Case report of rare presentation of schistosomiasis: delayed diagnosis of genitourinary schistosomiasis in an adolescent

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Abstract

Schistosomiasis is a tropical infection endemic to developing nations that can result in chronic liver damage, renal failure, infertility, and bladder cancer. Genitourinary localization is marked by dysuria, visible hematuria, and urinary obstruction. We present the case of a 17-year-old male adolescent from a rural area of Central Africa, who arrived in Italy two years prior, exhibiting hematuria and urinary symptoms. He came to our attention with a history of terminal hematuria, dysuria, and intermittent abdominal pain since the age of ten. We conducted initial blood tests, urine analyses, and ultrasonography, all yielding negative results. Cystoscopy was conducted with biopsy of an atypical bladder lesion due to the persistence of hematuria. Histopathology revealed morphological findings indicative of Schistosoma haematobium. The patient received praziquantel treatment and was monitored through parasitological urine analyses. Bladder schistosomiasis should be considered in children exhibiting terminal hematuria from endemic regions. Diagnosis can be established through a urinary microbiological examination. An endoscopic evaluation may assist in the diagnosis if the results are negative.

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Introduction

Schistosomiasis knows as "snail fever" or "bilharzia", is a parasitic disease, caused by the Schistosoma, a trematode, endemic in sub-Saharan Africa and the Middle East, where the most affected population is represented by the poorest among the poor living in the remotest, hardest-to-reach parts of these countries. They often include ethnic minorities, nomadic and migrant populations, and other minority or marginalized populations. It is included in the list of "neglected tropical diseases". It is an infection that frequently involves the urinary tract and the intestine. A persistent and chronic infection increases the risk of developing liver damage, kidney failure, infertility and in adult bladder cancer. The urogenital disease is caused by Schistosoma Haematobium. Symptoms include dysuria, painful terminal haematuria, and loin pain.[1-11] Sometimes an obstructive urinary disease could be expression of Schistosomiasis due to the immunopathological reactions against Schistosome's eggs which are trapped in the tissues, while an asymptomatic proteinuria, nephrosis and/or nephritic syndrome can be a clinical manifestation of Schistosomal glomerulopathy. This parasitic infection is reported in early infancy, but the peak of incidence occurs in early adolescence because of frequent bathing in contaminated pools of water. Diagnosis is obtained with parasitological urine/stools examinations; radiological imaging could be useful, above all ultrasound of the genitourinary tract, for evaluation of injuries.[2,5] Treatment, as recommended by World Health Organization (WHO), is medical with Praziquantel.[12] We report a case of urogenital schistosomiasis of a 17-years old African adolescent, in Italy since 2 years, affected by persistent terminal hematuria since the age of 10 years old.

Case Report

We present a case of an adolescent, male, of 17-years-old, arrived in Italy from a Country of sub-Saharan Africa two years ago. He arrived to our attention for a persistent terminal macrohematuria since the age of 10 years (at the end of each urination) associated with dysuria and occasional abdominal pain. Shortly after his arrival in Italy he was hospitalized in the Nephrology Department, for proteinuria and anaemia due to probable malnutrition.

Clinically, the presence of macrohematuria with urinary and abdominal symptoms lead us to consider different possible diagnostic hypothesis: from bladder/urethral polyps to bladder inflammatory process, from possible neoplastic process (less probable for long-time symptoms onset) to "nutcracker syndrome"(affecting the renal vessels) not excluding a possible parasitic infection.

Blood tests revealed only hyper-eosinophilia. Anaemia, dysionemia, alteration of liver and kidney function were excluded. Creatinine was always in normal range. Urine test highlighted hyperproteinuria (264 mg/24h) and haemoglobinuria with elevated red blood cells count (1213/uL) and white blood cells count (711/uL) in the urinary sediment. The search of microbiological agents (bacteria/parasites) as parasitic Bence Jones protein test were negative. Instead, the Farley test revealed dysmorphic red blood cells. In order to exclude a glomerular pathology, we completed the diagnostic assessment with following examinations: i) protein electrophoresis which showed an hyper-gammaglobulinemia and hypo-albuminemia; ii) coagulation profile (PTT, PT, Fibrinogen), and complement factors, which were normal. In addition, Anti-lupus, anti-ds-DN antibodies, C-ANCA, P-ANCA, anti-B2GPI1 IgM and IgG Abs, Anti-HCV and HbaAg were checked resulting in the normal range. We performed also abdominal ultrasound showing regular bladder, kidneys with normal cortical-medullary differentiation and no dilation of the urinary tract.

After a multidisciplinary discussion with paediatric nephrologists, for a strong suspicion of a glomerular disease they proposed a kidney biopsy founding us in disagreement. We decided to start first with an endoscopic procedure performing a cystoscopy. During endoscopy multiple small whitish rod-like formations wit blackish concretions were observed difficult to interpret (Figure 1). At the level of the bladder neck, there were papular formations. We performed also three samplings of the concretions visualized. Histopathological examination described cystitis and oval calcified formations compatible with parasitic eggs, indicating an infection by Schistosoma Haematobium. At least, a parasitological urine examination was repeated confirming the eggs presence of Schistosoma haematobium.

