

CYSTOSCOPY IN THE DIAGNOSIS AND FOLLOW-UP OF URINARY SCHISTOSOMIASIS IN BRAZILIAN SOLDIERS RETURNING FROM MOZAMBIQUE, AFRICA

Iran Mendonça da SILVA(1), Roberto THIENGO(2), Maria José CONCEIÇÃO(3,4), Luis REY(3), Edson PEREIRA FILHO(1) & Paulo Cesar RIBEIRO(1)

SUMMARY

The assessment of urinary schistosomiasis in individuals coming from endemic areas often requires diagnostic resources not used in areas of exposure in order to determine complications or to establish more precise criteria of cure. Cystoscopy and 24-hour urine examination were performed, after treatments with praziquantel 40 mg/kg body weight, single dose, on 25 Brazilian military men who were part of a United Nations peace mission to Mozambique in 1994. The median age of the individuals was 29 years and all presented a positive urine parasitological exam. The alterations detected by cystoscopy were hyperemia and granulomas in the vesical submucosa in 59.1% of the individuals and only granulomas in 40.9%. A vesical biopsy revealed granulomas in all patients and viable eggs in 77.3% even after a period during which the patients no longer excreted eggs in urine. Cystoscopy after treatment, followed by biopsy and histopathological evaluation, performed in areas where the evolution of the disease can be better monitored, was found to be a safe criterion of parasitological cure.

KEYWORDS: Urinary schistosomiasis; Cystoscopy.

INTRODUCTION

Urinary schistosomiasis occurs in 53 countries on the African continent and in the Middle East (CEGET-CNRS/OMS-WHO 1987); however, no autochthonous case has been reported in Brazil thus far. Brazil has historical ties with Africa as a result of the migratory flows that occurred during the colonization of the country. Although to a lesser extent, migration continues to occur until today due to the search for better socioeconomic conditions (CASTRO, 1981). Several cases of individuals infected with *S. hematobium* coming from endemic areas have been reported in the literature (GANEM & MARROUM, 1998, NOZAIS *et al.*, 1993, HERNÁNDEZ & SUARÉZ, 1991), thus indicating the need to investigate the diagnosis, especially the presence of hematuria and the history of travel to endemic areas (SULTANA *et al.*, 1995, THALLER & WANG, 1999).

In addition to HERNANDEZ *et al.* (1985), who were able to differentiate old from recent infections in a series of patients with endoscopic alterations, other authors (ABDEL-WAHAB *et al.*, 1992, 1993, ADOBOR *et al.*, 1998, GANEM & MARROUM, 1998) demonstrated the importance of the cystoscopy in the investigation of the disease (BURKI *et al.*, 1986). KROLIKOWSKI *et al.* (1995), studying women with pelvic inflammatory disease from regions endemic for schistosomiasis, used cystoscopy and laparoscopy to investigate pelvic pain and obtained a diagnosis of urinary schistosomiasis in 21.5% of the patients.

Cystoscopy is an important exam for the detection of the case of hematuria and other affections of the bladder. This approach is indicated in cases in which semiological assessment by noninvasive methods is unable to establish a diagnosis (PATIL *et al.*, 1992, ROTKOPF *et al.*, 1993, TORRICELLI *et al.*, 1998, HATZ *et al.*, 1998, HERWALDT *et al.*, 1995, LIANG *et al.*, 2000), and especially in cases in which the disease may develop complications that need to be identified by a direct exam (NOZAIS *et al.*, 1993, PALASCAK *et al.*, 2001, ABDEL-HADI & TALAAT, 2000).

The aim of this study is to describe the value of the cystoscopy in the diagnosis of schistosomiasis haematobia.

PATIENTS AND METHODS

The protocol of this study was approved by the Research Ethics Committee of Instituto de Biologia do Exército, Rio de Janeiro, Brazil. An appropriate informed consent was obtained for all the patients and the guidelines for human experimentation of the National Health Council were followed in the conduct of clinical research.

