

Unexpected events of ureteric schistosomiasis in Saudi Arabia

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Abstract

The incidence of schistosomiasis in the Kingdom of Saudi Arabia (KSA) is low; although the presence of ureteric schistosomiasis is low, its presence in association with the other complications is considered a rare event among males, especially in a country like KSA. The objective was to study a 56-year-old Saudi Arabian male, who presented with schistosomiasis in ureter with the development of transitional-cell carcinoma instead of squamous-cell carcinoma. An investigation was carried out in this case by repeated cystoscopes and biopsies for histopathological examinations, as well as several imaging procedures such as plain X-ray, CT, and MRI along with several lab assessments. The presence of all these complications in this patient makes this a case of special interest. This will reflect on conducting further research workup for accurate estimation of schistosomiasis in Saudi Arabia.

KEYWORDS: Schistosomiasis, TCC, pyelonephritis, glomerulonephritis

Introduction

Schistosoma spp. infect 250 million people worldwide.^[1] Schistosomiasis is an endemic in many countries, being not only in sub-Saharan Africa, but also the far East, South and Central America, and the Caribbean.^[2] Obstructive uropathy is the most common and dangerous complication of *Schistosoma haematobium* infection of the interstitial and juxtavesicular portions of the ureter. Chronic renal failure and immune-complex-mediated glomerulonephritis may result. The urinary collecting system, the ureters, bladder, seminal vesicles, prostate gland, urethra, vas deferens, and testes may become affected.^[3,4] In the ureter, mostly the lower portion is affected because of the blood supply anatomy. Eggs are found in all layers of the ureter causing mural fibrosis, loss of the muscle layer, and fibrosis. Stricture may occur. Acute symptoms may include renal colic with pyelonephritis and hydronephrosis. Long-standing obstruction may present with silent obstruction or anuria. Most cases of ureteral involvement also have bladder involvement.^[5,6]

In the Middle-Eastern countries where the trematode *S. haematobium* is endemic, bladder cancer is the most

common adult cancer. Unlike bladder cancers in the Western countries, that are predominantly transitional-cell carcinoma (TCC), these schistosomiasis-associated bladder cancers are predominantly squamous-cell carcinoma (SCC).^[7,8] The histopathological entities of bladder cancer associated with schistosomiasis have certain distinct features that differ from those of bladder cancer found in the Western countries. In many areas of endemic schistosome infection, a much higher proportion SCC of the bladder was seen compared to those occurring in Europe or North America.^[8] In Egypt, for example, SCC occurred in 10 of 1000 adults infected with *S. haematobium* but only in 0 to 3 of 1000 schistosome-free patients.^[9,10] The extent of *Schistosoma* infection apparently plays a significant role in the induction of different types of carcinoma, since SCC is usually associated with moderate-and/or high-worm burdens whereas TCC occurs more commonly in areas associated with lower degrees of infection.^[11] In other countries also (e.g., Iraq), a strong correlation between *S. haematobium* infection and SCC is maintained.^[12,13] The proportion of SCC varied from 54% to 81% of all bladder cancer cases in different areas of endemic infection, which contrasts to the Western countries, where the frequency of SCC in bladder cancer cases is much lower (3–10%).^[13] In general, the major histological cell type of bladder cancer associated with schistosomiasis of the urinary tract is SCC.^[14] The new WHO classification of urothelial carcinomas of the urinary bladder (1999) discriminate the minimally invasive papillary urothelial carcinomas in those with infiltration of the lamina propria above the muscularis mucosae (pT1a), the infiltration of the lamina muscularis mucosae (pT1b), and the extension beyond the muscularis mucosae (pT1c). The recurrence rate increases from stage pT1b. This sub staging

