Pancreatitis in systemic juvenile idiopathic arthritis

Sirs,

Systemic juvenile idiopathic arthritis (sJIA) is a unique subset of JIA that is distinct from other types of JIA in terms of disease pathogenesis and severity (1). Complications of sJIA include macrophage activation syndrome (MAS), erosive arthritis, osteoporosis, cardiac tamponade, coronary artery dilatation, hyperlipidaemia, pulmonary artery hypertension, interstitial lung disease and amyloidosis (2, 3). To the best of our knowledge, pancreatitis has never been reported with sJIA.

Case 1

A 9-year-old girl was diagnosed as sJIA (Table 1), and was initially started on prednisolone (1mg/kg/day). However, in view of poor response, subcutaneous methotrexate and oral cyclosporine were added. A month later, she acquired hepatitis A infection and developed features of MAS- fever, cytopenia [haemoglobin 96 g/L, leukocyte count- $4.0x10^9$/L, platelet count $75x10^9$/L], raised ferritin (3000 ng/ml), raised fasting triglyceride level (320 mg/dL), and bone marrow showing haemophagocytosis. Subsequently, she also developed features of acute pancreatitis in form of severe pain abdomen, bulky pancreas in the ultrasonography (USG) of abdomen, elevated serum levels of amylase (234 U/L) and lipase (186 U/L). Clinical and laboratory parameters partly improved with intravenous immunoglobulin (1g/kg) along with oral prednisolone. She was managed conservatively for pancreatitis. Intravenous tocilizumab (8 mg/kg) was also given for systemic symptoms, and these symptoms also recovered. However, 2 months later, she had recurrence of abdominal pain, and investigations revealed main portal vein thrombosis, walled off necrosis and loculated perisplenic collections (Fig. 1). Pig tail was inserted to drain collection. High dose prednisolone or tocilizumab could not be used for arthritis, as she had moderately severe acute pancreatitis and both the drugs are known to be associated with pancreatitis (4, 5). Arthritis was managed with low dose steroids (0.2 mg/kg/day) and naproxen. She gradually recovered and at 1-month follow-up, her arthritis was passive and pancreatitis was improving.

Case 2

A 6-year-old boy presented with fever of prolonged duration and was diagnosed as sJIA based on the clinical features (Table 1). He was initiated on oral steroids (1 mg/kg/day) and methotrexate (10 mg/m^2), to which he showed a considerable improvement in symptoms. Medications were tapered over next 2 years and continued on low dose oral steroids (2.5 mg alternate days) and oral methotrexate (5 mg weekly). He then developed features of both sJIA flare and acute pancreatitis. Serum amylase was elevated (980 U/L) and USG showed bulky pancreas. Investigations did not reveal any evidence of MAS. Arthritis was managed with naproxen and subcutaneous methotrexate (12 mg/week). He subsequently had 3 episodes of acute pancreatitis over the next 2 years, each time coinciding with sJIA flare and responded to intermittent hike in the dose of corticosteroids. He was investigated for causes of recurrent acute pancreatitis and none was found. MRCP revealed mildly bulky pancreas in tail region and normal pancreato-biliary confluence. He had no features of exocrine and endocrine pancreatic insufficiency during follow up visits.