After the appearance of genitourinary signs and symptoms among Brazilian soldiers returning from ONU peace mission in 1994, in Mozambique (Africa), we evaluated by clinical and laboratorial exams, 132 men that came from the mission. Some of them swam in Licungo river (Africa) and, after this, they presented haematuria, dysuria,

(1) Seção de Vigilância Epidemiológica, Subdivisão de Pesquisa, Divisão de Ensino e Pesquisa, Instituto de Biologia do Exército, Rio de Janeiro, Brasil.

(2) Serviço de Urologia, Hospital Central do Exército, Rio de Janeiro, Brasil.

(3) Laboratório de Biologia e Controle de Esquistossomose, Departamento de Medicina Tropical, Instituto Oswaldo Cruz, FIOCRUZ, Rio de Janeiro, Brasil.

(4) Hospital Universitário Clementino Fraga Filho, Rio de Janeiro, Brasil.

Correspondence to: Iran Mendonça da Silva, MD, Seção de Vigilância Epidemiológica, Subdivisão de Pesquisa, Divisão de Ensino e Pesquisa, Instituto de Biologia do Exército, Rua Francisco Manuel 102, Benfica, 20911-270 Rio de Janeiro, RJ, Brasil. Phone: 55 21 38600442 ramal 228, Fax: 55 21 38603510, e-mail: silva.iran@ig.com.br

polakiuria, and lumbar pain. The first laboratory evaluation was the urine parasitological assay, and 18.9% (25/132) presented eggs of *Schistosoma haematobium* in urine. So, these men were considered eligible to the study, when after detailed explanation about the previous methods in the study, they signed the free and informed consent. The age of the patients ranged from 26 to 36, with a median of 29 years.

Three of 24-hour urine samples were collected at minimum intervals of one week for selective and initial diagnosis. One part (200 mL) of the total urine volume was transferred to glass chalices and left to stand for 24 hours. After this, 10 mL of the initial sediment was removed with a glass pipette held close to the bottom of the chalice and centrifuged at 3500 g for 5 min. One-hundred microliters of the centrifuged material was removed with a glass pipette held close to the bottom of the tube, mounted on slides, coverslipped, and observed under a microscope at magnifications of 100X and 400X. Three urine examinations, with the same technique, were performed after six months to do the control after treatment with praziquantel 40 mg/kg body weight, single dose.

In the follow up, the patients were submitted to cystoscopy with Olympus 19 CH with a 30° eyepiece. It was done, after six months in each treatment, to investigate complications and to control the cure of the patients. The urinary bladder biopsy was done when were observed alterations in the vesical mucosa. If the histopathological examination showed granulomas and viable eggs, the treatment was repeated. After the minimum interval of six months, a cystoscopy was repeated.

RESULTS

Alterations upon cystoscopic examination were observed in 88.0% (22/25) of the patients. Macroscopic alterations included hyperemia (Fig. 1) and granulomas in the vesical submucosa were observed in 59.1% (13/22) of the patients, and only granulomas (Fig. 2) were found in 40.9% (9/22). Histopathological analysis identified viable eggs in 77.3% (17/22) of the patients. The eggs were filled with miracidia, in which intact internal structures, such as nervous system cells,

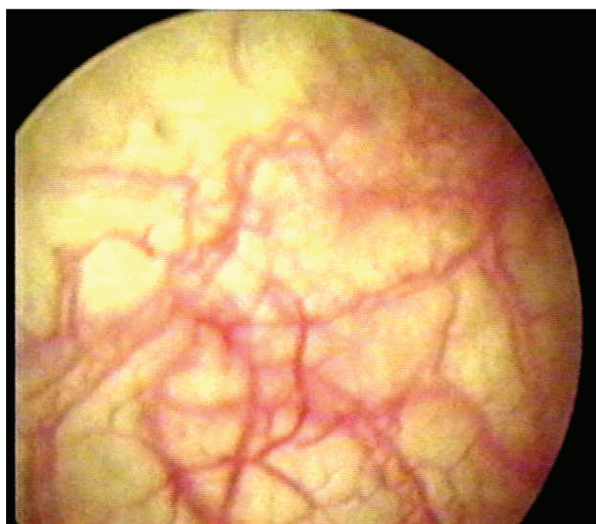


Fig. 1 - Cystoscopy demonstrating hyperemia.