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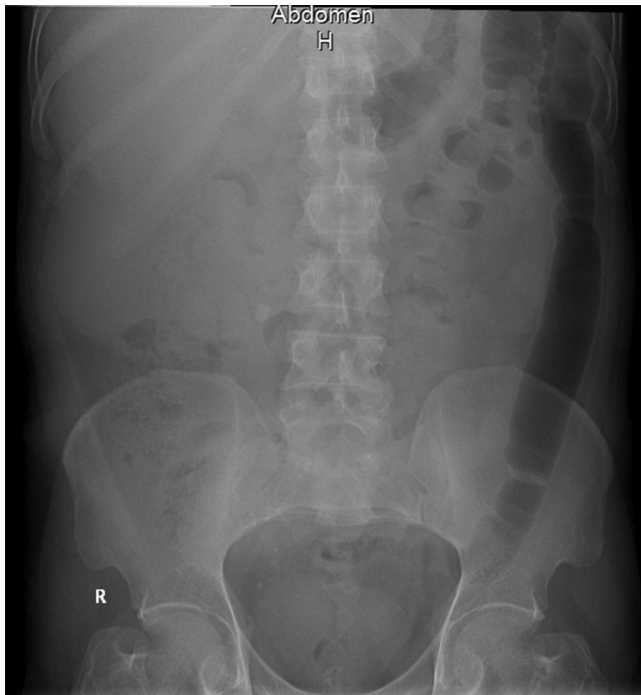


Figure 1: Plain film of the abdomen showed right upper and middle quadrant soft tissue mass density, small rounded radio-opaque shadow at level L3-L4.

may be of therapeutical relevance.^[14] A large series of schistosomiasis-associated bladder tumors for genetic alterations was assessed by Shaw et al., who carried out a partial allelotype of 70 tumors from patients with schistosomiasis. They revealed that there is LOH on all chromosome arms studied (3p, 4p, 4q, 8p, 9p, 9q, 11p, 11q, 13q, 14q, 17p, 18q). The most frequent regions of LOH were 9p (65%), 17p (58%), 3p (40%), 9q (39%), and 8p (37%). LOH on 17p, where the TP53 gene is located, was more common in Egyptian TCC than in SCC. Similarly, 8p LOH was more common in TCC than SCC.^[15]

Case Report

A Saudi male patient, 56 years of age, presented to the outpatient department with right flank pain associated with dysuria, abdominal pain, and fever 1 month prior. His medical history showed urinary retention and suprapubic catheterization. He had neither gastrointestinal symptoms nor gross hematuria. The patient denied any trauma or recent sexual activity. Review of symptoms was negative for any ophthalmic or rheumatologic complaints. Family history was negative for any significant illnesses. The patient was a heavy smoker for 35 years, with two packets daily for the first 20 years and one packet daily for the last 15 years.

On examination, the patient had normal vital signs; abdominal examination showed palpated mass in the right upper quadrant area of approximately 5 cm × 5 cm.



Figure 2: CT shows severe right hydroureter and hydronephrosis, right ureteric stones, focal distal ureteric short segment soft tissue density enlargement and urinary bladder wall calcifications.

Investigations showed that complete blood count and liver function tests were normal; creatinine was 90 mg/dL, and urinalysis showed the presence of red cells, 100 cells/H.P.F. Plain film of the abdomen showed the right upper and middle quadrant soft tissue mass density, small rounded radio-opaque shadow at level L3–L4 (Figure 1). A CT scan was carried out for the palpated mass that revealed severe right hydroureter and hydronephrosis, right ureteric stones, focal distal ureteric short-segment soft-tissue density enlargement, and urinary bladder wall calcifications (Figure 2). A cystoscopy and a retrograde pyelogram were carried out and a biopsy from ureter was taken for histopathological examination. Retrograde right ureterogram was conducted through cystoscopy that showed complete obstruction to the level of middle segment of the ureter. The histopathological report showed noninvasive high-grade papillary urothelioma grade PT1a (Figure 3). Radical nephroureterectomy with bladder cuff was carried out through a right paramedian incision and 1.6 L of pus was drained from the kidney. All resected tissue was sent for histopathology lab, which showed the presence of noninvasive ureteric high-grade papillary urothelial (transitional cell) carcinoma PT1 (Figures 4–7). Renal biopsy revealed a picture suggestive of chronic pyelonephritis (Figure 8) and chronic glomerulonephritis. After recovery from the operation, the patient was discharged in a good condition with readmission for transurethral resection of the bladder tumor (TURBT).

