [1]

Initially, Choi et. al proposed a response criteria, in which size and density were the elements for assessing the responses to treatment. In some cases, the size of the tumor can increase due to a side effect of the development of an intratumoral hemorrhage or myxoid deterioration. [2,3]

II. Targeted Therapies

Selective inhibitor tyrosine kinase agents are employed for the treatment of GIST (molecular targeted therapy) that specifically acts in biomolecular changes that onset the disease and that exclusively targets the tumural cells. The use of this treatment has allowed a 5 year increase in up to 43% of the patients with this metastatic disease. [4,5]

The protocol for GIST treatment at IMSS (Mexican Social Security Institute) UMAE CMN Siglo XXI is based on the histological grading of malignancy according to its mitotic index. The first-line medication treatment used post-surgery is Imatinib Mesylate, which acts through specific inhibition of the ennzyme tyrosine kinase. A 400mg to 800mg dose is administered; depending in the histological grade, there is a one year follow-up for mild cases and up to three years for severe cases. If there are any indications of progression of the disease observed through imaging methods, or clinically observed side effects due to the medication, second-line Sunitinib is then administered.

III. Assesment through Imaging

Computed tomography (CT), is the imaging method of choice for the diagnosis, staging, monitoring and assessment to treatment response of the GIST; 5 cm tumors are identified as large tumors, well-defined, heterogeneous, and exophytic component or with a polypoid intraluminal. . The central portion may contain tumor areas of lower attenuation secondary to necrosis, hemorrhage and cystic degeneration; the presence of calcifications is unusual. [6,7,8]

Malignant GISTs are large and well defined (86 %), with heterogeneous soft tissue of low density and necrotic center. They frequently come from the wall of the stomach or small intestine. The attenuation by liquid or central necrosis occurs in approximately 67% of the cases. [9,10]

The period for follow-up in patients who have GIST may be modified by variables such as if received surgical treatment (neoadjuvant or adjuvant), [11]

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presences of metastatic disease (liver, peritoneum and other sites) and changes in treatment (for adverse effects to the medication or the progression of the disease). High-risk patients are evaluated from 1 to 2 years at the end of the adjuvant therapy and low-risk patients can have greater intervals of evaluation.[12] The group of sarcomas in Europe suggested to routinely assess every 3-6 months during adjuvant therapy in the first year and on an annual basis in the following 5 years. Patients with GIST of low risk can be evaluated every 6-12 months by for a period of five years.[13]

Table 1 : Comparative table between RECIST and CHOI criteria

Criteria	CHOI	RESIST 1.1
Complete Response	Disappearance of all target lesions No new lesions	Disappearance of all target lesions No new lesions
Partial Response	Decrease ≥10% in the sumof the LD or shrinkage ≥15% in Hounsfield Units (tumoral density). No evidence of new lesions	Decrease ≥ 30% in the sum of the LD of target lesions
Stable Disease	Neither sufficient shrinkage to qualify for PR nor sufficient Increase to qualify for PD	Neither PRnor PD
Progressive Disease	Increase in size≥10% with no criteria in Partial Response of the tumor density Appearance of new lesions, intramural nodules, increase in existing nodules or tiissue increase in a hypodense lesion	Increase ≥ 20% in the sum of the LD of target lesions

There are no studies reported in the literature on the experience of the Oncology Hospital Siglo XXI that include criteria CHOI as a basis for monitoring response to molecular targeted therapy. Some authors include in their studies specific criteria such as tumor size, histological grade and track interval once white therapy has begun.

It is therefore important for the Medical Oncologist to know the significance of the tomographic reportfor follow-up of patients with gastrointestinal tumors. The objective of this study was to describe with CTs the response to the treatment of GIST in patients from the Oncology Hospital of twenty-first century, using the criteria of CHOI.

