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SYSTEMIC LUPUS ERYTHEMATOSUS AND ACUTE PANCREATITIS: CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Background: Systemic lupus erythematosus (SLE) is usually accompanied with gastrointestinal complaints, especially abdominal pain. The coexistence of SLE and pancreatic diseases is very low and does not reach 5% according to published series in Europe and the USA. The association between SLE and pancreatic diseases is based on the episodes of acute pancreatitis. Acute pancreatitis as the initial manifestation of systemic lupus erythematosus has been very rarely documented.

Methods: We report the case of a 41 years old woman patient with fever, abdominal pain and vomiting, elevated levels of pancreatic enzymes, and other laboratory abnormalities. Further investigation led to a diagnosis of SLE and acute pancreatitis. There are a small number of publications about SLE and acute pancreatitis, so a literature search was undertaken.

Conclusions: It is not clear whether SLE or the steroids are the cause of acute pancreatitis. It still remains controversial. On the other hand, the treatment of SLE pancreatitis is steroids. As SLE is a systemic disease, it can involve any organ system, so it is important to identify other coexisting abnormalities during SLE and treat them as soon as possible.

Introduction

Systemic lupus erythematosus is a systemic autoimmune disorder characterized by a broad range of manifestations and the finding of antibodies in the blood directed against one or more components of cell nuclei [1]. It has a definite female predominance, especially after the onset of puberty, but has been known to occur in children as young as 3 years of age [2]. The most common involvement is the joint and cutaneous system, with nonspecific complaints of fever, malaise and fatigue, and renal disease [3]. Gastrointestinal (GI) manifestations are common in SLE patients; 19.2%–50% of SLE patients presented with gastrointestinal symptoms [4, 5, 6, 7]. Acute pancreatitis is a rare manifestation in SLE patients [8, 9, 10, 11, 12, 13]. The association between systemic lupus erythematosus (SLE) and pancreatitis was first documented by Reifenstein et al. in 1939 [14]. According to the existing studies, pancreatitis occurred in about 0.7%–8.2% of patients with SLE [4, 5]. The annual incidence of acute pancreatitis is approximately 0.4–1.1‰ [10, 11, and 12]. Most of the data about SLE-related acute pancreatitis (AP) are mostly based on individual case reports or small case series [8, 15, 16].

The initial manifestation, however, can involve any organ system either singly or in combination, which frequently makes diagnosis difficult. The American Rheumatism Association recommends 4 of the following 11 revised criteria for the diagnosis of SLE: malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorder, neurologic disorder, hematologic disorder, immunologic disorder on serologic testing, and antinuclear antibodies [17].

Case Report

M.L, a 41-year-old woman, previously well, presented at the University Hospital Center complaining of a 2-week history of lower abdominal pain and occasional dysuria. She reported one week history of fever, loss of appetite, generalized weakness, and episodes of nausea and vomiting. Her son had the same symptoms three weeks before, so she thought it was a simple flu. As the situation continued, she consulted her family doctor, who prescribed an antibiotic for a presumed diagnosis of upper respiratory tract infection and pelvic inflammatory disease.

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She complained of general weakness, nausea, vomiting, hair loss, general myalgia, hematuria, and rectoragia, photosensibility with eritematous elements in her face, hands and back. She was febrile, with a temperature round 39.5°C.

In her past medical history, she reported that she had episodes of abdominal pain, treated as outpatient. She also reported that she had been hospitalized a year ago and diagnosed with Discoid lupus, with systemic tendencies. She had two normal deliveries, and 5 miscarriages. At that time, she was treated with IV prednisone and local corticoid creams. She was still in corticoid therapy. She denied any other drug or alcohol use. She reported thinning of her hair and hair loss for the past 6 months, and a weight loss of 10 kg within the past 3 months.