TURBT showed multiple growths on bladder and around prostatic fossa 5 months later. Histopathological report showed multiple calcified schistosomiasis ova with focus of cystitis

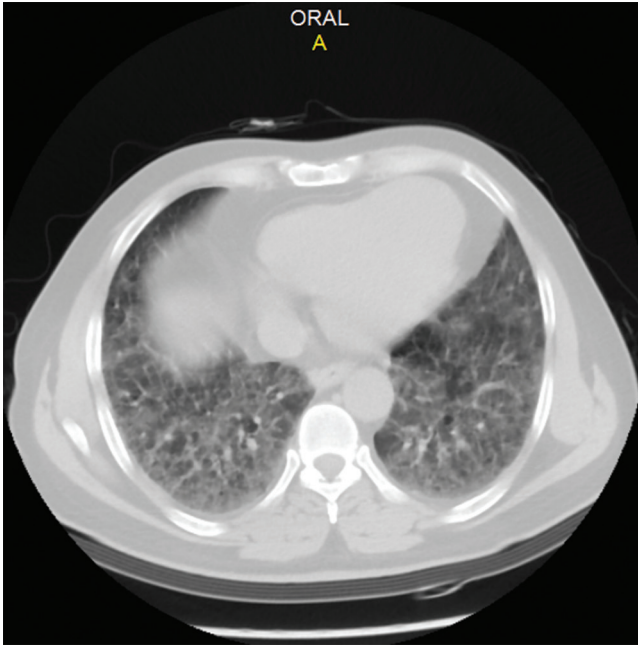


Figure 3: CT chest shows ground glass attenuation of lungs bases, bilateral sub-pleural reticulations, multiple small bilateral apical and basal small cystic airspaces mounting to honey combing, right lung middle lobe sub-pleural nodule measuring 9 mm, right paratracheal subcentemetric lymph node not reaching the pathological size.

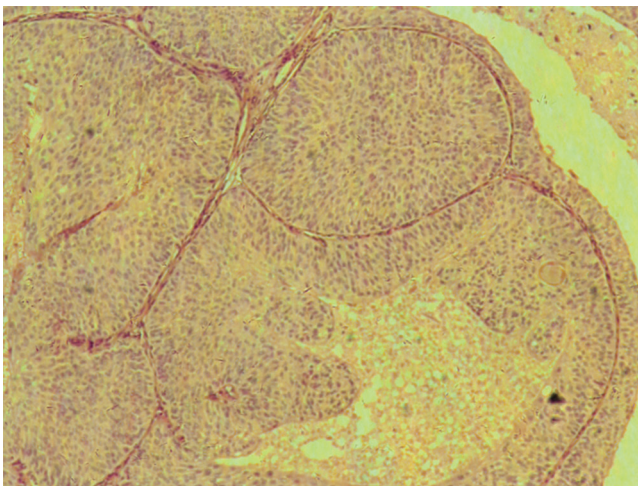


Figure 4: Papillae covered by more than seven layers of transitional cell layers showing cytotypic atypia with CT core of variable thickness with no invasion into lamina propria. Some cells in papillae still retain its perpendicular appearance on basement membrane. All lamina propria seen is intact (x100).

cystica (Figure 9–11). Bladder cytology at this time revealed high-grade urothelial carcinoma.

After one course of Bacillus Calmette-Guerin (BCG) was received by the patient along 6 weeks, a follow-up cystoscopy was conducted that showed a growth again on the lateral wall

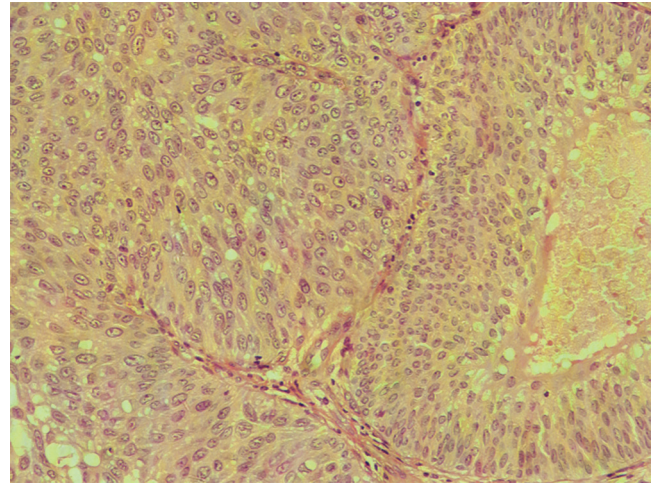


Figure 5: This microphotograph shows more than seven layers of transitional cells revealing marked cellular atypia in the form of nucleomegaly, slight pleomorphism and presence of inconspicuous nucleoli with retaining of some of its perpendicular character on basement membrane. Still no invasion beyond basement membrane (x200).

