Brazilian Journal of TRANSPLANTATION

https://doi.org/10.53855/bjt.v26i1.532_ENG

CASE REPORT

Is There Still a Role for Urine Cytology in Kidney Transplantation? Experience Report in a Teaching Hospital

Ana Luisa Figueira Gouvêa[1,*], Fabiana Rabe Carvalho[2], Ana Lucia Rosa Nascimento[3], Rachel Ingrid Juliboni Cosendey[4], Camila de Melo Carvalho Nascimento[2], Jorge Reis Almeida[2]

1.Universidade Federal Fluminense – Hospital Universitário Antônio Pedro – Departamento de Patologia – Niterói/RJ, Brazil. 2.Universidade Federal Fluminense – Hospital Universitário Antonio Pedro – Laboratório Multiusuário de Apoio à Pesquisa em Nefrologia e Ciências Médicas – Niterói/RJ, Brazil. 3.Universidade Estadual do Rio de Janeiro – Instituto de Biologia Roberto Alcântara – Departamento de Histologia e Embriologia – Rio de Janeiro/RJ, Brazil. 4.Universidade Estácio de Sá – Instituto de Educação Médica – Campus Vista Carioca – Rio de Janeiro/RJ, Brazil.

*Corresponding author: anafigueira@id.uff.br

Section editor: Ilka Boin

Received: Sep. 09, 2023 | Accepted: Oct. 20, 2023.

How to cite: Gouvêa ALF, Carvalho FR, Nascimento ALR, Cosendey RIJ, Nascimento CMC, Almeida JR. Is There Still a Role for Urine Cytology in Kidney Transplantation? Experience Report in a Teaching Hospital. BJT. 2023.26 (01):e3323. https://doi.org/10.53855/bjt.v26i1.532_ENG

ABSTRACT

Introduction: Urinary cytology has been used as a monitoring strategy for kidney transplant patients, live under chronic immunosuppression, as it is a non-invasive and low-cost method. The early detection of infections can prevent possible dysfunction and graft loss. However, its use has been decreased. **Methods:** We conducted a prospective study on voided urine samples from 29 consecutive patients undergoing kidney transplantation over a continuous period of 17 months, collected during their first-year post-transplantation. One technician prepared the samples by cytocentrifugation, Papanicolaou staining, and one pathologist analyzed them. Decoy cells (DCs) positive samples were prepared, by other two technicians, for contrast phase analysis, ultrastructural study, and immunofluorescence for SV40 T antigen. **Results:** We evaluated 252 urine samples from 26 patients. Two consecutive samples (0.8%) out of five, from the same patient (3.8%), referring to the fourth- and fifth-week post-transplant, showed low-grade squamous intraepithelial lesions; only rare epithelial cells with atypia of undetermined significance were detected (0.4%) in the sample corresponding to the sixth month post-transplant. The patient's subsequent gynecological examination and Pap smear revealed no changes. Pseudohyphae and fungus yeasts were found in five samples (2.0%) from four patients (15.4%). *Trichosporon* sp. was identified in the urine of one of these patients. Decoy cells were detected in 25 samples (9.9 %) from six patients (23.1%). Two patients had sustained DCs shedding; one of them, presenting dirty background smears, developed Polyomavirus-associated nephropathy. Ultrastructural study of DCs showed icosahedral viral particles. Immunofluorescence (SV40 T antigen) was positive in DCs nuclei. Analysis by contrast phase was successful in samples with numerous DCs. **Conclusion:** Systematic urinary cytology after transplantation helps detect some infection signs. Patients with sustained DCs shedding and dirty background smears deserve special clinical attention. Electron microscopy and immunofluorescence (SV40 T antigen) are alternative techniques to detect polyomavirus reactivation. The findings suggest that urinary cytology still plays a role in kidney transplantation.

Descriptors: Urinary Sediment Analysis; Kidney Transplantation; Opportunistic Infections; Diagnosis; Cytology; Biological Monitoring.