IV. Materials and Methods

A retrospective study from January 2009 to January 2014. The patients included in the study had to have a confirmed diagnosis of GIST by histopathology; a CT scan performed in the oncology service at the IMSS, with realization of three-phase protocol (arterial, venous and portal); treatment of white therapy (Imatinib or Sunitinib) and a baseline and follow-up CT. Simple frequency and dispersion measurements were taken through the program SPSS.

V. Results

From 2009 to 2014 31 cases were obtained with the inclusion criteria mentioned, of whom 54.8 % were women and 45.2 % were men with a median age of 57 years (range 36 to 84 years); all with a study of abdominal computed tomography. The organs affected by GIST were 51.6 % (16) stomach, 22.6 % (7) jejunum, 12.9 % (4) rectum, 6.5 % (2) duodenum, 3.2 % (1) peritoneum and 3.2 % (1) retroperitoneum (Table 2). 32.3 % (10) of the patients were surgically treated before starting with Imatinib. 67.7 % received first-line molecular targeted therapy with Imatinib, and 32.3 % received second line with Sunitinib. We assessed the response to treatment with a CT scan in an average of 1 to 24 months. According to the criteria of CHOI, we observed 45.2 % (14) complete response, 19.4 (5) stable disease, 19.4 (6) partial response and 16.1 % (5) disease progression (Table 3) Figures 1,2, 3. During that time, metastatic activity was observed in 14 patients representing a 45.1 %, with predominant involvement in the liver with a percentage of 35.5 % of the total (Table 4) Figure 4.

Table 2 : Organs affected by GIST

Affected Organ	Number of Patients	Percentage
Stomach	16	51.6
Jejunum	7	22.6
Rectum	4	12.9
Duodenum	2	6.5
Peritoneum	1	3.2
Retroperitoneum	1	3.2
Total	31	100%

Table 3 : Patient responses to targeted therapy treatment in patients with GIST according to CHOI criteria

Responses according to CHOI criteria	Number of Patients	Percentage
SD	6	19.4
PD	5	16.1
PR	6	19.4
CR	14	45.2
Total	31	100 %

Table 4 : Follow-up of GIST patients with metastasis treated with targeted therapy SD (Stable Disease). PD (Progressive Disease). PR (Partial Response). CR (Complete Response)

Site of metastases	Number	Percentage
Peritoneum	1	3.2
Liver	11	35.5
Retroperitoneum	1	3.2
Uterus	1	3.2
Total	14	45.1

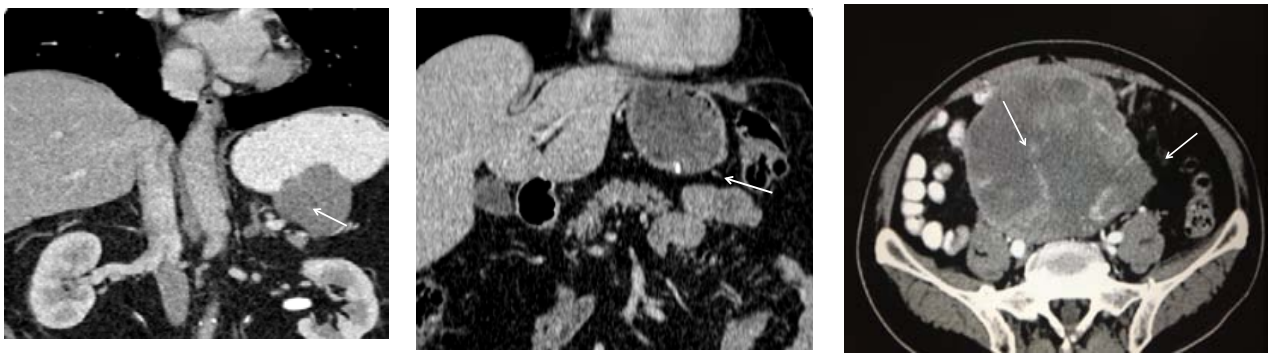

Figure 1: Partial Response to treatment. 2a. Retroperitoneal tumor with density of 49 UH, predominantly hypodense aspect. 2b. Control tomographic study with decrease in greatest diameter to 10% in maximum diameters, heterogeneous density, peripheral enhancement. 2c. 6 month follow-up with decrease greater than 10 % of diameters, increased vascular enhancement not more than 15 % at 2 years of treatment with an interval of 6 months between the assessments.