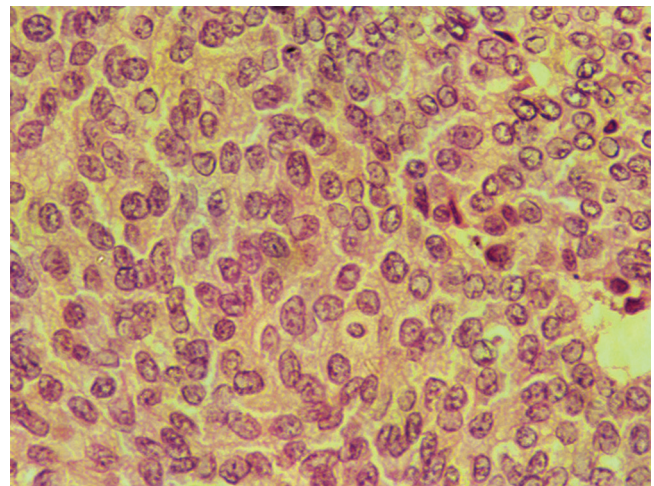


Figure 6: This microphotograph revealed nuclear features of cytologic atypia is in the form of nucleomegaly, rounded nuclei with some irregularities of nuclear contour. Also there is fine to slightly abnormal chromatin distribution. Nucleoli is present in most nuclei, but still are inconspicuous (x200).

of bladder with some patches on the right side and base and growth on the bladder neck. TURBT was conducted again 2 months later and histopathology report revealed mucosal ulceration with variable mixed inflammatory cells in the left lateral wall tissue and low-grade papillary urothelial carcinoma PT1a (invasive into lamina propria) at the bladder neck tissue.

Four months later; a follow-up cystoscopy was conducted that showed new growth on its lateral wall of bladder. TURBT was conducted and histopathology showed grade-I noninvasive papillary urothelial carcinoma PT1a. Follow-up CT and

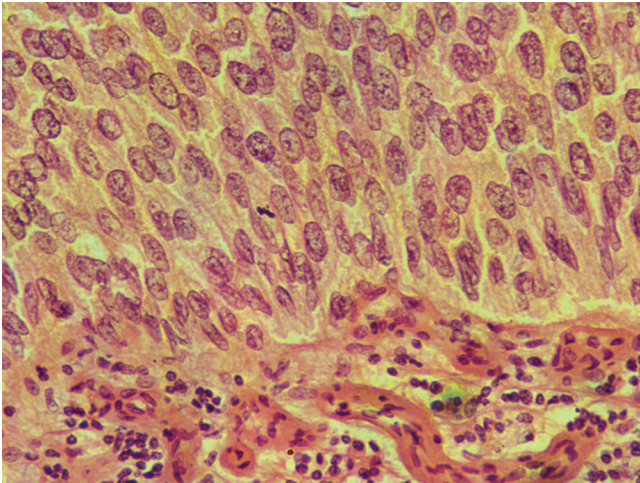


Figure 7: Transitional cell layers showing cytotypic atypia and marked inflammatory infiltrate in submucosa are evident (x400).

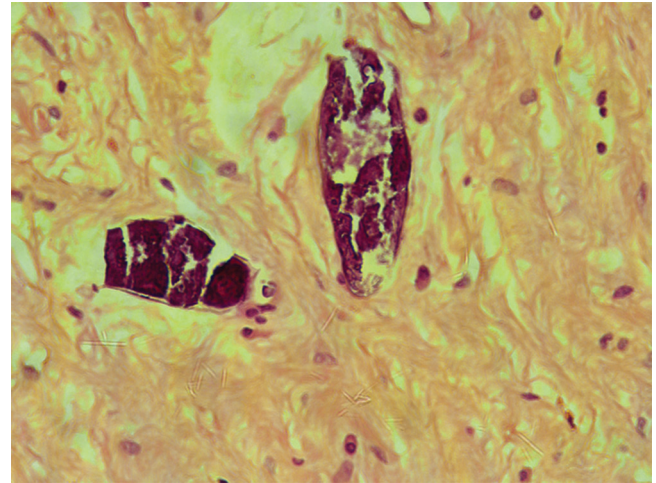


Figure 9: The submucosa of ureteric wall shows multiple calcified bilharzial ova with sparse eosinophils (x400).

