



Case report

Aseptic abscess syndrome associated with traveler's diarrhea after a trip to Malaysia



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ABSTRACT

The first, to our knowledge, case of the aseptic abscesses syndrome as a complication of traveler's diarrhea after a trip to Malaysia is presented. The patient failed to respond to several antimicrobials. The diagnosis was histologically confirmed and the patient only responded to immunomodulatory therapy with corticosteroids and methotrexate. Travel physicians should be aware of this entity reviewed herein in the context of traveler's diarrhea.

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Introduction

The aseptic abscesses syndrome is a rare clinical entity characterized by aseptic necrotic lesions containing neutrophils [1]. Exclusion of other clinical entities together with histological confirmation is paramount in establishing the diagnosis.

A case of a patient with the aseptic abscesses syndrome in an otherwise healthy individual is presented. Extensive work-up excluded other diagnoses. The diagnosis was histologically confirmed.

Case report

A 37 year old male presented in a tertiary care University Hospital with the chief complaint of prolonged fever after return from a business trip to Malaysia. While in Malaysia, the patient developed an episode of diarrhea for 4 days followed by high fever,

rigors and malaise. He described a self-resolved similar episode in a co-traveler that lasted for 5 days.

He returned to Greece on the fifth day of his syndrome. Five days later, due to prolonged fever, he was admitted to the department of Medicine at a tertiary care university hospital. He reported no significant medical history and was receiving no medications at the time of evaluation.

The physical exam was unremarkable, except for a temperature of 39 °C, a blood pressure of 120/80 mmHg, a heart rate of 88 beats per minute and an oxygen saturation of 97%. The abdominal examination revealed no tenderness or organomegaly. There were no enlarged peripheral lymph nodes, joint findings or rash.

Laboratory work-up at admission revealed polymorphonuclear leukocytosis with 25,800 white blood cells (82% polymorphonuclear cells, 11% lymphocytes, 5% monocytes, eosinophils 2%), Hct: 35.7% and CRP: 198 mg/L (normal < than 6 mg/L). He was admitted to the hospital for investigation and treatment. During his stay he underwent an extensive evaluation including: a) repeat complete blood testing that disclosed persistent leukocytosis, a severe normocytic anemia with a hematocrit as low as 25% (that required administration of 3 packed red blood cell units), thrombocytosis (as high as $594 \times 10^9/L$) and an elevated CRP (as high as 234 mg/L) and erythrocyte sedimentation rate of 100–110 mm/hour; b) multiple blood, stool and urine culture sets were taken that were

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negative for any pathogen; c) repeat stool cultures that were negative for *Salmonella* spp., *Shigella* spp., *Yersinia* spp., *Campylobacter* spp. and *Aeromonas* spp.; d) repeat stool ova and parasite testing that was negative for parasites; e) negative stool culture for *C. difficile* as well as negative *C. difficile* toxin assay; f) negative *Giardia lamblia*, cryptosporidium and entamoeba antigen; g) negative interferon gamma release assay; h) negative HIV, HTLV I and II, CMV, EBV, *Echinococcus granulosus*, *Toxoplasma gondii*, *Brucella melitensis*, *leishmania* spp, syphilis, hepatitis A, B and C serologies and; i) a bone marrow aspirate examination with normal results.

The patient did not respond to several courses of antimicrobials including sequential use of ciprofloxacin and metronidazole followed by piperacillin-tazobactam, followed by meropenem with vancomycin, and last a combination of docycycline and gentamycin.

A computed tomography of the abdomen revealed multiple enlarged and necrotic mesenteric lymph nodes, and edema in the wall of the distal ileum and the entire colon. A colonoscopy showed aphthous ulcerations in many parts, especially in the cecum, the ileocecal junction and the first part of the terminal ileum; histology was nonspecific. Twenty days into his course a new CT scan disclosed exacerbation of the disease with a lot of enlarged necrotic mesenteric lymph nodes and 2 focal deformities in the spleen about 1 cm in size. By this time the patient developed arthritis in the left ankle joint and an atypical bilateral rash in the shins resembling nodular panniculitis. At that point a quadruple anti-tuberculous regimen was initiated. Tissue samples obtained during an exploratory laparotomy from the abnormal mesenteric lymph nodes, showed acute purulent and focally granulomatous suppurating lymphadenitis with extension of acute inflammation into the perinodular mesenteric fat adjacent adipose tissue; PAS and Grocott stains disclosed no fungi, whereas PCR for *Mycobacterium tuberculosis* was negative.

The patient was diagnosed with aseptic abscesses syndrome and was treated with systemic administration of corticosteroids (40 mg of prednisone) together with methotrexate (15 mg/week). After tissue PCR results came back negative for TBc, the anti-TBc regimen was discontinued.

The patient had an excellent response to the immunosuppressive treatment with rapid clinical improvement with restoration of all his abnormal laboratory parameters during a 6 month follow-up. He is followed by a gastroenterologist for the possibility of development of inflammatory bowel disease.

Discussion

We describe, to our knowledge the first case of the aseptic abscess syndrome in an otherwise healthy traveler from Malaysia after a traveler's diarrhea episode with no identified bacterial cause. The patient presented with prolonged fever and his diagnosis was made after exclusion of other causes of protracted

fever. Interesting features of this case include the presence of large non-infectious necrotic abdominal lymph nodes that resembled tuberculous lymph nodes, the presence of spleen abscesses, the occurrence of arthritis in the left ankle joint and of an atypical bilateral leg rash resembling nodular panniculitis. The patient did not respond to antibiotics but only to immune modulation with corticosteroids and methotrexate.

