Urine Cytology Screening among Renal Transplant Recipients for Presence of Atypical Changes

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Abstract- Objectives: The aim of this study was to screen transplant patients for the presence of inflammatory and atypical cytological changes, and to correlate cytological finding with demographical, clinical data and type of immunosuppressive drug in use.

Methods: A total of 300 voided urine samples were collected from patients, 242 males and 58 female, their ages were ranged from 11 to 71 and mean age 41 years. All patients were using immunosuppressive drugs including cyclosporine, Tacrolimus, mycophenolate motilf, with highest ratio of patient taking tacrolimus (38.6%), and the least were taken cyclosporine (13%). The average period of transplant was 8.4 years, with the highest group (64.3%) were 0 – 4.2 years.

Results: 300 cases were identified, including 262(87.34%) reported with normal cytology, the remainder 38(12.6%) were inflammatory, in which 6(2%) have a nonspecific inflammation, 17(5.67) consist from viral infections that includes (3 BKV, 2 CMV and 12 HPV), 10(3.34%) Bacterial infections, 3(1%) fungal infections constitute from candida albicans and 2 were mixed of bacterial and fungal infections.

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Conclusion: The study concluded that urine cytology is an excellent tool for routine follow up of renal transplant recipients to detect a variety of inflammatory and infectious agents, and need to be a widely recognized among physicians.

I. Introduction

Renal transplantation has markedly increased over the years. The two major factors for successful renal transplantation are better control of rejection and better prevention and treatment of infection. Infectious complications are frequent in renal transplant recipients. The term opportunistic infections are applied to an infection occurring in an immunocompromized host with impaired defense mechanisms. Such infections have been on the increase for a variety of reasons. New immunosuppressive drug that, can foster the genesis of new opportunistic infections (1).

Most of the opportunistic infections occurring in renal allograft recipients are Polyma virus, Cytomegalovirus, Epstein- Barr virus, Herpes zoster virus; Asparagellus, Candida and other infection many of them have characteristic appearance in the urine cytology. Urine cytology can be used to detect, infection, atypical changes and follow patient with bladder cancer. Despite many attempts to develop another test with greater sensitivity and specificity, cytology remains the single best inexpensive, quick and reliable way to diagnose a variety of bladder lesions (2).

II. Material and Methods

During a period of 6 months from November 2011 to April 2012, a total of 300 Patients were attained to renal transplant hospital in Khartoum state, the data were taken from patients by questionnaire asking them about their names, age, and transplant period as well as any clinical signs and symptoms. Then we took a voided urine sample from each ones. The samples were centrifuges for 5 minutes, followed by addition of suspending media and leaved it for 30 mins, followed by centrifugation and discard the supernatant and we added to sediment an acid alcohol and leaved it for 30 mins and followed by centrifugation and discard the supernatant and then from the sediment we make the smears and allow it to dry. Then the smears are fixed and stained by Papaniclaou procedures (3). The staining was assessment by expertized cytologist the nucleus display blue color while the cytoplasm displays different shades of green color.

The cytological diagnosis was grouped in four categories: 1: negative benign or reactive changes, 2: cases showing acute inflammatory changes, 3: inconclusive case and 4: malignant.

III. Results

Three hundred (300) renal transplant recipients were screened using urine cytology, 242 (80.7%) male and 58 (19.3%) were females. Their ages were ranged from 11 to 71 years the age was mean 41 years. The study population were classified in to age groups, large number of them were within the age group 41 to 50 years age (36%) and few number were more than 71 years (0.3%).

All patients were using immunosuppressive drugs including cyclosporine, Tacrolimus (prograf), mycophenolate motefil (cellcept) and steroids which includes predinsoline and imuran. With highest ratio of patients taken prograf and steroids (38.6%) and the least were taken cyclosporine and cellcept (13%). The
average period of transplant was 8.4 years with the highest group 193 (64.3%) were 0-4.2 years.

The cytological results of study groups showed that 262 (87.34%) reported with normal cytology, the remainder 38 (12.6%) were inflammatory in which 6 (2%) found to have none specific inflammation and cast, 17 (5.67%) viral infections that include (Three BKV, two CMV and 12 were HPV), 10 (3.34%) Bacterial infections, three (1%) fungal infections and two (0.67%) were mixed bacterial and fungal infections.

