Pancreatitis as a rare manifestation of Behçet disease

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BACKGROUND

Behçet disease (BD) is a chronic idiopathic vasculitis characterized as a triad of papulopustular skin lesions, uveitis, and genital-oral ulcers.[1] Gastrointestinal (GI) manifestations of BD are associated with significant morbidity and mortality, as mucosal inflammation and large vessel disease result in intestinal ischemia and infarction.[2] Although the incidence of GI involvement varies, rates are reported to be as high as 60% in Japan.[3] Pancreatitis is a rare manifestation of BD that has scarce documentation in the literature. It has been suggested that Behçet pancreatitis may be underdiagnosed, as an autopsy series of 170 cases from Japan found 5 previously undiagnosed cases of pancreatitis.[4]

Abbreviations used:

BD:	Behçet disease
CT:	computed tomography
EUS:	endoscopic ultrasound scan
GI:	gastrointestinal

CASE REPORT

We report on a 56-year-old man with BD who presented with acute pancreatitis requiring repeated hospital admission. Per the International Study Group Criteria for BD, the patient initially had BD diagnosed in 2005 after a 5-year history of various cutaneous lesions and recurrent genital-oral ulcers.[5] He had 2-mm inflamed follicular papules on his face and numerous 0.5- to 1-cm indurated deep red papulopustular lesions along his chest, back, thigh, and buttocks (Fig 1). Subsequent punch biopsies found a dense dermal neutrophil infiltrate, which was in keeping with BD (Figs 2 and 3). His BD was well controlled while being treated with topical corticosteroids and varying regimens of colchicine, dapsone, and methotrexate.

The patient was initially admitted in 2011 after presenting with severe abdominal pain and a concurrent flare of his BD in which he had an increasing number of cutaneous lesions. Although both endoscopy and computed tomography (CT) enterography were normal, a CT of the abdomen showed pancreatic fat stranding, which was suggestive of pancreatitis. However, because the lipase was not significantly elevated, an exact cause was not determined. The rheumatology service attributed his presentation to BD, and he was started on azathioprine, 50 mg daily. After resolution of his pancreatitis, the patient was seen in follow-up, and it was noted that his cutaneous lesions were also resolving. Although the patient self-stopped the medication after 6 weeks because of increasing fatigue, he did not have any recurrence of abdominal pain until 2015.

In 2015, the patient was admitted again after having a 2-week duration of worsening right upper quadrant pain that radiated to the back and was worse after meals. Although he had no other GI symptoms, he also experienced night sweats, chills, malaise, and general weakness. The patient again noted a concurrent flare of his BD with an increased number of erythematous papulopustular lesions along his trunk and extremities (Fig 1). There was no evidence of oral or genital lesions during this admission.

Initial investigations found a leukocyte count of 12.3 $\times$ 10^9/L with an elevated C-reactive protein level at 175 mg/L (normal, 0-10 mg/L). Although liver enzymes were normal, the lipase level was elevated at 69 U/L

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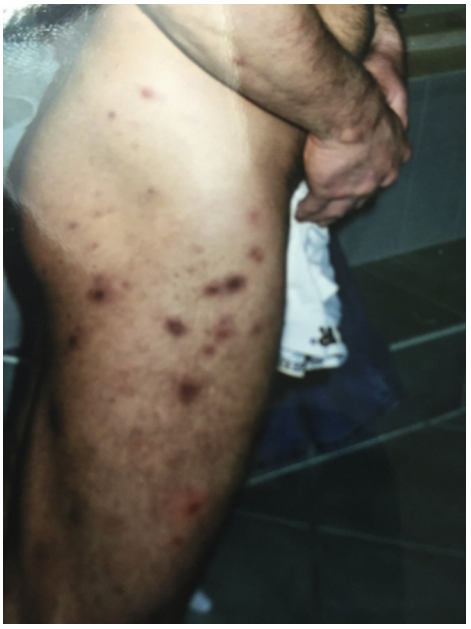

Fig 1. Photographic image taken by patient of lateral aspect of thigh and leg shows several dark red round papules.

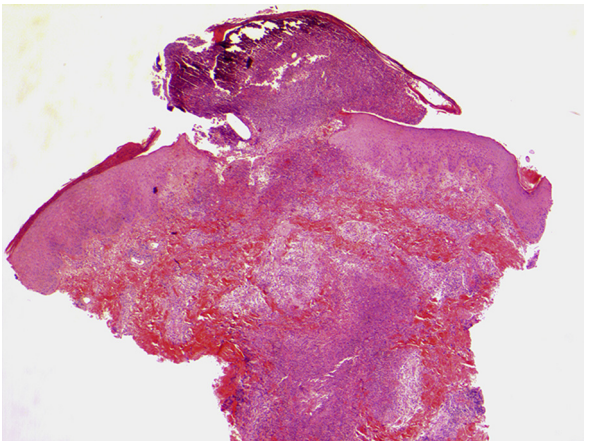

Fig 2. Punch biopsy shows dense dermal suppurative neutrophilic infiltrate with surface ulceration. (Hematoxylin-eosin stain; original magnification: ×25.)

and was as high as 185 U/L (normal, 0-60 U/L) the day before admission. Upper endoscopy was normal, but CT enterography did show pancreatic fat stranding, which is a sign of inflammation. There were no findings to suggest gallstones, biliary sludge, microlithiasis, or biliary obstruction as the cause of his pancreatitis.

In the hospital, the patient's symptoms were treated conservatively. He rapidly improved as his abdominal pain settled and C-reactive protein and lipase returned to normal.

METHODS

Two searches using Discovery Service for University of Alberta Libraries and Pubmed were performed in July 2015. Of 45 articles, 6 studies were case reports of Behçet pancreatitis.