Existe Ainda um Papel para a Citologia Urinária no Transplante Renal? Relato de Experiência em um Hospital Universitário

RESUMO

Introdução: A citologia urinária tem sido utilizada como estratégia de monitoramento dos pacientes transplantados renais, que vivem sob crônica imunossupressão, por ser um método não invasivo e de baixo custo. A detecção precoce de infecções pode prevenir possíveis disfunções e perda do enxerto. No entanto, a sua utilização tem decrescido. **Métodos:** Realizamos um estudo prospectivo em amostras

de urina provenientes de 29 pacientes consecutivos, submetidos ao transplante renal ao longo de um período contínuo de 17 meses, coletadas durante seu primeiro ano pós-transplante. Um mesmo técnico preparou as amostras por citocentrifugação, coloração de Papanicolaou e um único patologista as analisou. Amostras positivas para "*decoy cells*" (DCs) foram preparadas por dois outros técnicos, para análise por microscopia de contraste de fase, estudo ultraestrutural e imunofluorescência (antígeno T SV40). **Resultados:** Foram avaliadas 252 amostras de urina de 26 pacientes. Duas amostras consecutivas (0,8%) dentre cinco, de uma mesma paciente (3,8%), referentes à quarta e quinta semana pós-transplante, apresentaram lesão intraepitelial escamosa de baixo grau; na amostra referente ao sexto mês pós-transplante foram detectadas apenas raras células epiteliais com atipias de significado indeterminado (0,4%); o posterior exame ginecológico da paciente e teste de Papanicolaou não revelaram alterações. Pseudohifas e esporos fúngicos foram encontrados em cinco amostras (2,0%) de quatro pacientes (15,4%). *Trichosporon* sp. foi identificado na urina de um desses pacientes. *Decoy cells* foram detectadas em 25 amostras (9,9%) de seis pacientes (23,1%). Dois pacientes tiveram eliminação sustentada de DCs; um deles, apresentando esfregaço de fundo sujo, desenvolveu Nefropatia associada ao poliomavírus. O estudo ultraestrutural das DCs mostrou partículas virais icosaédricas. A imunofluorescência (antígeno T SV40) foi positiva nos núcleos das DCs. A análise por microscopia de contraste de fase foi bem-sucedida em amostras com numerosas DCs. **Conclusão:** A citologia urinária sistemática após o transplante é útil na detecção de alguns sinais de infecção. Pacientes com eliminação sustentada de DCs e esfregaços de fundo sujo merecem atenção clínica especial. A microscopia eletrônica e a imunofluorescência (antígeno T SV40) são técnicas alternativas para detectar a reativação do poliomavírus. Os resultados sugerem que a citologia urinária ainda desempenha um papel no transplante renal.

Descritores: Análise do Sedimento Urinário; Transplante de Rim; Infecções Oportunistas; Diagnóstico; Citologia; Monitoramento.

INTRODUCTION

Renal transplant patients are exposed to the action of several pathogens due to their immunosuppressive state.[1,2] Infections can cause chronic dysfunction and loss of graft.[3,4] Urine cytology is a noninvasive and low-cost technique that favors serial examinations.[5–7] It can offer important information about the health of the renal graft; so it can be an efficient way of monitoring these patients, providing the detection of different infectious agents.[8]

Polyomavirus BK (BKV) reactivation can be diagnosed by the detection of decoy cells (DCs) in urine tests.[7–10] Identification of DCs allows the selection of patients who are more prone to develop BKV-associated nephropathy (BKVAN), a condition that can lead to loss of graft function in up to 5% of renal transplant patients.[11] Cytomegalovirus (CMV), Herpesvirus, Human papillomavirus, and *Candida* sp. are other pathogens that can be effectively diagnosed in urine by sediment exam.[2,8,12,13]

However, nowadays, urinary cytology has been less explored in transplant centers, possibly due to the greater accessibility to molecular diagnostic techniques.Our objective is to investigate urinary cytopathological findings in a group of patients, during their first year after kidney transplantation.

METHODS

We conducted a prospective study on urine samples from 29 consecutive patients submitted to kidney transplant at the Hospital Universitario Antonio Pedro, Rio de Janeiro state, Brazil, in a period of consecutive 17 months. The voided urine samples were collected during their first-year post transplantation, on follow-up consultations at the kidney transplant outpatient clinic of the Hospital Universitario Antonio Pedro. Three technicians were responsible for preparing the samples and one pathologist analyzed them.

This study protocol was reviewed and approved by the Ethics Committee of Universidade Federal Fluminense. Reference number 24490913.9.0000.5243 (trial: 506.290). Written informed consent was obtained from each patient for the publication of this research and any accompanying images.

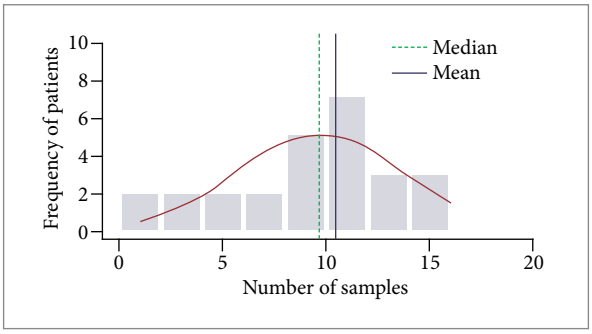
The first morning urine was collected, and a 15 ml aliquot was immediately processed. Urine was centrifuged at 3,000 rpm for 10 min. The sediment button was suspended in a small volume of urine. Three slides from each patient were prepared, after cytocentrifugation at 900 rpm for 3 min. Cytospin smears were fixed in ethyl alcohol and stained with Papanicolaou staining. Samples were analyzed for fungus and viral cytopathic effects. Decoy cells were identified according to the description of Singh et al.[14] and quantitatively evaluated in 10 contiguous high-power fields (HPF), in the most cellular smear.

