



Case report

A case of encapsulating peritoneal sclerosis in a patient with chronic schistosomiasis



Paraskevi C. Fragkou^a, Emmanouil Karofylakis^{a,*}, Nikolaos Oikonomopoulos^b, Evangelia T. Piperaki^c, Sotirios Tsiodras^a, Dimitra Kavvatha^a

^a 4th Department of Internal Medicine, Medical School, National and Kapodistrian University of Athens, "Attikon" University Hospital, 1 Rimini Str, Chaidari, Athens, 12462, Greece

^b 2nd Laboratory of Radiology, Medical School, National and Kapodistrian University of Athens, "Attikon" University Hospital, 1 Rimini Str, Chaidari, Athens, 12462, Greece

^c Parasitology Unit, Microbiology Laboratory of Medical School, National and Kapodistrian University of Athens, Mikras Asias 75, Goudi, Athens, 11527, Greece

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ABSTRACT

Encapsulating peritoneal sclerosis (EPS) is a debilitating condition, mainly associated with long-term peritoneal dialysis, where up-regulation of intra-abdominal inflammatory pathways leads to a fibrocollagenous peritoneal membrane formation resembling a cocoon. EPS causes intestinal encapsulation leading to bowel obstruction and dilatation. Chronic schistosomiasis is characterized by dysregulation of pro-inflammatory and anti-inflammatory cytokines. EPS has never been reported before in patients with chronic schistosomiasis. We report the first, to our knowledge, case of a 57-year-old male originated from Burkina Faso with chronic intestinal and urogenital schistosomiasis and EPS. Although causality cannot be established solely by this case, we hypothesize that EPS may be the result of chronic inflammatory activation, due to immune dysregulation driven by chronic schistosomiasis. The potential pathogenetic linkage between these two conditions should be further explored.

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Introduction

Schistosomiasis, known also as bilharziasis, is a parasitic infection caused by trematode worms of the genus *Schistosoma* [1]. The parasites' intermediate hosts are freshwater aquatic or amphibian snails, which shed the infective form, cercariae, in water. Humans and other definitive hosts acquire the parasites in contaminated water by direct penetration of the skin. Schistosomiasis is endemic in tropical and sub-tropical countries.

The parasite may cause either an acute syndrome, known as Katayama syndrome, or a chronic parasitic infection in gastrointestinal or genitourinary tract by invading the target organs' blood vessels. The organism has developed mechanisms in order to escape the host's immune surveillance by interfering and modulating both innate and acquired immune responses [2]. The efficient egg transit through the tight barrier of the

endothelium and subsequently, completing the life cycle of the worms, incorporates the regulation of new vessel formation, the modulation of pro-inflammatory and anti-inflammatory cytokines and the expression of adhesion molecules [3].

The encapsulated peritoneal sclerosis (EPS) or cocoon abdomen is a debilitating, but rare, condition that is characterized by the formation of a fibrocollagenous peritoneal membrane caused by the upregulation of inflammatory pathways [4]. The stiff peritoneum encases the gastrointestinal tract leading to recurrent bowel obstruction [5,6]. Depending on the etiology, it may be either primary (or idiopathic) or secondary with the most acknowledged causative factor being continuous peritoneal dialysis [5,6]. Although it is still controversial to which extend the helminthic products promote or ameliorate autoimmune and inflammatory processes in the human hosts, to date there are no reports of EPS associated with schistosomiasis. Here, we present the first case, to our knowledge, of a patient who was diagnosed simultaneously with chronic schistosomiasis from *Schistosoma haematobium* and EPS.

Case report

A 57-year-old man from Burkina Faso, resident of Greece for the last 8 years with no travel or past medical history, presented with

* Corresponding author at: 4th Department of Internal Medicine, Attikon University Hospital, 1 Rimini Str, Chaidari, Athens, 12462, Greece.

E-mail addresses: evita.fragou@gmail.com (P.C. Fragkou), manoskarofilakis@gmail.com (E. Karofylakis), noikonom1959@gmail.com (N. Oikonomopoulos), epiper@med.uoa.gr (E.T. Piperaki), Sotirios.tsiodras@gmail.com (S. Tsiodras), dimitra.kavatha@gmail.com (D. Kavvatha).

abdominal pain, constipation, nausea, vomiting, dysphagia and unintentional weight loss, progressively worsening during the last 6 weeks. On examination, the patient was emaciated, with pitting edema up to the calves, diminished breath sounds on the lower lungs bilaterally as well as distended and uncompressible abdomen (Grade 3 ascites).