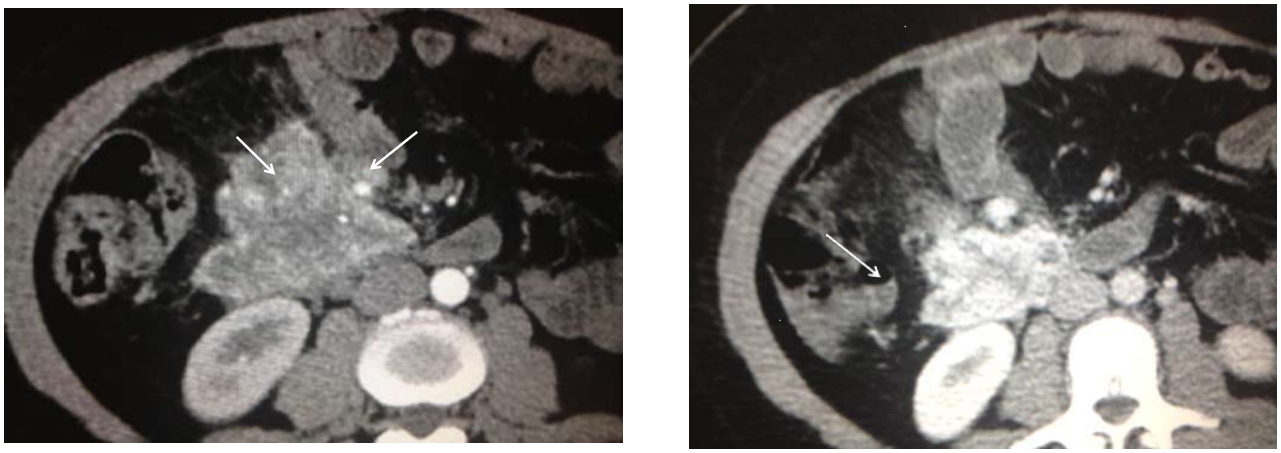

Figure 2 : Progression of the disease. 3a. Peritoneal implants and nodular ascites fluid. 3b. Ascites fluid in peritoneal cavity.