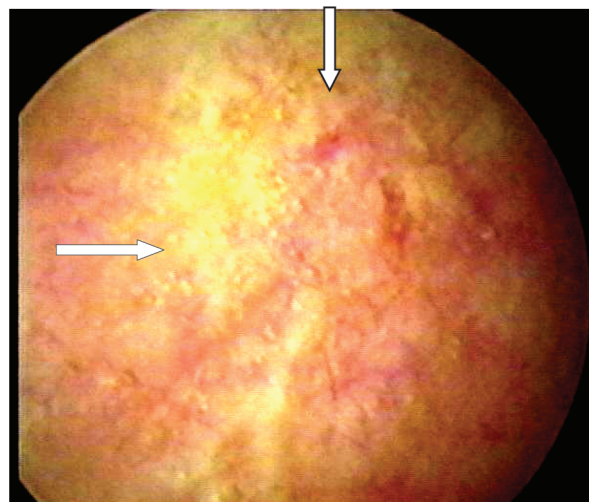


Fig. 2 - Cystoscopy demonstrating hyperemia and granulomas (white arrows).

germinative cells and glands, could be differentiated. We observed, like LENZI *et al.* (1998), multiple granulomas in the exudative and exudative-productive phase and few granulomas in the involutinal phase. After the second treatment, considering all patients, the cystoscopic control showed that 36.0% (9/25) of them were still with granulomas and viable eggs, in spite of urine assay being negative.

DISCUSSION

The alterations observed upon macroscopic examination of the bladder are peculiar and complications of this infection are generally identified by endoscopy, with an early diagnosis permitting efficient corrections (ABDEL-WAHAB *et al.*, 1992, NOZAIIS *et al.*, 1993, PALASCAK *et al.*, 2001, SHARFI & HASSN, 1994, SULTANA *et al.*, 1995).

In the present study, cystoscopy was not exclusively performed to establish a primary etiological diagnosis but to monitor and identify complications. Cystoscopy was abnormal in 88.0% of the individuals, who presented only granulomas or granulomas associated with hyperemia. A vesical biopsy was obtained from all patients and the etiological diagnosis was confirmed by the identification of viable eggs of *S. haematobium*. The patients did not return to endemic regions, and 36.0% (9/25), who continued to be followed up, still showed viable eggs, six to 24 months after treatment with praziquantel. Since parasite eggs had no longer been detected in the urine of these patients, cystoscopy followed by biopsy and histopathological examination markedly contributed to this finding.

Our results corroborate the opinion of several authors. They suggest that the cystoscopy should be used in the case of chronic schistosomiasis of the urinary tract, mainly in accidentally exposed individuals, since poor elimination of eggs in this condition may yield a false-negative diagnosis when determining eggs in urine (ORTIZ RODRIGUEZ-PARETS *et al.*, 1995, SULTANA *et al.*, 1995, THALLER & WANG, 1999, TORRICELLI *et al.*, 1998). This is the situation that we have got among our patients. We observed that this is also indicated for

patient follow-up as a criterion of cure and when complications are suspected (ABDEL-HADI & TALAAT 2000). Our study was conducted with both aims, and although we did not detect complications, we observed therapeutic failures that were not being detected in urine parasitological assays.

Cystoscopy is indicated in cases in which non-invasive semiological evaluation does not lead to a diagnosis, and especially in cases in which the disease may develop complications that need to be identified by direct observation.

In endemic areas, the main objective of post-treatment assessment based on urine samples is the control of transmission and morbidity. However, in individual cases with evidence of tumor complications, cystoscopy should be performed in view of reports of the occurrence of vesical neoplasia in young individuals (AMONKAR *et al.*, 2001, HERNÁNDEZ *et al.*, 1984).

In our study, even after the treatment with praziquantel has been offered for three times, the patients remained positives with viable eggs in the urinary bladder. So, cystoscopy was essential to verify the therapeutic failure.