Praziquantel oral therapy (40mg/kg/day) into two day administrations was started lasting for three consecutive days. No complications occurred. The patient was discharged on fifth postoperative day.

Follow-up included parasitological examination on three urine samples at 4 weeks after cystoscopy that still showed Schistosoma Haematobium eggs with persistent terminal gross haematuria. Two months after treatment, we repeated: abdominal ultrasound, with no evidenced of pathological finding; blood tests that showed eosinophils 400/mmc; parasitological examination of stool and urine in three samples, which confirmed eradication of the infection. The patient was asymptomatic, with no more haematuria, dysuria and abdominal pain.

Discussion

Schistosomiasis (Bilharziasis) is a Neglected Tropical Disease (NTDs). It is the second after malaria for rate of incidence and burden of disease.[13] In some countries, it still represents a fatal condition.[11] Both men and women are affected with an incidence that reaches its peak in adolescence between 11 and 15 years.[7] Different species of Schistosoma are detected: *Schistosoma Haematobium*, *Schistosoma Mansoni* and *Schistosoma Japonicum* which cause infection in humans; others are *Schistosoma Intercalatum* and *Schistosoma Mekongi*. Only *S. Haematobium* causes urogenital disease[13] while the remaining species gastrointestinal infection. Schistosoma haematobium is prevalent in Africa and the Middle East, regions where the disease is endemic, due to inadequate sanitation and contaminated waters.[3,11] In endemic regions, infection usually occurs before the age of 2 years, and symptoms worsen during the first decade of life.[14] The variability of clinical and biological presentations makes diagnosis complex. Often schistosomiasis remains asymptomatic, especially in children and hematuria is often misinterpreted. Actually, Schistosomiasis represents one of the most imported disease in children coming from endemic area.[15,16] Schistosomiasis is transmitted through contact with contaminated water. S. haematobium lives in the genitourinary plexus where female worms reproduce and deposit eggs.[8-10] The eggs penetrate the skin and through the

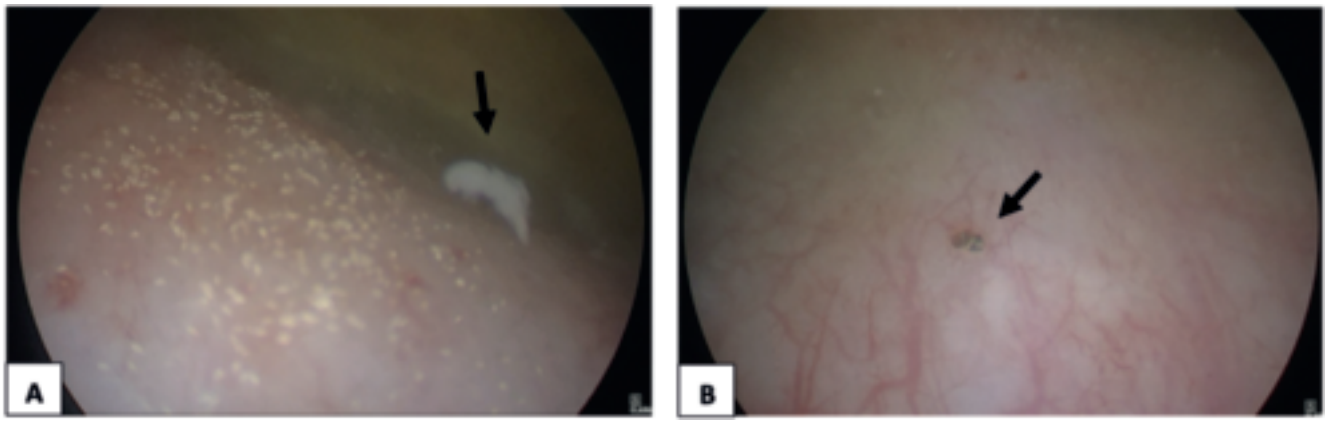

Figura 1. Represented of multiple small whitish rod-like formations (A) with blackish concretions (B).