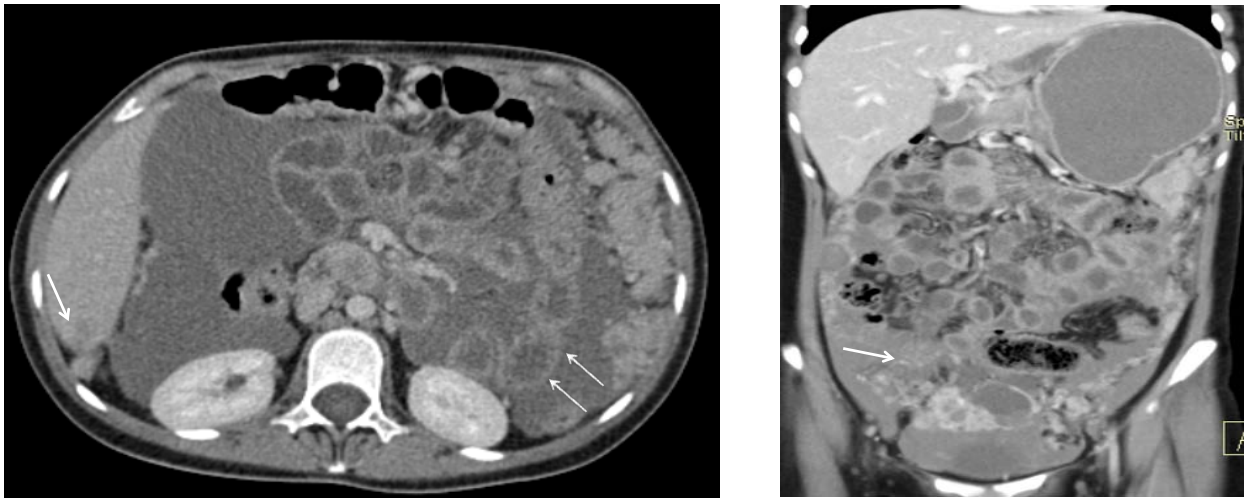

Figure 3 : Total Response to treatment.4a. GIST tumor in greater curvature aspect of hypodense, extraluminal, lobed, before the surgery. 4b. Postsurgical control where no lesions in the gastric wall are observed.

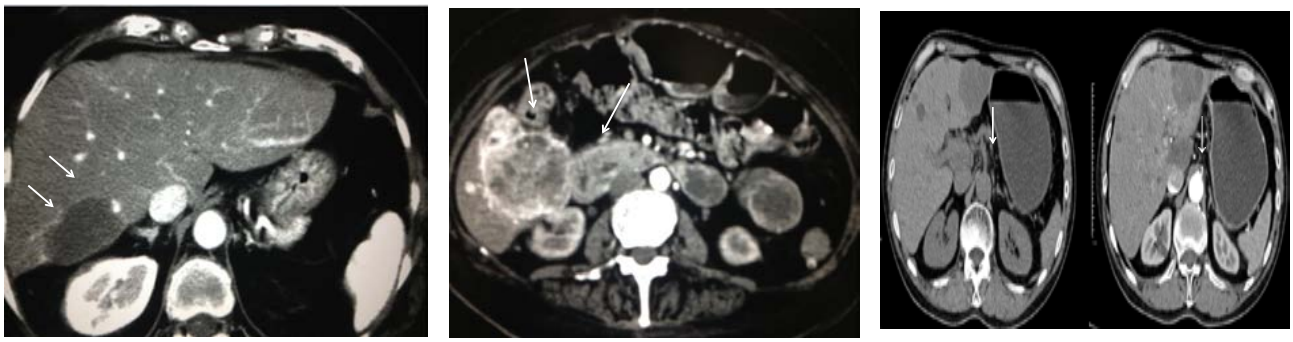

Figure 4 : Liver metastases.1a. Hepatic metastases by gastric GIST. Hypodense aspect, without enhancement after contrast administration. 1b. Liver metastasis of heterogeneous aspect, with peripheral vascular enhancement and focal zones hypodense probably linked to necrosis. 1c. Hypodense hepatic metastases in simple and arterial phase.

VI. Discussion

Neither the time of survival nor the histologic grade of malignancy was considered in our review as Toyokawa et al recommends.[12] A prospective study would consider the survival. In recent publications the partial answer is the predominant result when evaluating with criteria of CHOI, which does not differ with the gains of the study. [12,13.]

The length of time of follow-up was from 6 months. In patients undergoing surgery, the period of follow-up was one year. It was noted that the progression of the disease was determined by the stage at the time of diagnosis and the location that made the unresectable tumor. The molecular targeted therapy in patients with liver hypovascular metastases areas remained as stable disease or partial response to treatment, with a similar percentage to what is reported in the literature. The follow-up every 4-6 months the first two years and annual the following years were a period of time made on average.

The organy most frequently affected (stomach) and the most frequent metastatic disease (liver) is similar to that reported in the literature.

VII. Conclusions

It is necessary as radiologists to become familiar with the existence of white therapies and criteria for evaluation of response, to achieve the appropriate integration in the multidisciplinary management. CT scans allows us to evaluate the response to white therapy in patients with GIST using the criteria of CHOI. It also allows us to identify the primary tumor, stage of the disease and detect metastatic diseases. The criteria of CHOI reported by CT help the clinician with the patient management, decision for surgical treatment, grant white therapy, to change white therapy line and prognosis. GIST requires a tomographic assessment using criteria of CHOI, with a period of time as a minimum of 6 months.

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