Considering the results, we suggest that cystoscopy should be part of the diagnostic assessment of patients coming from areas endemic for urinary schistosomiasis under the following conditions: parasite eggs undetectable in three 24-hour urine samples obtained from symptomatic individuals; as a criterion of post-treatment parasitological cure even when three negative urine samples were obtained; suspicion of complications during any period of evolution and at any age. We also recommend to the individuals that travel to endemic areas not to swim where they are not sure about the possible water contamination, or where they see snails. If it is not possible to avoid the exposure, they have to do a medical evaluation with urine parasitological assay, after nine to 11 weeks pos-exposure.

ACKNOWLEDGMENTS

The authors thank the "Serviço de Urologia do Hospital Central do Exército, Rio de Janeiro, Brazil", for technical support.

RESUMO

Cistoscopia no diagnóstico e seguimento de esquistossomose urinária em militares brasileiros retornando de Moçambique, África

A avaliação de esquistossomose urinária em indivíduos procedentes de áreas endêmicas, freqüentemente requer recursos diagnósticos não usados nas áreas de exposição, para determinar as complicações ou estabelecer um critério de cura mais preciso. A cistoscopia e o exame de urina de 24 horas foram realizados, após tratamentos com praziquantel na dose de 40 mg/kg de peso, dose única, em 25 militares brasileiros que participaram de uma Missão de Paz pela ONU em Moçambique no ano de 1994. A idade média dos indivíduos foi de 29 anos e todos apresentavam exame parasitológico de urina positivo. As alterações detectadas pela cistoscopia foram hiperemia e granulomas na submucosa vesical em 59.1% dos indivíduos e somente granulomas

em 40.9%. A biópsia vesical revelou granulomas em todos os pacientes e ovos viáveis em 77.3%, mesmo após um período durante o qual os pacientes não mais eliminavam ovos pela urina. Após o tratamento, a cistoscopia seguida por biópsia e avaliação histopatológica, realizada em áreas onde a evolução da doença pode ser monitorada melhor, demonstrou ser um critério mais seguro de cura parasitológica.

REFERENCES

1. ABDEL-HADI, A.M. & TALAAT, M. - Histological assessment of tissue repair after treatment of human schistosomiasis. *Acta trop.*, 77: 91-96, 2000.
2. ABDEL-WAHAB, M.F.; RAMZY, I.; ESMAT, G.; EL KAFASS, H. & STRICKLAND, G.T. - Ultrasound for detecting *Schistosoma haematobium* urinary tract complications: comparison with radiographic procedures. *J. Urol.*, 148: 346-350, 1992.
3. ABDEL-WAHAB, M.F. & STRICKLAND, G.T. - Abdominal ultrasonography for assessing morbidity from schistosomiasis. 2. Hospital studies. *Trans. roy. Soc. trop. Med. Hyg.*, 87: 135-137, 1993.
4. ADOBOR, R.D.; JOHANSEN, T.E. & MAJAK, B. - *Schistosomiasis* of the urinary bladder. *Tidsskr. Nor. Laegeforen*, 118: 1041-1042, 1998.
5. AMONKAR, P.; MURALI, G. & KRISHNAMURTHY, S. - *Schistosoma* induced squamous cell carcinoma of the bladder. *Indian J. Path. Microbiol.*, 44: 363-364, 2001.
6. BURKI, A.; TANNER, M.; BURNIER, E. *et al.* - Comparison of ultrasonography, intravenous pyelography and cystoscopy in detection of urinary tract lesions due *Schistosoma haematobium*. *Acta trop.*, 43: 139-151, 1986.
7. CASTRO, T. - *África: geohistória, geopolítica e relações internacionais*. Rio de Janeiro, Biblioteca do Exército, 1981. p. 17-204.
8. CEGET-CNRS / OMS-WHO - *Atlas of the global distribution of schistosomiasis*, 28: 223-230, 1987.
9. GANEM, J.P. & MARROUM, M.C. - Schistosomiasis of the urinary bladder in an African immigrant to North Carolina. *Sth. med. J. (Bgham, Ala.)*, 91: 580-583, 1998.
10. HATZ, C.F.; VENNERSVALD, B.J.; NKULILA, T. *et al.* - Evolution of *Schistosoma haematobium* - related pathology over 24 months after treatment with praziquantel among school children in southeastern Tanzania. *Amer. J. trop. Med. Hyg.*, 59: 775-781, 1998.
11. HERNÁNDEZ, A.D.; LOPETEQUI, O.L.; PEREZ, A.R.; GARCIA, A.R. & AVILA, J.P. - Schistosomiasis y cancer de vejiga. *Rev. cuba. Med. trop.*, 36: 258-263, 1984.
12. HERNÁNDEZ, A.D.; FERNÁNDEZ, T.R.; PÉREZ, A.R. *et al.* - Esquistossomiasis a *Schistosoma haematobium*: manifestaciones clínicas y hallazgos endoscópicos en pacientes cubanos y extranjeros. *Rev. cuba. Med. trop.*, 37: 278-287, 1985.
13. HERNÁNDEZ, C.S.G. & SUARÉZ, M.F. - Estudio de la schistosomiasis en pacientes cubanos ingresados en el Instituto de Medicina Tropical "Pedro Kouri". *Rev. cuba. Med.*, 30: 17-22, 1991.
14. HERWALDT, B.L.; TAO, L.F.; VAN PELT, W.; TSANG, V.C. & BRUCE, J.I. - Persistence of *Schistosoma haematobium* infection despite multiple courses of therapy with praziquantel. *Clin. infect. Dis.*, 20: 309-315, 1995.
15. KROLIKOWSKI, A.; JANOWSKI, K. & LARSEN, J.V. - Laparoscopic and cystoscopy findings in patients with chronic pelvic pain in Eshowe, South Africa. *Cent. Afr. J. Med.*, 41: 225-226, 1995.
16. LENZI, H.L.; KIMMEL, E.; SCHECHTMAN, H. *et al.* - Histoarchitecture of schistosomal granuloma development and involution: morphogenetic and biomechanical approaches. *Mem. Inst. Oswaldo Cruz*, 93 (supl. 1): 141-151, 1998.

