



Chronic Relapsing Lupus Pancreatitis

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Key words: pancreatitis, systemic lupus erythematosus, corticosteroid, pathogenesis

IMAJ 2007;9:44–45

Acute pancreatitis is an uncommon manifestation of systemic lupus erythematosus. Recently, Nesher et al. [1] reviewed 80 such patients reported during the last 30 years. The etiology and pathogenesis of pancreatitis in lupus patients are not well determined. In most cases the pancreatitis is related to hepatobiliary disease, alcoholism, metabolic disease or to various medications. Lupus pancreatitis, defined as pancreatitis that is directly related and caused by SLE, is a diagnosis of exclusion, especially when there are no other signs of lupus disease activity. We describe a patient with relapsing lupus pancreatitis responding to corticosteroid treatment.

Patient Description

A 53 year old man had a history of discoid lupus without any systemic involvement for 24 years. Three years before the current admission he developed systemic manifestations, including high titers of antinuclear and anti-ds-DNA autoantibodies, lymphopenia, arthritis and glomerulonephritis with proteinuria (up to 9 g/24 hours), and elevation of creatinine levels to 4 mg/dl (normal < 1.4 mg/dl). Percutaneous kidney biopsy, which was performed at that time, demonstrated diffuse proliferative glomerulonephritis (activity index 7/18 and chronicity index 6/12). Treatment with high dose steroids (methylprednisolone 1000 mg/day for 3 days followed by prednisone 1 mg/kg/day) and pulse cyclophosphamide therapy

was initiated 3 years prior to the current admission (monthly for 6 months and then every 3 months for 2 years, according to the National Institutes of Health protocol) resulted in clinical remission with significant improvement of all clinical manifestations. The glucocorticoid dosage was slowly tapered to a dose of 5 mg prednisone per day. The patient also received several other medications: furosemide, nifedipine and clonidine for hypertension, famotidine for peptic disease, and calcium supplementation.

At the present admission the patient presented with severe abdominal pain accompanied by a rise of serum amylase levels up to 3500 u/L (normal < 100 u/L). In addition, he also complained of recurrent similar "attacks," which did not require hospitalization in the last year preceding his current admission. The patient and his family denied alcohol abuse. There were no other clinical or laboratory signs for any lupus-related disease activity. Anti-ds-DNA and anticardiolipin autoantibodies were negative. Complement levels and serum calcium levels were normal and triglycerides were only mildly elevated (< 350 mg/dl). Abdominal ultrasound, endoscopic ultrasound and endoscopic retrograde cholangiopancreatography were all normal. Abdominal computed tomography was also normal except for a diffuse enlargement of the pancreas, suggesting the diagnosis of pancreatitis. All medications, including steroids, were withdrawn without any clinical or laboratory improvement. A diagnosis of lupus pancreatitis was made, and prednisone at a dose of 60 mg/day

was initiated with rapid disappearance of all abdominal complaints and normalization of serum amylase levels.

Several months elapsed with no further attacks, but any attempt to reduce the steroid dose below 15 mg/day resulted in the reappearance of his abdominal pain accompanied by elevation of serum amylase levels. The recurrent attacks of lupus pancreatitis were not accompanied by any other lupus-related disease manifestations. During the next 3 years of follow-up, the patient had multiple episodes of lupus pancreatitis, mostly following attempts to reduce the corticosteroid dose. All episodes subsided with immediate normalization of sera amylase levels when the corticosteroid dose was raised.

Comment

Pancreatitis, either acute or chronic relapsing, is not common among SLE patients. Saab et al. [2] identified, retrospectively, only eight lupus patients with acute pancreatitis over 10 years of follow-up. More recently, Derk and colleagues [3] reported 25 hospital admissions of lupus patients with pancreatitis out of 2947 SLE admissions (0.85%) over a 20 year period. The pathogenesis of pancreatitis in SLE patients is variable. It may result from hepatobiliary disease, alcohol abuse, trauma, metabolic disorders (e.g., hypertriglyceridemia and hypercalcemia) or structural abnormalities of the pancreas. Other etiologies include drug-induced pancreatitis due to lupus-related (e.g., azathioprine) or unrelated medications (e.g., estrogens), and lupus pancreatitis

SLE = systemic lupus erythematosus

defined as pancreatitis that is directly caused by SLE [1].

The pathogenesis for the development of lupus pancreatitis is not precisely defined. Possible mechanisms include pancreatic vascular thrombosis associated with the presence of antiphospholipid antibodies, pancreatic vasculitis, or pancreatic inflammation due to T cell infiltration and complement activation. Since necropsy studies of SLE patients with pancreatitis are lacking, the exact role of the above mechanisms is not known. Lupus pancreatitis may present with other lupus-related clinical manifestations as one component of lupus disease activity. Alternatively, like in our patient, it may be the only manifestation of lupus activity. Rarely, acute pancreatitis is the presenting symptom of SLE. It is worth noting that mild elevation of sera amylase levels (in the presence of normal renal function) without clinical symptoms of pancreatitis is quite common among SLE patients (about 50%, Sthoeger et al., unpublished data). Most lupus patients with lupus pancreatitis have a single attack, but a chronic and relapsing course similar to the one witnessed in our patient was also reported [4].

Corticosteroids, which are commonly used by SLE patients, are frequently incriminated for the development of pancreatitis. Nevertheless, several studies failed to demonstrate such a cause-effect association [5]. Moreover, in some reports of patients

with pancreatitis assumed to be related to corticosteroids, many of those patients had SLE, thus their pancreatitis may have resulted from lupus, like in our patient, rather than from the steroid treatment. Furthermore, in animal models of acute pancreatitis, corticosteroids were shown to reduce inflammation and improve survival [5]. Taken together, despite the uncertain role of corticosteroids in the pathogenesis and course of pancreatitis, it appears that steroid treatment is beneficial in the treatment of lupus pancreatitis [1,2] as was clearly demonstrated in our patient.

The physician facing a lupus patient with acute abdominal pain should first consider, as with any other patient, the need for immediate surgical exploration. In SLE patients with acute pancreatitis who do not require surgical intervention, one should first search for all non-lupus causes (e.g., hepatobiliary disease, alcohol, metabolic disorders or medications). Only after all those etiologies are excluded can the diagnosis of lupus pancreatitis be established and steroid treatment (initiation of therapy or increasing the dosage) given to the patient.

In patients who do not respond to high dose steroid treatment, cytotoxic agents and/or plasmapheresis [1,5] have to be initiated. In some lupus pancreatitis patients, like the one described here, a good response to corticosteroid treatment is observed. Nevertheless, any attempt to discontinue or to significantly reduce

the dosage of the corticosteroid results in exacerbation of the condition. In those patients, other therapeutic modalities such as high dose immunoglobulins or cytotoxic agents (mainly cyclophosphamide and methotrexate since azathioprine itself can cause pancreatitis) should be considered in order to achieve both a clinical response and steroid-sparing effect to avoid long-term adverse effects [1,4,5].

References

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