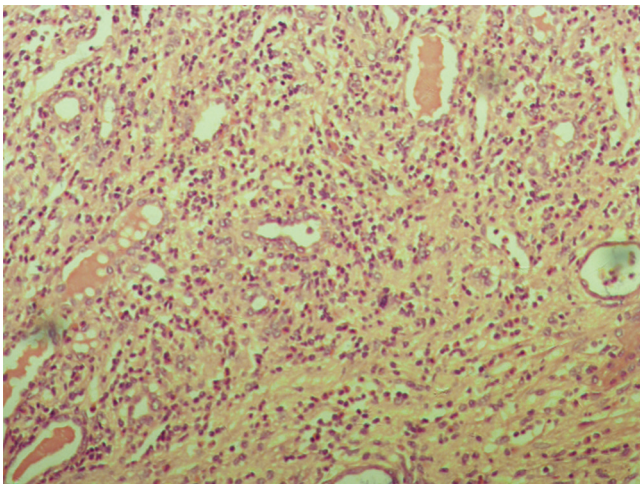


Figure 8: Marked interstitial lymphocytic infiltrate, some tubules appear narrowed and others show dilatation with thyroidization. These findings are suggestive of chronic pyelonephritis (x100).

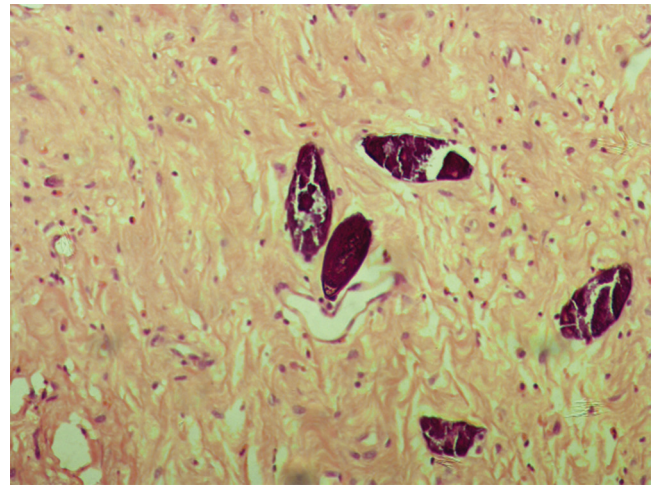


Figure 10: The submucosa of ureteric wall shows multiple calcified bilharzial ova with sparse eosinophils (x200).

IV contrast (Figures 3 and 12) were conducted (metastatic workup) that showed the following: ground-glass attenuation of lung bases, bilateral subpleural reticulations, multiple small, bilateral, apical, and basal small cystic airspaces mounting to honeycombing, right-lung middle-lobe subpleural nodule measuring 9 mm, right paratracheal subcentimetric lymph node not reaching the pathological size. No pathological hilar or mediastinal lymph nodes.

Discussion

This case was presented with renal symptoms on account of ureteric obstruction caused by a ureteric mass that diagnosed histopathologically as TCC that developed on top of bilharzial

lesion seen in all ureteric layers. Development of TCC top of bilharzial lesion is an unusual and the usual finding is the occurrence of SCC as reported in many studies.^[14,15] Appearance of bilharzial ova in ureteric wall and subsequent developing transitional cell carcinoma is the unusual presentation of this case that the bilharziasis is more seen in bladder mucaosa than ureteric mucosa, despite of both sites seem to be suitable to inhabit the bilharzial ova.^[6,14-16] Of these, the study carried out by Zahran et al.^[16] who reported that the heavy deposition of ova in the submucosa of the bladder leads through its mechanical and toxic irritation to marked epithelial and premalignant changes that pave the way for the disturbing frequency of carcinoma of the bladder in the patients with bilharzia, which is not the case in the ureter. Presence