17. LIANG, Y.S.; COLES, G.C. & DOENHOFF, M.J. - Detection of praziquantel resistance in schistosomes. **Trop. Med. Int. Hlth**, **5**: 72, 2000.
18. NOZAIS, J.P.; DANIS, M. & GENTILINI, M. - Symptoms and development of *Schistosoma haematobium* infestation seen in a metropolis. **Rev. Prat. (Paris)**, **43**: 428-431, 1993.
19. ORTIZ RODRIGUEZ-PARETS, J.; SILVA, J. & GARCIA MACIAS, M.C. - Bladder schistosomiasis. Report of a case. **Arch. esp. Urol.**, **48**: 642-643, 1995.
20. PALASCAK, R.; GAME, X.; MILCENT, S. *et al.* - Verrucous epidermoid carcinoma of the bladder unrelated to schistosomiasis. **Progr. Urol.**, **11**: 695-699, 2001.
21. PATIL, K.P.; IBRAHIM, A.I.; SHETTY, S.D.; EL TAHIR, M.I. & ANANDAN, N. - Specific investigations in chronic urinary bilharziasis. **Urology**, **40**: 117-119, 1992.
22. ROTKOPF, L.; HELENON, O.; CHRETIEN, Y. *et al.* - Radiological exploration of hematuria. **J. Urol.**, **99**: 192-209, 1993.
23. SHARFI, A.R. & HASSAN, O. - Evaluation of haematuria in Khartoum. **E. Afr. med. J.**, **71**: 29-31, 1994.
24. SULTANA, S.R.; BYRNE, D.J. & McCULLOUGH, J.B. - The value of a travel history in urology. **Scot. med. J.**, **40**: 83, 1995.
25. THALLER, T.R. & WANG, L.P. - Evaluation of asymptomatic microscopic hematuria in adults. **Amer. Fam. Phycn.**, **60**: 1143-1152, 1999.
26. TORRICELLI, M.; CERRI, M.; LEVA, E. *et al.* - An unusual case of macroscopic hematuria in pediatric age. **Pediat. med. chir.**, **20**: 81-83, 1998.

Received: 17 December 2004

Accepted: 29 September 2005