Samples presenting only a few epithelial cells (<5/cytospin) with mild nuclear changes were called suspicious, but not diagnostic of DCs. Decoy cell positive samples were prepared for phase contrast microscopy analysis: 10 ml of urine was centrifuged at 2,000 rpm for 5 min and a smear was prepared from a drop of the sediment. Two samples with abundant DCs were prepared for ultrastructural study and indirect immunofluorescence for SV40 T antigen. Ultrastructural study: 1 ml of sediment was fixed in

1 ml of 5% glutaraldehyde in 0,2 M sodium cacodylate buffer and included in Araldite resin, after processing. Grids were prepared with 70 nm sections, contrasted with 5% uranyl acetate and lead citrate. Indirect immunofluorescence: fixed cytospin smears were incubated with Mouse Monoclonal Antibody Anti-SV-40, clone MRQ-4 (Cell Marque, California USA, dilution 1:200), and Goat anti-Mouse IgG (H+L) Highly Cross-Adsorbed Secondary Antibody Alexa Fluor™ Plus 488 (Invitrogen, USA, dilution 1: 200). The slides were finalized with DAPI (4',6-diamidino-2-phenylindole) mounting medium.

RESULTS

Three of the 29 patients were excluded from the analysis, because they did not contribute urine samples, due to the death of one and loss of graft by renal vein thrombosis in two of the patients. A total of 252 urine samples were obtained from 26 patients (mean age 44.3±14.5). Fourteen (53.8%) were males and twelve (46.2%) were females. Urine samples ranged from one to 16 samples per patient, with an average of 9.7±4.1 samples per patient (Fig. 1).



Source: Elaborated by the authors.

Figure 1. Distribution of 252 urine samples from 26 patients

A total of 207 samples (82.1%) presented normal findings. The remaining 45 (17.9%) presented cytological abnormalities (Table 1): Low-Grade Squamous Intraepithelial Lesion in two consecutive samples from a female patient in second month (fourth and fifth weeks) post-transplantation. The same patient had two normal samples in first month post-transplant, and a few Atypical Squamous Cells of Undetermined Significance in the sixth month after transplantation.

Table 1. Cytological abnormalities in urine samples from renal transplant patients

Cytological abnormalities	Samples N = 252	Patients N = 26
Low-Grade Squamous Intraepithelial Lesion / Human papillomavirus	2 (0.8 %)	1 (3.8 %)
Atypical Squamous Cells of Undetermined Significance	1 (0.4 %)	1 (3.8 %)
Inconclusive for decoy cells	8 (3.2 %)	5 (19.2 %)
Decoy cells	25 (9.9 %)	6 (23.1 %)
Yeasts	4 (1.6 %)	3 (11.5 %)
Pseudohyphae and yeasts	5 (2.0 %)	4 (15.4 %)

Source: Elaborated by the authors.

Six patients (23.1%) presented DCs-positive samples, comprising 25 samples (9.9%). Five patients (19.2%) presented samples with a significant number of DCs (>10/10 HPF). Four of them (15.4%) had sustained DCs shedding (for more than four weeks) and had the first detection of DCs within the first three months after transplantation.

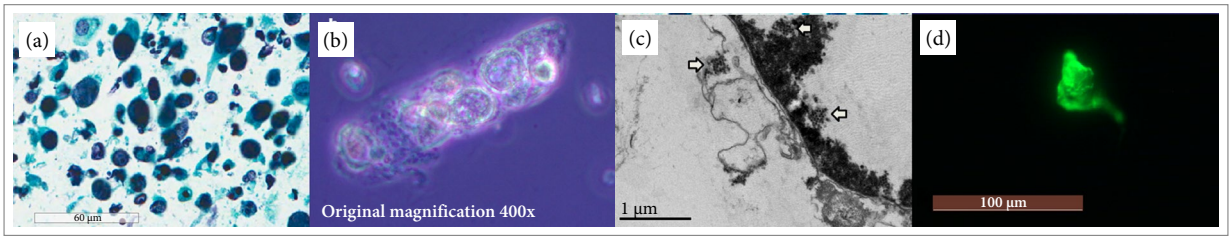
Phase-contrast microscopy revealed easily identifiable DCs, with a huge ground glass nucleus. Some DCs presented inclusion body as a dark and ill-defined core. The delicate clear area involving the inclusion body, presented as a shiny halo, was especially identifiable when the micrometric screw is rotated. We observed that the cellular morphology appeared to be more preserved at phase contrast microscopy, with well-defined cellular and nuclear contours, in contrast with the corresponding samples stained with Papanicolaou.