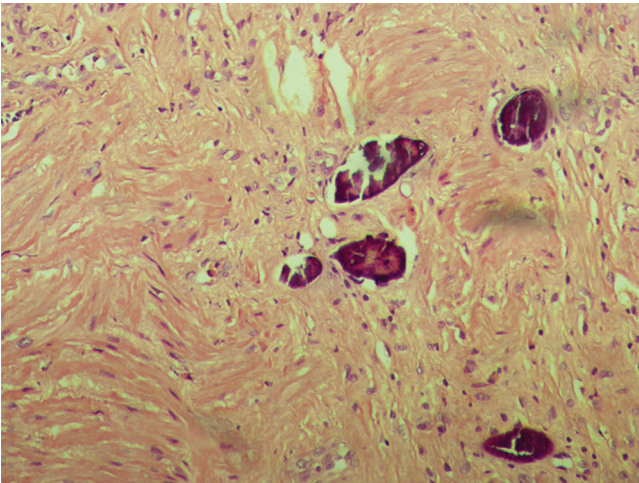


Figure 11: This photomicrograph shows calcified bilharziasis ova in the muscularis of ureteric wall ($\times 200$).

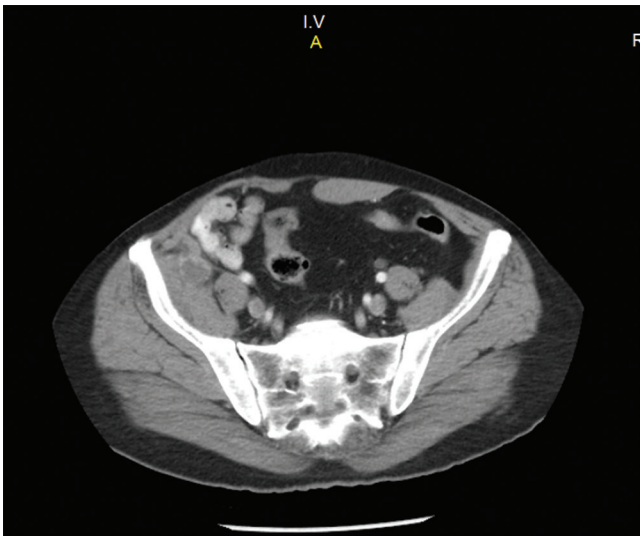


Figure 12: CT with IV contrast shows abdomen and pelvis: evidence of right uretero-nephrectomy. Ill-defined heterogeneously enhancing lesions are seen at the right lumbar and iliac fossa regions. Streaky densities from the lesions are seen adherent to the psoas, iliacus, and internal oblique muscles. Compensatory hypertrophy of the left kidney showed good excretory functions. Mild circumferential vesical mural thickening with faint spotty calcifications along the right superolateral wall likely post intervention no pathological pelvi-abdominal lymph nodes (LNs), no ascites.

of TCC exophytic lesion toward the ureteric lumen resulted in ureteric obstruction manifested by development of back pressure in the form of hydroureter and hydronephrosis with superimposed infection and complicated by pictures of chronic pyelonephritis and chronic glomerulonephritis that ended by development of chronic glomerulonephritis manifested both in laboratory and clinically.

Several new growths were seen on the bladder wall that were not present before and were diagnosed histopathologically as low grade papillary TCC, PT1 invasive into lamina propria. These new growths developed again after the BCG course. The explanation of this growth is either on account of direct spread of tumor to bladder or direct seeding as that occur as one of the methods of spreading of malignant tumor through natural passages, that is from ureter to bladder wall or from instrumentations through different cystoscopies by catastrophe or has been related to some genetic alterations as reported by Shaw et al.^[16] and has different pathogenesis out of relation to schistosomiasis.

Conclusion

Scistosomiasis in ureter has a low incidence in comparison to that of bladder; this case reported ureteric schistosomiasis with development of TCC instead of SCC making our case unusual. The development of new growths on bladder wall was of mystery and subsequently TRUBT was conducted for the removal of these growths and explanation for these new growths in this short period to a large extent is on account of direct seeding of malignant tissue through manipulation with repeated cystoscopes or the advent of tumor may have genetic alteration out of schistosomiasis and our patient may be in need of genetic assessment for LOH in q9 as explained by Shaw et al.^[16] The presence of lung nodule is highly suspicious to be metastatic to this primary urothelial tumor. Moreover, this patient is a Saudi male and the incidence of schistosomiasis in this country is very rare and in addition, presence of all these complications in this patient makes this a case of special interest. This will reflect on conducting further research workup for accurate estimation of schistosomiasis in Saudi Arabia.

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