Her family history was unremarkable for autoimmune or gastrointestinal disorders.
In the objective examination, she was alert, well appearing woman. She was afebrile, her pulse rate was 100 beats per minute, and her blood pressure was 100/60 mmHg. She had no skin lesions or lymphadenopathy. Her eyes were normal on examination. Her chest sounds were clear with no friction rubs, and she had no murmurs or rubs. Her abdomen was soft, sensitive in the epigaster, with mild tenderness, minimal guarding, and no rebound tenderness. Bowel sounds were present. She had no vaginal discharge, cervical motion tenderness, or adnexal masses. Her uterine size was normal. Her extremities showed no joint swelling or tenderness. Neurologically, she was unremarkable.
Laboratory studies disclosed the following values: sodium 139 mEq/L, potassium 3.8 mEq/L, chloride 105 mEq/L, bicarbonate 21 mEq/L, blood urea nitrogen 75 mg/dL, creatinine 0.73 mg/dL, glucose 84 mg/dL, aspartate aminotransferase 58 U/L (normal 14–50 U/L), alanine aminotransferase 65 U/L (normal 10–65 U/L), protein 5.4 g/dL, albumin 2.3 g/dL, calcium 8.5 mg/dL, and total bilirubin 1.6 mg/dL (normal 0.2–1.3 mg/L). A complete blood count showed a white cell count of 6.8 x 10^3/mm3. Hemoglobin was 9.6 g/dL, hematocrit 28.9 %. Pancreatic enzymes were elevated, with amylase level of 690 U/L (normal 30–110 U/L) and a lipase level of 467 U/L (normal 20–200 U/L). Urinalysis showed a white cell count of 12–20 per high-power field (HPF), granular casts 1–2/HPF, no bacteria, and some epithelial cells. Urine pregnancy test was negative. A chest radiograph showed an inflammatory lymph node in the right basal lung. C3 58.3 (79.0–152 mg/dL), C4 14.5 (16 – 39 mg/dL). An abdominal ultrasound showed a normal liver, normal appearing gallbladder. The pancreas appeared edematous, hipoechogenic.

Antinucler antibodies (ANA) were positive +++ with a titer 1:520 (pozitiv >1:320).
A computed tomographic (CT) scan of the abdomen without contrast showed no evidence of gallbladder stones or abnormality of the pancreas.
A sonogram on day 3 of admission showed a possible left pleural effusion, edematous pancreas with a peripancreatic liquid collection, the other findings were normal.
The patient was admitted to the hospital with a differential diagnosis of urinary tract infection, and possible perihepatitis complicating pelvic inflammatory disease. She was allowed nothing by mouth, given intravenous fluids, and started empirically on antibiotics. Tests for gonorrhea, chlamydial infection, and HIV were all negative.
By day 3 of admission her pancreatic enzymes were elevated, serum amylase was 990U/L (normal 28-100 U/L), serum lipase 612 U/L (normal 20 -200 U/L) and her white cell count had dropped to 3 x 10^3/ mm^3. Her gastrointestinal discomfort worsened, she had nocturnal colics, and a surgeon was consulted, there were no surgical emergencies. Two hours later the symptoms had resolved, and she reported feeling better.
A diagnosis of SLE pancreatitis was made on the fourth day of admission, and steroids were started. Pancreatic enzyme levels continued to rise, peaking on day 10 of admission despite continuous steroid therapy and strict orders of nothing by mouth. Her elevated temperatures continued despite withholding her antibiotics for possible drug fever. Repeated CT scan was performed on day 10, to rule out micro abscesses as a source of her fever. The pancreas was enlarged and edematous, but no other lesions were seen.
During her steroid therapy she developed a discoid rash in both ears and an oral ulcer, both of which disappeared with continued steroid therapy. She was discharged after near normalization of her pancreatic enzymes (amylase 73 U/L, lipase 192 U/L) and disappear Systemic Lupus Erythematosus. She received a tapering dose of oral prednisone on discharge. Her discharge diagnosis was SLE pancreatitis.
When she returned for a follow-up visit after 3 months, she had normal pancreatic enzymes (amylase 88 U/L, lipase 197 U/L), with corresponding normalization of complement (C3 100 mg/dL, C4 30 mg/dL). Her white cell count was normal at 5.27 10^3/ L, and a urinalysis was negative for protein and casts.

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Discussion

SLE-related AP is relatively rare compared to other organ injury involved in lupus. The incidence of clinical AP associated with SLE varies from 0.7 to 4% [5, 12], with the annual incidence of 0.4–1.1‰ [10, 11]. Most previous studies on this issue were individual case reports or small case series. The Hopkins lupus cohort [29] reported the largest case series with 63 SLE-attribute pancreatitis out of 1740 SLE patients (3.5%), and a Taiwan series reported 40 out of 2976 SLE patients (1.34%). In a Chinese cohort, 27 out of 4053 SLE patients were diagnosed as SLE-related AP, with the prevalence of 0.67%, and annual incidence of 0.56‰, which is comparable with the findings of previous literatures [5,10,12,18,16].