Five of six patients with DCs shedding had samples with a clean background, free of inflammatory cells or cell debris, on Papanicolaou staining. In contrast, the sixth patient had many DCs in all his 11 urine samples, collected from the third month to the first-year after transplantation, presenting a dirty background, full of leukocytes, cell debris (Fig. 2a), and casts of DCs, which were also observed by phase-contrast microscopy (Fig. 2b).

The ultrastructural exam was performed on two different samples from this same patient. The first sample, at the ninth month after transplantation, revealed degenerated DCs and a great number of isolated or aggregated icosahedral viral particles in the

extracellular space, cytoplasm, and nucleus. Decoy cells showed huge nuclei with clumped chromatin at the nuclear periphery and viral particles more centrally located in the fragmented and rarefied chromatin residue (Fig. 2c).

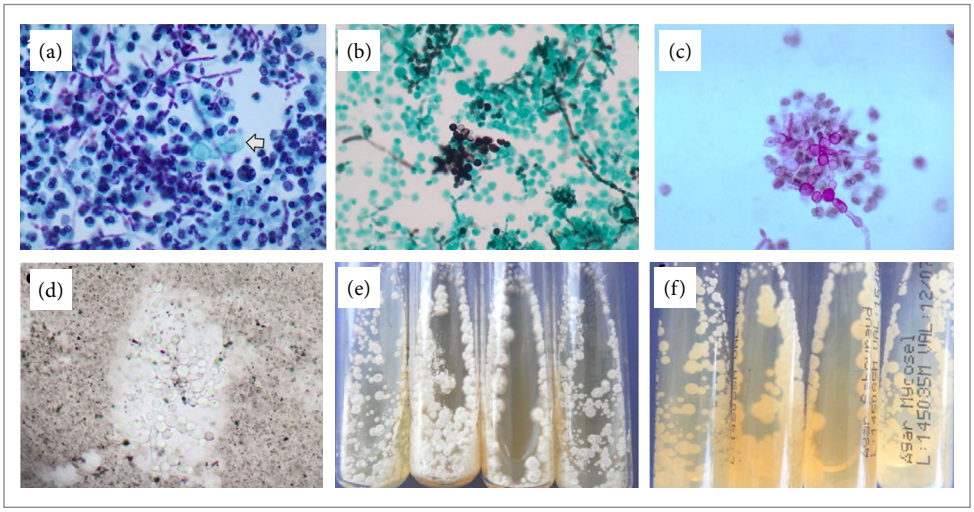
The second sample, collected one year after transplantation, when BKVAN was diagnosed, showed a higher number of DCs presenting marked signs of degeneration, plentiful intranuclear viral particles. Sometimes in a crystalloid pattern, placed in the center or periphery of the nucleus, close to the nuclear membrane. The cytoplasm revealed some swollen mitochondria and viral particles involved in cellular membranes. The extracellular space showed viral particles isolated or arranged in small low cohesive aggregates intermingled with cellular debris. Indirect immunofluorescence revealed DCs with double nuclear positivity for the DAPI and SV40-T antigen (Fig. 2d).



Source: Elaborated by the authors.

Figure 2. a) Decoy cells in a smear with dirty background – Pap Stain; b) Decoy cells cast - phase contrast microscopy; c) Degenerated decoy cell with "empty" nuclei and viral aggregates (arrows) - transmission electron microscopy. d) Decoy cell nuclear positivity for SV-40 – immunofluorescence

Two samples, from the same patient, presenting pseudohyphae and yeasts, showed some rounded yeasts, a bit larger than the also present classical oval ones, sometimes arranged in small aggregates, from within abundant pseudohyphae, eosinophilic or refractive, poorly, or not stained by Pap stain (Fig. 3a). This pattern was also observed with Grocott and Periodic Acid-Schiff stains (Fig. 3b, c). The rounded yeasts showed a gentle halo on direct examination with the preparation of the China ink (shown in Fig. 3d). Culture in Sabouraud 2% agar and Mycosel agar grew numerous white, wrinkled yeast colonies, consistent with *Trichosporon* sp (Fig. 3e, f). The API 20 C AUX 5.0 System (ControlLab, RJ) identified *Trichosporon mucoides*.