Apart from mild thrombocytopenia (140/ μ L), complete blood count, including eosinophils, was normal. C-reactive protein (CRP) was moderately elevated on admission (32.6 mg/dL). Biochemistry panel disclosed significantly elevated creatine kinase (CK) and lactate dehydrogenase (LDH), impaired liver function tests, hypoalbuminemia, and renal impairment with a serum creatinine and urea of 2.7 mg/dL and 196 mg/dL respectively. Clotting screen demonstrated an elevated international normalized ratio (1.37). Microscopic hematuria with 10–15 red blood cells per high-power field was evident on urinalysis. Ascitic fluid microscopy revealed 880/ μ L white blood cells (90 % lymphocytes), 1840/ μ L red blood cells and a serum ascites albumin gradient of 2.2 g/dL consistent with portal hypertension. Blood, urine and ascitic fluid cultures were all negative for bacteria, parasites and mycobacteria as were serology tests for hepatitis B, hepatitis C and human immunodeficiency virus (HIV).

Abdominal computed tomography (CT) scan revealed bowel wall thickening, dilatation of the entire gastrointestinal (GI) tract and symmetric peritoneal thickening consistent with encapsulating peritoneal sclerosis (EPS) (Fig. 1 A–E). Moreover, CT scan demonstrated periportal fibrosis and multiple intestinal sub-serosal calcified foci (usually associated with *Schistosoma mansoni* infection) as well as bladder wall thickening and calcified intramural lesions, characteristic of *Schistosoma haematobium* infection (Fig. 1 A–E). Although, upper GI endoscopy demonstrated esophageal dilatation, necrotic reflux esophagitis and varices, sigmoidoscopy was unrevealing. Biopsies were obtained from both upper GI and sigmoid colon.

No parasites were found in stool microscopy, but sigmoid mucosa crush biopsy revealed *Schistosoma haematobium* ova (Fig. 1 F), while upper GI biopsies demonstrated necrotic esophagitis and mild duodenitis. Oral praziquantel was initiated. Repeated large volume paracenteses were performed as an interim measure to decrease intra-abdominal pressure until renal function permitted the initiation of diuretics. However, on the 10th day of admission, the patient deteriorated rapidly due to septic shock caused by *Candida tropicalis* and expired 48 h later. The patient's critical condition during his admission did not allow the performance of laparoscopy in order to obtain peritoneal biopsies and to directly visualize the abdominal cavity; request for post-mortem examination was declined by the next of kin.

Discussion

We present the first reported case of a patient concurrently diagnosed with EPS by CT scan and chronic schistosomiasis confirmed by sigmoid colon crush biopsy. The CT findings of symmetrical peritoneal thickening, bowel tethering and GI dilatation were compatible with EPS. Ascites was attributed to periportal fibrosis caused by chronic schistosomiasis. Renal impairment, elevated muscle enzymes and necrotic reflux esophagitis were attributed to the presence of a massive ascites inside a non-compliant peritoneal cavity, causing abdominal compartment syndrome, leading to elevated CK and LDH, along with pre-renal azotemia due to the reduced oral intake. The patient's symptoms were attributed to the ascites caused by portal hypertension as well as to the underlying intestinal encapsulation.

EPS is a disabling and potentially life-threatening condition, with a mortality rate of 60–93 % if left untreated; however, with precise treatment at specialized referral centers a reduction of

mortality up to 25 % is feasible [7]. EPS is driven by activated intra-peritoneal inflammatory pathways that lead to proliferation and hyperplasia of mesothelial cells; this results in the formation of a dense fibro-collagenous peritoneal membrane resembling a “cocoon” [8]. In its early stages, the disease is characterized by non-specific gastrointestinal symptoms whereas later in the course of the disease, intestinal encapsulation by the non-compliant fibrous peritoneum causes bowel obstruction [9]. The observed GI tract dilatation in our patient was attributed to the intestinal encapsulation. Direct visualization of the peritoneum and/or consistent histological findings would have confirmed the EPS diagnosis in this case. However, the characteristic CT findings in the context of a compatible clinical syndrome along with high CRP on admission, obviated the need for invasive procedures to confirm EPS in our patient [10,11] (Fig. 1A–E).