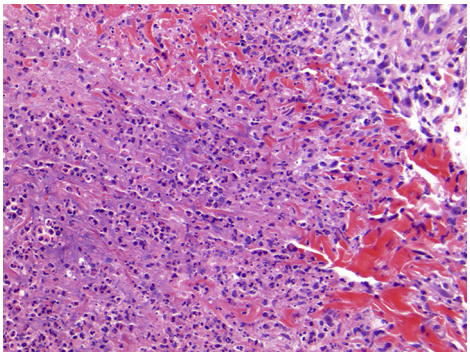

Fig 3. High-power examination shows dense dermal neutrophilic infiltrate. (Hematoxylin-eosin stain; original magnification: ×200.)

DISCUSSION

Because an obvious cause for pancreatitis was not found, other etiologies were considered. Autoimmune pancreatitis was ruled out because IgG-4 was within normal limits.[6] Review of the patient's medications found frequent use of ranitidine, which has been implicated in some cases of pancreatitis.[7] However, a retrospective cohort study suggests that there is no association between pancreatitis and ranitidine.[8] Another possible culprit was azathioprine, which has been associated with idiosyncratic pancreatitis (relative risk, 8), typically with onset of acute pancreatitis 3 to 5 weeks after starting azathioprine and resolution after cessation of therapy.[9-11] In this case, the patient had stopped azathioprine 4 years prior, making azathioprine an unlikely cause. Other risk factors were also absent: the patient is a nonsmoker and consumes alcohol only on a social basis, there were no preceding infections, calcium value was within normal limits, and triglycerides were only mildly elevated.[12] Because no other etiology was apparent, the patient's concurrent flare of BD and pancreatitis suggests that there is an association between the 2 disease processes.

Despite the high prevalence of intestinal BD, similar cases of associated pancreatitis are rare in the literature. To our knowledge, our patient is the 11th reported case of pancreatitis in patients with BD (Table I).[4,13-17] Clinically, symptoms suggestive of pancreatitis such as epigastric pain, vomiting, or diarrhea are also common in intestinal BD.[18] In reviewing these cases, we find that there is no predilection for gender (Table I).[4,13-17] In addition, the age of onset seems to be in young adults with an average age of 31 (median, 32). The most common presenting complaint was epigastric pain radiating to

Table I. Pancreatitis in patients with BD: Review of the literature

Study	No. of patients	Age	Gender	Clinical presentation	Diagnostic findings	Treatment
O'Duffy et al[13]	1	43	F	Sharp midepigastric pain radiating to the back, 30-lb weight loss	↑Amylase	—
Lakhanpal et al[4]	5	—	—	No preclinical data available	Autopsy data	—
Le et al[14]	1	24	M	Vomiting, epigastric pain, 13-kg weight loss	↑ Amylase (77) ↑ Lipase (537) U/S, CT normal EUS findings	Prednisone, 60 mg daily × 3 months
Backmund and Schomerus[15]	1	32	M	Fever, mild epigastric pain	↑ Amylase (1054-2146) ↑ Lipase (8333) U/S, CT findings	Cortisone, pentoxifylline prednisolone
Alkim et al[16]	1	37	M	2-year duration of epigastric pain radiating to back, 12-year history of 100 to 150 g/w of alcohol	Normal lipase U/S, CT findings Pseudoaneurysm of superior mesenteric artery	Pancreatic sphincterotomy
Yaghlene et al[17]	1	18	F	Severe epigastric pain, 7 kg weight loss	↑Lipase (4-5x N) U/S, CT findings, EUS confirmed pseudoaneurysms of celiac arteries	Prednisolone, 1 mg/kg/d × 5 months; cyclophosphamide, 900 mg q3w × 6 cycles Colchicine/aspirin

q3w, Every 3 weeks; *U/S*, ultrasound.

the back followed by significant weight loss. Other GI symptoms are uncommon, as vomiting was only present in 1 patient. Thus, patients with BD that present with unexpected epigastric pain and weight loss may warrant additional workup for pancreatitis. Because lipase was elevated in 83% (5 of 6), bloodwork should include lipase in addition to other inflammatory markers such as leukocyte count and C-reactive protein (Table I).[13-15,17] The single patient with a normal lipase level had a history of chronic, rather than acute, abdominal pain, which may explain his normal lipase level.[16] Imaging the pancreas by CT enterography may be helpful, as 80% of cases (4 of 5) had positive CT findings (Table I).[14-17] Endoscopic ultrasound scan (EUS) may help confirm the diagnosis of pancreatitis and rule out biliary stone disease and examine for vasculopathy.

In previous cases, the main treatment was oral steroids; however, immunosuppressives, colchicine, and symptomatic treatment were also effective (Table I).[4,13-17] Currently, however, there is no consensus for treating pancreatitis associated with BD. Of note, 2 of the case reports documented the presence of pseudoaneurysms in the celiac and superior mesenteric artery.[16,17] These observations suggest that the underlying large vessel vasculitis found in intestinal BD may also contribute to acute pancreatitis in BD such that systemic therapies for intestinal BD may also be effective for pancreatitis.[18,19]

We report a rare case of acute and recurrent pancreatitis associated with BD. Because GI symptoms are nonspecific to both pancreatitis and intestinal BD, we suggest that pancreatitis should be considered in the differential diagnosis in patients with BD who present with abdominal pain. With better recognition, more data will be available to generate higher-quality studies, allowing current therapeutic strategies to be refined. Because intestinal BD is often severe enough to require hospitalization, controlling and preventing GI manifestations of BD may improve overall morbidity and mortality.

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