Source: Elaborated by the authors.

Figure 3. a) Small aggregates of rounded unstained yeasts (arrow) - Pap Stain (400x). b) Pseudohyphae and yeasts – Grocott (400x); c) Pseudohyphae and yeasts – Periodic Acid-Schiff Stain (400x); d) Rounded yeasts with a gentle halo on the direct examination - China ink preparation; e) Numerous white, wrinkled, yeast colonies - Culture in Sabouraud agar 2% and Mycosel agar; f) Colorless reverse of yeast colonies.

DISCUSSION

Viruses are one of the most common opportunistic infectious agents in renal transplanted patients, often resulting from the reactivation of the host's latent infection. Immunosuppression, antirejection therapy, inflammation, and tissue injury are conditions that can contribute to viral reactivation after transplantation.[1,2]

We found DCs in 25 samples (9.9%) from six patients (23.1 %). Decoy cell shedding in kidney transplant varies between 17.9% and 28.6% of the patients, in different studies,[6,15–19] with the first detection around the second and third months after transplantation[16,17] up to the fourth month after transplantation.[20] In fact, four (66.7%) out of six DCs-positive patients started DCs shedding in the first three months post-transplant. When the charts were reviewed, we observed that all the six DCs-positive patients presented some clinical event before the period of shedding: two patients were submitted to graft biopsies presenting Calcineurin inhibitor nephrotoxicity and Acute T-Cell Mediated Rejection. Four patients presented positive antigenemia for CMV (pp65); one of which developed CMV nephritis diagnosed by graft biopsy.

The patient who presented HPV reactivation in the second month after transplantation developed graft dysfunction in the first month after transplantation. The graft biopsy was suspicious of acute rejection mediated by T cells with multifocal tubular necrosis. These findings corroborate the proposition that some conditions predispose to viral reactivation in the post-transplant period. Her subsequent gynecological exam and pap smear sample did not present any specific abnormality.

Four of six patients presented sustained DCs shedding. Two of them stood out: one patient presented a mean of 104 DCs/10 HPF in six of his samples, over 16 weeks, in a clean smear background. The other presented a mean of 71 DCs/10 HPF in eight of his samples, over 45 weeks, in an always dirty background, with leukocytes, red cells, and cellular and acellular casts. This patient was the only one to develop BKVAN, diagnosed one year after transplantation, when graft biopsy was indicated, after an abrupt increase in serum creatinine. The presence of a necroinflammatory background in DCs-containing urine samples can accurately identify patients with active nephritis, although this observation is not specific by itself.[14,21] The negative predictive value of DCs for BKVAN is 100%, although the positive predictive value is around 25%.[6,22] The positive predictive value can be increased if other information is considered, such as dirty smear background, graft function, sustained DCs shedding (more than six weeks) and detection of DCs casts.[6,14,23,24]

The identification of DCs using phase contrast microscopy has been highlighted as a more effective strategy than conventional cytopathology examination, in terms of cost and time, in the hands of trained professionals.[25] Phase-contrast microscopy of the samples with many DCs provided us with the opportunity to train and gain experience in DCs identification. This technique turned out to be simple to perform and easy to detect cytological changes by a trained professional. Poloni et al.[26] stress the value of recognizing macrophage morphology, which can be quite variable and may be mistaken for DCs, by a less experienced professional. For us, the fine adjustment with the micrometric screw was of great help in defining the nuclear contour and observing the delicate refractive halo, observed around most nuclear inclusions.

Immunofluorescence and electron microscopy are techniques with good correlation to cytopathological examination in the detection of DCs antigens and viral particles. They can be used in diagnostic routines, especially in cases with poor cellularity or lack of conclusive data for DCs.[21,27] In our experience, fluorescence microscopy with the SV40 marker for polyomavirus was effective in the detection of viral antigens. The use of DAPI was important for nuclear identification and control of fluorescent signal location, to avoid misinterpretation with nonspecific deposits. We performed an ultrastructural exam on a urine sample from a patient in the course of BKVAN. Electron microscopy of voided urine has been considered a non-invasive technique for the diagnosis of BKVAN by the detection of 'Haufen', defined as polyomavirus cast-like aggregates;[28] however, we used a standard method for sample preparation, not the negative contrast technique, with the specific technical details developed by Singh et al.[28] Also, the cast-like viral aggregates we found were little cohesive and associated with cytoplasmic debris, contrasting with the definition of 'Haufen'.