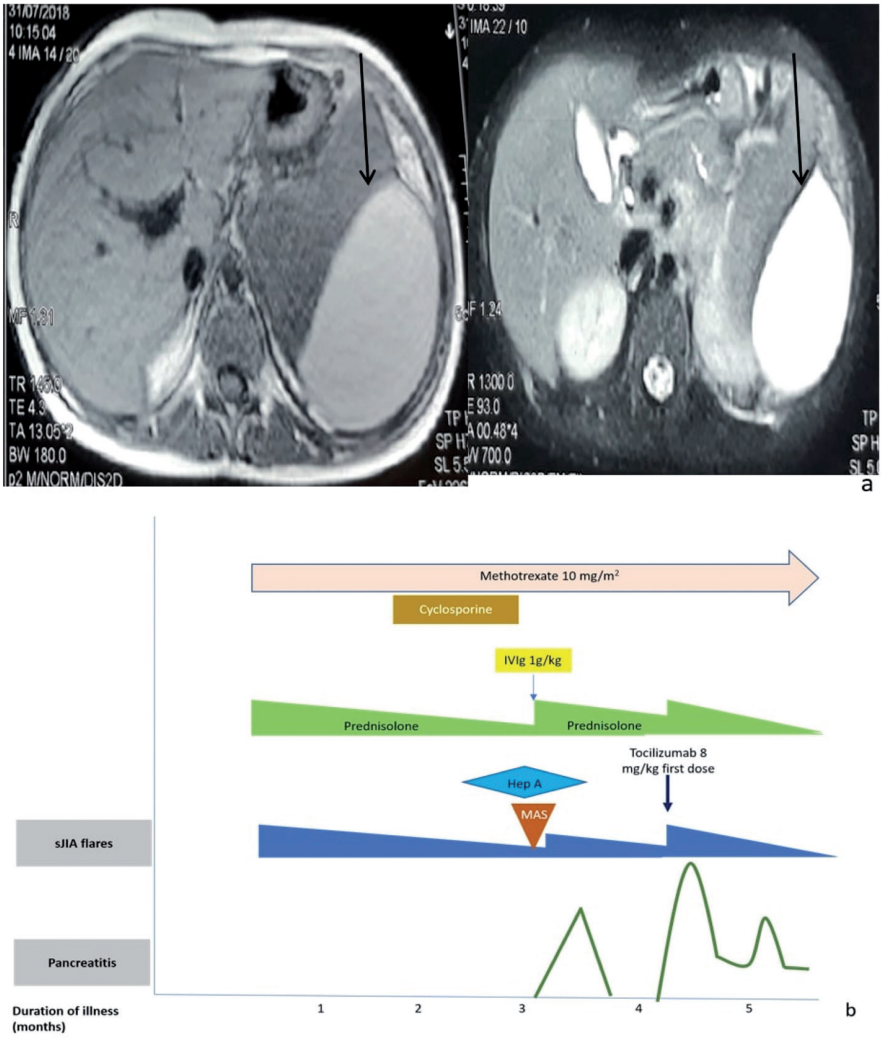


Fig. 1. (**a**) CT abdomen revealing pseudopancreatic cyst in lesser sac; (**b**) Timeline of case 1.

Table 1.

	Case 1	Case 2
Clinical profile	Fever, evanescent rash, arthritis and hepatomegaly for 6 months duration	Fever, arthritis, evanescent maculopapular rash, lymphadenopathy and hepatosplenomegaly
TLC	$23.7x10^9$/L	$23.0 X 10^6$/L
DLC	$P_{85} L_{12}$	$P_{70} L_{22}$
Platelets	$653x10^9$/L	$541X10^9$/L
ESR	85 mm 1st hour	60 mm in 1st hour
CRP	108 mg/L	
Serum ferritin	934 ng/ml	

Systemic JIA is now considered an autoinflammatory disease, and the spectrum expands from arthritis to severe multisystem involvement (1). MAS can be a life-threatening complication in these patients (6). Pancreatitis has been reported with lupus associated with MAS, some autoinflammatory diseases (7), and rarely in adult-onset Still's disease.

The possible mechanism of pancreatitis in sJIA could be disease activity, drugs, MAS, or infections. Kurushima *et al*. recently

reported an adult male with Still's disease with MAS and pancreatitis (8). Mice studies have shown that increased expression of TLR8 mRNA resulted in features of sJIA and pancreatitis (9). Recently, tocilizumab has also been implicated as an offending drug for pancreatitis (5). It has also been recognized that trypsin released in acute pancreatitis can activate macrophages and theoretically aggravate MAS (10).

Management of pancreatitis in sJIA can be clinically very challenging. The first patient, on one hand, had a moderately severe acute pancreatitis and on other hand, had a frank sJIA flare. As the drugs used in sJIA are known to aggravate pancreatitis, managing both the conditions becomes difficult. In the second case, cause of recurrent acute pancreatitis remained an enigma. He had no features of MAS throughout the course. In this case, pancreatitis was most probably a part of disease process coinciding with episodes of sJIA flares. We were not able to perform any genetic tests to determine any underlying genetic aetiology for severe pancreatitis.

To the best of our knowledge, ours is the first report of pancreatitis in sJIA.

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