The pathogenic mechanism of SLE-related AP is very complex and multifactorial. Vascular damage (including vasculitis, intimal thickening, immune complex deposition, occlusion of arteries, and arterioles), autoantibody production, abnormal cellular immune response, and drug toxicity may be responsible for the development of pancreatitis [8]. In a chinese cohort, more than half patients (51.85%) developed acute pancreatitis within 1 year of the onset of SLE, and all 27 patients were active SLE with dramatically elevated SLE DAI scores and other simultaneous SLE manifestations, especially the hematologic and renal involvement. SLE patients with AP presented with higher SLEDAI scores compared to patients without AP. Previous studies [10, 11, 18, and 19] also demonstrated that episodes of SLE-related pancreatitis significantly increased in the active SLE group. AP is considered as one of the clinical features of active SLE and is associated with the activity of the disease itself. These results indicate that SLE itself can be the primary etiologic factor or cofactor predisposing to AP.

The diagnosis of pancreatitis by itself is usually based on clinical findings of abdominal pain, nausea, and vomiting supported by laboratory findings of abnormal pancreatic enzymes and suggestive tomographic findings. Clinically the disease can manifest in any manner from a benign self-limiting disease to one with a fulminant course. Within the context of SLE, besides the clinically evident cases of acute pancreatitis, there have also been cases of what is known as subclinical pancreatitis in which there is an elevation of pancreatic enzymes without clinical symptoms. The incidence of subclinical pancreatitis is believed to be much higher than clinical pancreatitis. One study found hyperamylasemia in 30.5% of asymptomatic SLE patients, suggesting that subclinical pancreatic damage might occur frequently in SLE [20].

CT findings in acute pancreatitis, which usually correlate with the severity of disease, have a diagnostic accuracy of only 70% to 90%, even in severe pancreatitis [20, 21, 26].

In the general population, the mortality rate of AP is about 3.8%~10% [22, 23, 24, 25]. Approximately 15~20% of all AP cases were SAP which accounted for a mortality rate of 16.3%~30% [27]. SLE-related AP patients had much higher mortality. Wang et al. [19] reported that the mortality rate was 27.5% in all SLE-related AP and 78.57% in SAP. Richer et al. [28] reported that 57% of childhood-onset lupus with pancreatitis developed SAP with the mortality of 45%. In the Chinese cohort, the overall mortality rate of SLE-related AP was 37.04% compared to o in SLE patients without AP ($P = 0.001$), and mortality rate in SAP was 75%. The severity of AP might be the most important risk factor for the mortality of SLE-related AP patients (OR 11.25, 95% CI (1.611, 78.57), and $P = 0.014$).

In accordance with other literatures, the manifestations of SLE-related AP in this cohort were nonspecific and similar to non-SLE acute pancreatitis. Abdominal pain (92.59%), fever (77.78%), and nausea/vomiting (74.07%) were the most common symptoms. These symptoms could also be attributed to other gastrointestinal diseases or adverse reactions of medication and may lead to misdiagnosis in general practice. It was reported that the rate of misdiagnosis of AP in SLE was up to 88.6% [29]. Delayed diagnosis and improper treatment may contribute to unfavorable prognosis, even life threatening. Likewise, the mortality rate of the Hopkins Lupus Cohort (3%) was considerably lower than average of other reported studies due to close monitoring, early diagnosis, and treatment [12]. So, it should be paid more attention to AP in any SLE patient with abdominal pain when mechanical obstruction or toxic-metabolic etiologies, infection, or trauma are ruled out.

Some immunosuppressants, such as corticosteroids, azathioprine, and cyclosporine have been implicated to cause pancreatitis in several case reports. These studies couldn't verify the relationship between azathioprine and acute pancreatitis in SLE patients. There is still a controversy over steroid treatment in SLE-related AP. Increasingly accumulated evidence showed that steroids do not trigger acute

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pancreatitis or cause increased mortality on AP [18], but instead, they have a possible therapeutic effect on SLE-related pancreatitis [12]. In the Hopkins cohort, appropriate treatment with corticosteroids added a survival benefit in SLE-related AP [29].

Conclusion

Incidence rate of AP in Albania is in low figures and the association of SLE and PA is a very rare condition; in our experience it is the first case. It should be paid more attention to AP in any SLE patient with gastrointestinal complaints when mechanical obstruction or toxic-metabolic etiologies, infection, or trauma are ruled out.Early diagnosis of acute pancreatitis in SLE patients, especially those with abdominal pain, and appropriate corticosteroid treatment is beneficial for a better therapeutic outcome in these patients.

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