Fungi, especially from the genera Candida, are important causative agents of infection in the urinary tract in post-transplant patients. Selvaggi[8] reported *Candida* sp. in 3.2 % of 7116 urinary samples from renal transplant patients. Most of the time, the treatment is useless due to the low clinical repercussions.[29] We found nine samples (3.6%) presenting yeasts morphologically suggestive of *Candida* sp. We found a sample with slightly different-shaped yeasts associated with abundant pseudohyphae.

It was the only one submitted to culture, characterizing the growth *of Trichosporon mucoides*. The *Trichosporon* spp. has been considered an emergent opportunistic agent and can represent the second or third most common nonCandida yeast infections causing invasive disease in patients with hematologic cancer[30] or in other contexts of immunosuppression, organ transplantation, and various conditions of debilitating diseases.[31,32]

Risk factors for this kind of infection are similar to *Candida* sp. and include neutropenia, immunosuppression, and loss of mucosal surface integrity. Bloodstream infection, sometimes combined with pneumonia and/or skin lesions, is a common clinical feature.[32] The patient was treated with fluconazole and itraconazole but evolved with a respiratory infection, decreased level of consciousness, and death. It is very difficult to distinguish morphologically the genera Candida and Trichosporon. Electron microscopy and special stains such as Alcian blue and colloidal iron can help their distinction in tissue samples;[33] however, the criteria are difficult to apply and reproduce. Microbiological tests are indicated to classify the fungus and choose the most effective medication in cases with clinical signs of urinary tract infection.

CONCLUSION

The results indicate that the first six months after transplantation appear to be critical in terms of reactivation of latent viral infections; hence the importance of systematic urinary monitoring, especially during this period.

Sustained DCs shedding and smears with a dirty cytological background can indicate a risk of BKVAN development, even in the absence of clinical graft dysfunction.

Ultrastructural examination and immunofluorescence for the SV-40 antigen in urinary sediment are alternative techniques for detecting the reactivation of BKV.

Microbiological tests are important in fungus-positive samples from patients with clinical indications of treatment, despite the morphological aspects of the pathogen. They are essential to correctly classify the fungus and select the appropriate medication.

Urine cytology presents an effective instrument for the diagnosis of viral reactivation in renal transplant patients, particularly BKV and HPV, as well as for the detection of genitourinary fungi, which can be important threats to the health of the graft.

Taken together, our findings suggest that there is still a role for urinary cytology in kidney transplantation.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Gouvêa ALF, Almeida JR, Carvalho FR, Nascimento ALR, Cosendey RIJ, Nascimento CMC; **Conception and design:** Gouvêa ALF, Almeida JR; **Data analysis and interpretation:** Gouvêa ALF, Almeida JR, Carvalho FR; **Article writing:** Gouvêa ALF, Carvalho FR; **Critical revision:** Gouvêa ALF, Almeida JR, Carvalho FR, Nascimento ALR, Cosendey RIJ, Nascimento CMC; **Final approval:** Gouvêa ALF, Almeida JR, Carvalho FR, Nascimento ALR, Cosendey RIJ, Nascimento CMC.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

FUNDING

Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro
https://doi.org/10.13039/501100004586
Grant No: 26/111.702/2013.

ACKNOWLEDGEMENT

The authors thank the Institute of Biology of Universidade Federal Fluminense for allowing us to use the JEM 1011 transmission electron microscope and the technical support of biologist Alan Moraes to operate and photograph. We also thank Anna Karoline Fausto da Silva for immunohistochemical stains for SV40 T-ag, Marcos Alegria for help with phase contrast microscope analysis, Dr. Jeferson Carvalhaes de Oliveira for fungal culture, Divisão de Previsão Numérica – Centro de Hidrografia da Marinha for creating the graph in figure 1, and Drs. Paulo Alexandre Menezes and Magda Magalhães Santos were the attending physicians of the patients.

REFERENCES

1. Cukuranovic J, Ugrenovic S, Jovanovic I, Visnjic M, Stefanovic V. Viral infection in renal transplant recipients. ScientificWorldJournal. 2012;2012:820621. https://doi.org/10.1100/2012/820621
2. Leon RM, Ranzi AD, Fardin GS, Keitel E, Brackmann RL, Prolla JC, et al. Immunosuppression and the occurrence of HPV in kidney transplant patients verified by urinary cytology. J Bras Patol E Med Lab. 2016;52:25–30. https://doi.org/10.5935/1676-2444.20160009

3. Dupont PJ, Manuel O, Pascual M. Infection and chronic allograft dysfunction. Kidney Int. 2010;78:S47–53. https://doi.org/10.1038/ki.2010.423