The association between inflammatory conditions and gender were 17(5.6%) among male and 21(7%) female patients these results analyzed statistically found to be significant using a Chi square test (P<0.00) This result was consistent with literature where infectious agents such Cytomegalovirus, herpes simplex, candida and HPV were all detected in large series of more 7000 samples (4). Compare to our study of less than 300 samples we were able to correctly detect candida, HPV, BKV and other inflammatory conditions. These considered as satisfactory indicator for the usefulness of urine cytology as a daily test for patients with renal transplantation in Sudan.

With regard to relation between age groups and urine cytology results we found the inflammatory condition was most frequently in patients ageing between 41to 50 years (13/38), and less frequent for patient above 71 years (1/38) these results is statistically significant (P<0.00).

The results of urine cytology and types of immunosuppressive drugs showed that most frequently positive in patients who received Tacrolimus and mycophenolate (Prograf and cellcept respectively) (14.4%) and least in patients with cyclosporine and steroids (9.67%) these results shown to be insignificant (P>0.05).

Cytomorphology of inflammatory/degenerative changes in general were described comparable to what has already mentioned in literature. In addition to karyorrhexic changes, and nuclear enlargement, we have reported somewhat inflamed changes in the chromatin were definitely washed away homogenously. Cell degeneration was alsoevident. In candida changes presence of organism in lytic background was observed. In this instance this smear considered taken at late secretary phase.

Human Papilloma-virus changes were observed in 12 patients (4%) the number and rate of occurrence were 11(3.67%) in females and 1(0.34%) in males and interpreted based koilocytic changes cytomorphologically. These cells contain large cytoplasmic vacuoles, with clear glassy background and display dyskaryotic chromatin. Which of HPV reflex testing this confusion could easily solved by the aid of molecular testing. In this study, HPV changes were reported correctly, the urologist however can refer his patients to gynecologist for more information.

As opportunistic findings “Clue cell” for gardnerella vaginalis was detected as a supporting findings to help physicians for further workup, in fact the same changes due presence of cytoplasm filling bacteria of epithelial cells.

Decoy cells nuclei appeared as uniform washed chromatin, large or small cell and the nuclei. No prominent nuclei were present. Decoy cell structure ranges from small to large cell with bizarre appearances such comet-like, oval and tall columnar cells. The identification of these cells was difficult when marked degeneration was observed. The chromatin clumps were large and there degenerative spaces which lead to confusion of chromatin window in cancer cells. Also the clue for accurate interpretation is that their nuclear membrane is uniform. Hyperechromasias due to diffuse and washed DNA content also a confusing factor for false positive diagnosis. Here a well prepared Hematoxylin is required; Harris Hematoxylin is somewhat strong and might lead false positive interpretation, and however this is not the case for skilled cytologist. However Gill.

Hematoxylin is recommended since it outlines the chromatin crisply and less heavy (5).

IV. Conclusion

Urine cytology is a safe, noninvasive, and reliable diagnostic tool for identifying viral cytopathic effects in urothelial cells, and deserves more widespread use in the monitoring of renal transplant patients. It is now seems that urine cytology need to be implemented in clinical settings for the benefit of patients and urologists. Polyoma virus infection detection among transplant patients helps urologists to early manage renal graft rejection which of invaluable benefit for patients, community, physicians and economy. We also acknowledge regular screening for transplant patients with urine cytology as a part of routine check with other laboratory findings.

Also we have observed that urine cytology procedure need to be enhanced for harvesting well preserved cells. Improving techniques support accurate screening and diagnosis. We also found the Papanicolaou’s stain is superior in many instances to all other relative stains including those for air-dried preparations. Each laboratory however, needs to be equipped with good personnel and standard procedures.

Our findings also showed that other inflammatory/infectious conditions also are frequent cytological findings, however fungal infections such as candida albicans, viral infections such as HPV and other infectious agents readily identified in urine cytology from transplant patients.
REFERENCES


Picture 3: Typical “classical decoy” cell, the cell is large with dense uniform “washed” chromatin, with inflamed purplish zones. The nuclear membrane is regular and the cytoplasm is thick but slightly vacuolated and granulated and abundant. (LBC X40)

Picture 4: Melamed-Wolinska Bodies accompany DeCoy cell present in the same case mentioned in Fig 3