Besides long-term peritoneal dialysis, medications, intra-peritoneal tuberculosis, organ transplantation, neoplasms, endometriosis, toxic substances, foreign bodies, surgery and systemic inflammatory diseases are also implicated in EPS development [9,12]. We propose that our case may represent a secondary EPS driven by intra-abdominal inflammation by *Schistosoma* infection.

The most common diagnostic approach of schistosomiasis is the detection of the parasite's ova in urine or stool specimens [13,14]. Nonetheless, egg detection assays fail to accurately diagnose up to 20–30 % of infections. The decreased sensitivity of egg detection in chronic schistosomiasis has been attributed to the egg entrapment within fibrotic tissues [15]. Biopsy is useful when multiple stool or urine samples are negative as in our case [13]. The histological finding of *S. haematobium* ova in the sigmoid colon is unusual, as this species shows a clear predilection for genitourinary tract. However, GI tract may be rarely affected [15]. A potential coinfection by *S. mansoni* and *S. haematobium* would also explain similar findings especially in a patient from an endemic area but *S. mansoni* was not identified [16,17].

The interplay between schistosomiasis and the host's immune responses remains largely enigmatic. Initially, invading cercariae stimulate T-helper (Th)-1 responses, that lead to release of interferon gamma (INF- γ) and interleukin (IL)-12 that contribute to granuloma formation. Later, during parasitic maturation, mating and egg production, Th1 responses subside and strong Th2 responses, driven by the egg antigens, progressively emerge [14]. Notably, animal studies have shown that extreme polarization towards either Th1 or by Th2 responses may lead to fatal consequences (severe hepatotoxicity or extreme fibrosis respectively), thus highlighting the importance of IL-10 in maintaining a balanced immune response during schistosome infection [18].

Until recently, the consequences of chronic schistosomiasis were attributed solely to the immune activation against the parasite ova [19]. New vessels and granulomas formation stimulated by inflammatory chemokines are crucial processes for the migration of eggs and parasite's survival [3]. On the contrary, there is increasing evidence indicating that *Schistosoma* parasites may also promote the expression of anti-inflammatory cytokines in order to escape immune surveillance and continue their reproduction [3,20]. The co-existence of chronic schistosomiasis with EPS in this patient may depict a possible interplay of immune dysregulation driven by the parasites that set the grounds for EPS development, although the exact underlying associated pathogenetic mechanisms still remain obscure.

In conclusion, both conditions may share common pathogenetic pathways. An underlying association between EPS and schistosomiasis is quite possible, although this theory cannot be solidified only by this case. The potential pathogenetic linkage between these conditions should be further explored.