4. Masutani K. Viral infections directly involved in kidney allograft function. Nephrol Carlton Vic. 2018;23 Suppl 2:31–7. https://doi.org/10.1111/nep.13285

5. Chatterjee P, Mathur SR, Dinda AK, Guleria S, Mahajan S, Iyer VK, et al. Analysis of urine sediment for cytology and antigen expression in acute renal allograft rejection: an alternative to renal biopsy. Am J Clin Pathol. 2012;137(5):816–24. https://doi.org/10.1309/ajcpqfz0gelh5zpn

6. Nickeleit V, True K, Detwiler R, Kozlowski T, Singh H. Risk assessment for polyomavirus nephropathy using urine cytology and the detection of decoy cells: cheap and efficient. Transplantation. 2012;94(7):e42-44; author reply e45. https://doi.org/10.1097/tp.0b013e31826784d8

7. Tummidi S, Kothari K, Agnihotri M, Naik L, Rojekar A. Diagnostic utility of urine cytology in detection of decoy cells in renal transplant patients: Report of five cases and review of literature. Diagn Cytopathol. 2020;48(3):222–7. https://doi.org/10.1002/dc.24337

8. Selvaggi SM. Cytologic detection of concurrent infectious agents in urines from renal transplant patients. Diagn Cytopathol. 2010;38(8):549–50. https://doi.org/10.1002/dc.21243

9. Vidas Z, Misić M, Pacić A, Jurenec F, Knotek M, Kardum-Skelin I. The value of urinary decoy cells finding in patients with kidney transplantation. Coll Antropol. 2010 [cited 2023 Mar 22];34(1):153–7. Available from: https://pubmed.ncbi.nlm.nih.gov/20432744/

10. Ranzi AD, Introíni GO, Prolla JC, Brackmann R, Bassani NC, Pasqualotto AC, et al. Correlation between the presence of degenerated inclusion-bearing cells in voided urine samples and the occurrence of polyomavirus infection. Cytopathol Off J Br Soc Clin Cytol. 2017;28(2):103–8. https://doi.org/10.1111/cyt.12358

11. Bohl DL, Brennan DC. BK virus nephropathy and kidney transplantation. Clin J Am Soc Nephrol CJASN. 2007;2 Suppl 1:S36-46. https://doi.org/10.2215/cjn.00920207

12. Siddig EE, Mohamed NS, Ali ET, Mohamed MA, Muneer MS, Munir A, et al. Urine cytological examination: an appropriate method that can be used to detect a wide range of urinary abnormalities [Internet]. F1000Research; 2019 [cited 2023 Mar 22]. Disponível em: https://f1000research.com/articles/8-1878

13. Pajenda S, Kapps S, Gerges D, Hoermann G, Wagner L, Buchtele N, et al. Cytomegalovirus in urinary sediment in patients with acute kidney injury. BMC Nephrol. 2021;22(1):169. https://doi.org/10.1186/s12882-021-02377-z

14. Singh HK, Bubendorf L, Mihatsch MJ, Drachenberg CB, Nickeleit V. Urine Cytology Findings of Polyomavirus Infections. Em: Ahsan N, organizador. Polyomaviruses and Human Diseases [Internet]. New York, NY: Springer; 2006 [citado 23 de março de 2023]. p. 201–12. (Advances in Experimental Medicine and Biology). Disponível em: https://doi.org/10.1007/0-387-32957-9_15

15. Geramizadeh B, Roozbeh J, Malek-Hosseini SA, Azarpira N, Ayatollahi M, Salahi H, et al. Urine cytology as a useful screening method for polyoma virus nephropathy in renal transplant patients: a single-center experience. Transplant Proc. 2006;38(9):2923–5. https://doi.org/10.1016/j.transproceed.2006.08.177

16. Thamboo TP, Jeffery KJM, Friend PJ, Turner GDH, Roberts ISD. Urine cytology screening for polyoma virus infection following renal transplantation: the Oxford experience. J Clin Pathol. 2007;60(8):927–30. https://doi.org/10.1136/jcp.2006.042507

17. Chakera A, Dyar OJ, Hughes E, Bennett S, Hughes D, Roberts ISD. Detection of polyomavirus BK reactivation after renal transplantation using an intensive decoy cell surveillance program is cost-effective. Transplantation. 2011;92(9):1018–23. https://doi.org/10.1097/tp.0b013e318230c09b

18. Funahashi Y, Kato M, Fujita T, Ishida S, Mori A, Gotoh M. Association Between the Polyomaviruses Titers and Decoy Cell Positivity Rates After Renal Transplantation. Transplant Proc. abril de 2016;48(3):921–3. https://doi.org/10.1016/j.transproceed.2016.02.045