bloodstream reach the liver where they mature in adult forms. Schistosoma's adult forms enter in the peri-bladder venous plexus by the hemorrhoidal one. The female worms deposit eggs into the venules of the bladder wall and ureter.[17] The deposit of Schistosoma eggs in the bladder's submucosa leads first to the formation of granulomas that after aggregation become pseudo-tubercles, surrounded by hyperaemic areas. The aggregation of the tubercles, the hyperplasia of the mucosa and the bladder's wall muscle hypertrophy lead into nodular or polypoid lesions as described by Ferrara *et al.*[5] that tend to ulcerate and bleed causing hematuria. In some cases, these lesions calcify, appearing as "sandy patches". The bladder mucosa loses is normal pink colour with the disappearance of the submucosal vascular network described as "ground glass" mucosa.[5-18] These modifications could be found in the ureter wall. Clinical manifestations of urinary schistosomiasis depend on the inflammatory response to parasite infection. Usually, symptoms are related to the bladder: hematuria (as in our patient) dysuria, urinary incontinence, and urinary frequency.[3] If the trigone is involved is possible to have urinary retention, while a localization to the upper urinary tract can lead to fibrosis with possible renal failure in not-treated long-term infection. Patients affected by urinary schistosomiasis are more susceptible to secondary bacterial infections leading to chronic cystitis.[3,9,10] Salmonella has been cited as an etiological cause by several authors.[9,11] Fibrosis of the muscle layer may contribute to the bladder contraction, leading also to urodynamic disorders including "hypertonic" or "atonic" bladder. The progression of the disease leads to other comorbidities such as obstruction of the bladder neck and ureters (usually when large polypoid masses are present). Furthermore, due to urinary obstruction, reflux and possible infections, obstructive nephropathy (hydronephrosis) and renal damage can occur. Some authors have described Schistosomal glomerulopathy, which manifests with proteinuria, haematuria and oedema. For this reason, initially, our Nephrologist, hypothesizing in our case, a glomerulopathy recommended a renal biopsy.[3,10]

Lower abdominal and pelvic pain, urinary urgency and incontinence define the "contracted bladder" syndrome as described by Maestro *et al.*[9] The chronic bladder inflammation caused by Schistosoma leads to cytological abnormalities, which increase the risk of developing bladder cancer, usually, squamous cell carcinoma in long-term infections. It and may occur up to 10–20 years after infection.[4,9] By a revision of the Literature there are different reports of late complication in adults. Abdou et al reported 7 cases of bladder dilatation in a cohort of 241 patients, 12 of ureteral dilatation and 15 of bladder cancer.[19] Hodel *et al.*, in his study reports the association of S. Haematobium infection with an increased risk of chronic renal failure;[20] Roure *et al.*, found 30% renal failure in their adult patients affected by imported schistosomiasis.[21,22] Biological diagnosis of Urogenital Infection is complex. It is made with a parasitological urine tests in three different samples, as described by the European Association of Urology.[11] This test is very specific but not very sensitive (particularly in the first six weeks after contagion); to increase its effectiveness, it should be recommended on three different samples after a session of physical activity.[2,5] Additionally, urinalysis and urine culture may be helpful by showing signs of microhaematuria and proteinuria.[10] Eosinophilia represent another useful finding which we had in our patient, since it is a sign of infection by helminths such as schistosomiasis, as supported by Darraj in his review,[8,10] but it is not always present.[23] Schistosomiasis could be diagnoses by a microscopic examination of the urine (*S. haematobium*) where eggs may be observed. In our patient eggs were not found in the urine. Considering the development of nodular or polypoid formations, therefore ultrasound represents a valuable tool to assess urinary system pathology due to Schistosoma, as recommended by the WHO.[6] Ultrasound permits the visualization of irregularities of bladder mucosa, possible alterations of renal cortical-medullary differentiation, detrusor thickness and dilation of the urinary tract.[5,24] However, in difficult and misdiagnosed cases, as our patient, with persistent terminal macrohaematuria and normal ultrasound, mininvasive diagnostic methods as cystoscopy, is useful: typical findings are submucosal nodules and sandy patches (microgranulomas) or a typical "cooked rice grain" appearance (macrogranulomas) and erythematous fibrous polyps.[3,10] Biopsies in these cases can be diagnostic by detecting Schistosoma eggs.[8] According to the World Health Organization, the drug of choice for all species of Schistosoma is Praziquantel (a pyrazinoisoquinoline derivative), safe and effective up to 90% of cases, and we can be used by pregnant and lactating women. Possible side effects are usually mild and include nausea, urticaria, and dizziness, which are thought to be related to the death of the parasites rather than the drug itself. The recommended dose for S. haematobium is 40 mg/kg per day orally in two divided doses that had taken 12h apart. A single treatment leads to resolution of infection in a range of patient of 66-95% which reach the 95-100% with the second treatment four to six weeks later. Usually the second treatment is recommended with persistence of eosinophilia.[6-10]

Conclusions

Schistosomiasis usually leads to kidney, urinary, or genital disease. S. Haematobium is involved in urogenital disease. Bladder schistosomiasis should be considered in patients with urological symptoms, such as dysuria and terminal gross haematuria, coming from endemic countries. Systematic screening of patients returning from endemic areas is therefore recommended. With a diagnostic suspicion, it is recommended to do parasitological examination of the urine on three samples. Instrumental evaluation such as ultrasound is useful for visualizing renal, ureteral and bladder alterations. Cystoscopy is considered an invasive procedure but according us a mini-invasive tool, useful to confirm the diagnosis (as in our case) and eventually to treat possible complications caused by bladder schistosomiasis as ureteral stenosis. Balloon dilatation or ureteral endoscopic incisions in this case are usually the gold standard especially with minimal lesion typical of the first stage of disease. Patients with schistosomiasis present frequent kidney, bladder and urinary involvement and renal failure could be one possible and irreversible complication. Enhancing medical knowledge of this pathology among Pediatrician is essential to improve care and outcomes, to prevent complicated forms of the disease and to limit the risk of autochthonous outbreaks.

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