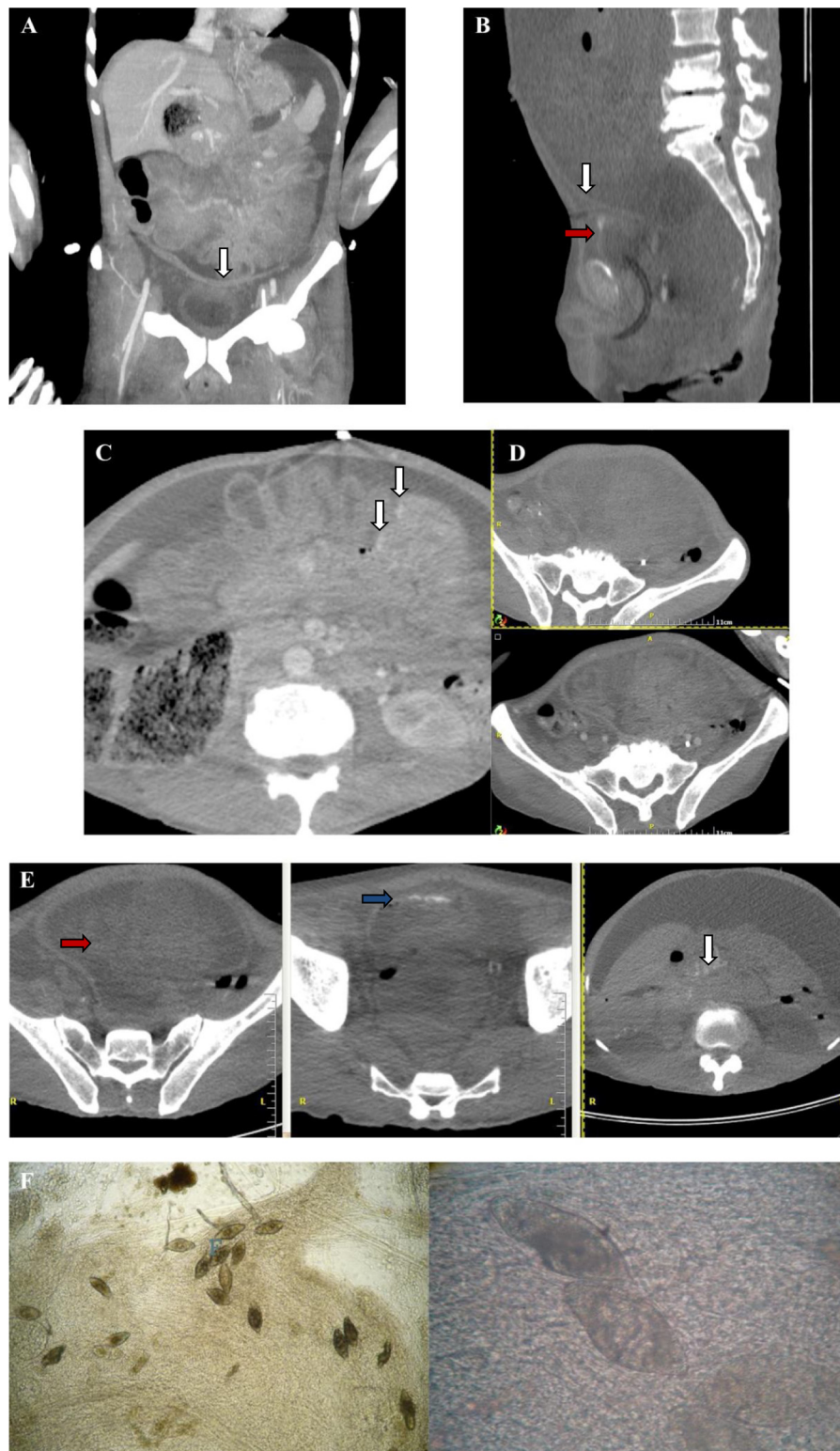


Fig. 1. Abdominal CT scan and rectosigmoid biopsy specimen images. **A.** Maximum intensity projection coronal plane: the image shows ascites, floating intestinal loops and peritoneal thickening. **B.** Sagittal plane: the image shows ascites, peritoneal thickening (white arrow) and bladder wall calcification (red arrow). **C.** Axial plane: the image shows ascites, floating intestinal loops and intestinal wall calcifications (white arrows). **D.** Axial plane images pre- and post-intravenous contrast media infusion, showing the thickening and the enhancement of peritoneum. **E.** Axial plane images showing the cocooning of the intestinal loops (red arrow), the bladder wall calcifications (blue arrow) and the intestinal wall calcifications (white arrow) without the administration of oral contrast media. **F.** Partially calcified *S. haematobium* ova with terminal spine (magnification 100x and 400x) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

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Ethical approval

No ethical approval was obtained for this case report. Written informed consent was obtained by the patient before the publication of this case report.

Consent section

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author statement

Paraskevi C. Fragkou: Contributed in the clinical management of the patient, collected the data, wrote the first draft of the manuscript and the subsequent revisions and approved the submitted manuscript.

Emmanouil Karofylakis: Contributed in the clinical management of the patient, collected the data, wrote the first draft of the manuscript and the subsequent revisions and approved the submitted manuscript.

Sotirios Tsiodras: Contributed in the clinical management of the patient, collected the data, wrote the first draft of the manuscript and the subsequent revisions and approved the submitted manuscript.

Dimitra Kavvatha: Contributed in the clinical management of the patient, collected the data, wrote the first draft of the manuscript and the subsequent revisions and approved the submitted manuscript.

Nikolaos Oikonomopoulos: Conducted the radiology tests, critically revised the manuscript and approved the submitted manuscript.

Evangelia T. Piperaki: Conducted the microbiology tests, critically revised the manuscript and approved the submitted manuscript.

Declaration of Competing Interest

The authors report no declarations of interest.

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