19. Maia TMC, Silva SFR, Silva SL, Holanda MC, Nascimento JM, Ferreira MVP. Polyomavirus-infected decoy cells in cytocentrifuged urine cytology specimens from renal transplant recipients. Acta Cytol. 2011;55(5):445–8. https://doi.org/10.1159/000329625

20. Hirsch HH, Knowles W, Dickenmann M, Passweg J, Klimkait T, Mihatsch MJ, et al. Prospective study of polyomavirus type BK replication and nephropathy in renal-transplant recipients. N Engl J Med. 2002;347(7):488–96. https://doi.org/10.1056/nejmoa020439

21. Drachenberg RC, Drachenberg CB, Papadimitriou JC, Ramos E, Fink JC, Wali R, et al. Morphological spectrum of polyoma virus disease in renal allografts: diagnostic accuracy of urine cytology. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2001 [cited 2023 Mar 22];1(4):373–81. Available from: https://pubmed.ncbi.nlm.nih.gov/12099383/

22. Sawinski D, Goral S. BK virus infection: an update on diagnosis and treatment. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2015;30(2):209–17. https://doi.org/10.1093/ndt/gfu023

23. Chen TW, Chen CY, Lin NC, King KL, Wu TH, Yang WC, et al. How to Improve the Positive Predictive Value of Urinary Decoy Cell Surveillance for Polyomavirus BK-Associated Nephropathy in Kidney Transplant Patients. Transplant Proc. 2016;48(3):924–8. https://doi.org/10.1016/j.transproceed.2016.02.044

24. Sekito T, Araki M, Yoshinaga K, Maruyama Y, Sadahira T, Nishimura S, et al. Presence of decoy cells for 6 months on urine cytology efficiently predicts BK virus nephropathy in renal transplant recipients. Int J Urol. 2021;28(12):1240–6. https://doi.org/10.1111/iju.14679

25. Fogazzi GB, Cantú M, Saglimbeni L. "Decoy cells" in the urine due to polyomavirus BK infection: easily seen by phase-contrast microscopy. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2001;16(7):1496–8. https://doi.org/10.1093/ndt/16.7.1496

26. Poloni JAT, Pinto GG, Giordani MSB, Keitel E, Inocente N, Voegeli CF, et al. Bright Field Microscopy to Detect Decoy Cells Due to BK Virus Infection in the Fresh and Unstained Urine Sediment in Kidney Allograft Recipients. J Clin Lab Anal. 2016;30(6):1044–50. https://doi.org/10.1002/jcla.21978

27. Nankivell BJ, Renthawa J, Jeoffreys N, Kable K, O'Connell PJ, Chapman JR, et al. Clinical Utility of Urinary Cytology to Detect BK Viral Nephropathy. Transplantation. 2015;99(8):1715–22. https://doi.org/10.1097/tp.0000000000000642

28. Singh HK, Reisner H, Derebail VK, Kozlowski T, Nickeleit V. Polyomavirus Nephropathy: Quantitative Urinary Polyomavirus-Haufen Testing Accurately Predicts the Degree of Intrarenal Viral Disease. Transplantation. 2015;99(3):609–15. https://doi.org/10.1097%2FTP.0000000000000367

29. Delgado J, Calvo N, Gomis A, Pérez-Flores I, Rodríguez A, Ridao N, et al. Candiduria in renal transplant recipients: incidence, clinical repercussion, and treatment indication. Transplant Proc. 2010;42(8):2944–6. https://doi.org/10.1016/j.transproceed.2010.08.019

30. Colombo AL, Padovan ACB, Chaves GM. Current knowledge of Trichosporon spp. and Trichosporonosis. Clin Microbiol Rev. 2011;24(4):682–700. https://doi.org/10.1128/cmr.00003-11

31. Iken M, Belkouch A, Bellarj B, Naoui H, Boumhil L, El Bouti A, et al. A rare case of urinary tract infection due to Trichosporon asahii in a diabetic patient. Pan Afr Med J. 2015;20:127. https://doi.org/10.11604/pamj.2015.20.127.6152

32. de Almeida Júnior JN, Hennequin C. Invasive Trichosporon Infection: a Systematic Review on a Re-emerging Fungal Pathogen. Front Microbiol. 2016;7:1629. https://doi.org/10.3389/fmicb.2016.01629

33. Obana Y, Sano M, Jike T, Homma T, Nemoto N. Differential diagnosis of trichosporonosis using conventional histopathological stains and electron microscopy. Histopathology. 2010;56(3):372–83. https://doi.org/10.1111/j.1365-2559.2010.03477.x