After the first description of the aseptic abscess syndrome [2] this condition remains a rare entity, a diagnosis of exclusion, characterized by the presence of intra-abdominal abscesses co-existing with other clinical manifestations [1,3,4]. Most cases have been reported from European medical centers while cases sharing similar features have been described in Japan [5]. Features of the syndrome from reported cases are summarized in Tables 1 and 2. The mean age at onset of the disease is 30 years and both sexes are equally affected. Fever, abdominal pain, leukocytosis and increased inflammatory indices are very common while diarrhea in the largest case series was seen in 20% of the cases (Table 1). Spleen involvement is almost always present and abdominal lymphadenopathy is very frequently seen (Tables 1 and 2). Ultrasound exam usually depicts multiple focal hypoechoic lesions in the organs involved while computed tomography discloses multiple focal hypodense lesions (Table 2) [1].

The main histologic characteristic of the aseptic abscesses syndrome is the presence of suppuration, often surrounded by palisading histiocytes [1]. Histological examination of tissue samples from the mesenteric lymph nodes was essential in establishing the diagnosis in the current case. Since inflammatory bowel disease (IBD), may precede, follow or concomitantly occur it is important to exclude this diagnosis in all cases [1]. The patient has been followed but has not developed IBD 2 years into the course of his disease. Evidence of other granulomatous or autoimmune conditions (e.g. Wegener's, Adamantiades-Behcet's syndrome) or malignancy (Hodgkin's and non-Hodgkin's lymphoma) was not found [1,6]. Of note, granulomas have recently also been reported in cutaneous aseptic abscesses [9].

Since our patient presented with a case of traveler's diarrhea we attempted to exclude infectious pathogens. Infectious causes associated with a similar presentation with abdominal necrotic lymph nodes include tuberculosis, *Yersinia* spp infection and Whipple's disease [1]. Slow-growing, uncultured or fastidious bacteria such as *Chlamydia trachomatis*, *Bartonella henselae*, fungi and non-tuberculous mycobacteria could be associated with a similar picture. Exclusion of a parasitic infection was important in view of his recent travel history to Malaysia [1,6,7]. We did not search for viral entities that could be associated with traveler's diarrhea due to the systemic, inflammatory state of the patient thus we may have missed a norovirus or rotavirus infection as an initiating event.

Similarly to our case, antimicrobials do not work and the syndrome completely responds to corticosteroids and/or other immunomodulatory medication like azathioprine or

Table 1
Clinical and laboratory findings in reported cases of the aseptic abscess syndrome.

Reference	Clinical findings						Laboratory work-up				
	Age	Gender	Fever	Abdominal Pain	Diarrhea	Cutaneous	Anemia	↑ PMNs	↑ CRP ± ESR	↑ LFTs	(+) p-ANCA
Andre et al. [1], n = 30 pts	29 (mean)	15 (50%)	27 (90%)	20 (66%)	6 (20%)	20 (66%)	14 (46%)	22 (73%)	28 (93%)	14 (46%)	5/24 (20%)
Ito et al. [5]	24	f	+	+	-	+	-	+	+	-	-
Bratucu et al. [6]	39	f	+	+	+	+	-	+	+	-	-
Maeshima et al. [8]	20	m	-	+	-	+	-	+	+	-	+
Salle de Chou et al. [9]	40	f	-	-	-	+	-	-	+	-	-
Fukuda et al. [10]	57	f	+	-	-	-	+	+	+	-	-
Kato et al. [11]	21	m	+	+	+	+	+	+	+	-	-
Reported Case	37	m	+	-	+	-	+	+	+	-	-

Table 2
Radiological data, treatment data and presence of other diseases in reported cases of the aseptic abscess syndrome.

Reference	Radiological findings			Treatment	Other comments
	Spleen involvement	Abdominal lymph nodes	Liver		
Andre et al and cases described therein [1]	27/30 (90%)	14/30 (46%)	12/30 (40%)	Immunosuppressive treatment 13/30 (43%)	IBD 21/30 (70%)
Ito et al. [5]	+	+	–	prednisolone	–
Bratucu et al. [6]	+	+	+	prednisone	Responded to tuberculosis treatment but relapsed after 6 months
Maeshima et al. [8]	+	–	+	prednisone	Behçet – Adamantiades syndrome
Salle de Chou et al. [9]	–	–	–	colchicine, mesalazine	Ulcerative colitis
Fujuda et al. [10]	–	–	–	Prednisolone, Methotrexate	–
Kato et al. [11]	–	–	–	Granulocyte and monocyte apheresis, prednisolone	Crohn's disease
Our case	+	+	–	Prednisolone + methotrexate	–

cyclophosphamide [1]; unfortunately a large percentage of patients relapse [1]. TNF- α blockade may be an effective treatment option but there is little data available [5].

In conclusion, we present a rare case of the aseptic abscesses syndrome as a complication of traveler's diarrhea after a trip to Malaysia. Travel physicians, should be aware of this rare entity in the context of traveler's diarrhea.

Conflict of interest

None.

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