Case Report
A case report and literature review of systemic lupus erythematosus with sustained elevated serum amylase and lipase levels

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Abstract: Systemic lupus erythematosus is a common autoimmune disease that can cause multiple organ damage, but the sustained increase of serum amylase and lipase without any corresponding clinical manifestations and imaging changes is relatively rare. We reported a case of systemic lupus erythematosus with pancreatic, salivary gland, central nervous system, skin, and thyroid involvement along with multiple organ damage accompanied by continuously increasing serum amylase and lipase levels. The patient was a young female who had suffered from the disease for about 13 years. After a relapse, her amylase and lipase levels continued to increase without any corresponding clinical manifestations or imaging changes. We followed up with the patient and summarized the changes in her serum amylase and lipase levels, and here we review the literature and analyze the reasons for the increases.

Keywords: Systemic lupus erythematosus, amylase, lipase, pancreas, multiple organ damage

Introduction
Systemic lupus erythematosus (SLE) is a chronic autoimmune disease involving multiple factors and with a largely unknown pathogenesis. Multiple organ dysfunction, including the skin, the cardiovascular system, the lungs, kidneys, joints, the digestive system, the blood, and the nervous system, is caused by the production of autoantibodies, namely anti-nuclear antibodies; however, the continued elevation of amylase and lipase is relatively rare. This article reports on a patient who has lived with systemic lupus erythematosus for 13 years and who demonstrated rising serum amylase and lipase levels after a relapse of the disease without any corresponding symptoms or signs. In addition, no abnormalities were seen in the pancreatic imaging examination, and the salivary glands, central nervous system, skin, and thyroid were involved. We summarize the patient’s clinical features, treatment process, and outcomes, and review the related literature.

Case report
A 24-year-old female was admitted to the hospital on February 25, 2019 because of “facial edema and rashes for 13 years, fever for 20 days”. She had erythema and papules 13 years ago that gradually spread to the face and scalp; she also presented with facial edema. The facial skin was hard, and flaky erythema had formed, but the erythema did not protrude from the skin’s surface. Her hands and feet appeared dark and were accompanied by tenderness, oral ulcers, photo allergies, lower extremity joint pain and fever (body temperature up to 39°C). The patient had no cough, her hands did not get cold and turn white and purple, she experienced no dry eyes or mouth and had no hair loss. The patient was diagnosed with “connective tissue disease” after the relevant examination and given intravenous methylprednisolone, oral hydroxychloroquine, and symptomatic treatment. She was discharged with oral methylprednisolone tablets (40 mg/day) and hydroxychloroquine; the oral methylpred-
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A physical examination demonstrated the following: Body temperature 37.3°C, heart rate 108 beats/min, breath 18 times/min, blood pressure 98/70 mmHg, conscious, memory loss, normal computing and orientation ability, dry tongue, and red rashes on the face. The bilateral parotid gland and submandibular gland were hard, and the double neck, armpit, and groin reached multiple swollen lymph nodes. The bilateral posterior lymph nodes were positive for tenderness, and there were no apparent abnormalities of the heart, lungs, or abdomen.

The laboratory data are shown in Table 1. A superficial local color ultrasound prompted bilateral parotid gland, submandibular gland inflammation, and diffuse lesions. Magnetic resonance images (MRI) of the head were performed (Figure 1), and total abdominal computed tomograms (CT) showed no obvious abnormalities of the pancreas (Figure 2A). Moreover, an electrocardiogram, an echocardiography, and a chest CT showed no obvious abnormalities.

Three months after her discharge, the patient was treated again in our hospital for elevated blood sugar. Her fasting blood glucose was 10.9 mmol/L, and her 2-hour postprandial blood glucose increased to 14.21 mmol/L. Insulin autoantibodies (IAA), islet cell autoantibodies (ICA), glutamate decarboxylase antibod-

### Table 1. The patient’s laboratory data

<table>
<thead>
<tr>
<th>Laboratory project</th>
<th>On admission</th>
<th>90 days later</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-ribosomal P protein</td>
<td>Positive (+)</td>
<td>positive (+)</td>
<td>negative (-)</td>
</tr>
<tr>
<td>Antinuclear antibodies</td>
<td>1:100 positive</td>
<td>1:100 positive</td>
<td>negative (-)</td>
</tr>
<tr>
<td>Anti-U1-nRNP/Sm</td>
<td>positive (+)</td>
<td>negative (-)</td>
<td>negative (-)</td>
</tr>
<tr>
<td>Anti-Sm</td>
<td>positive (+)</td>
<td>negative (-)</td>
<td>negative (-)</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>155.50 IU/ml</td>
<td>&lt; 100.00 IU/ml</td>
<td>&lt; 100.00 IU/ml</td>
</tr>
<tr>
<td>Anti-neutrophil perinuclear antibody (pANCA)</td>
<td>positive (+)</td>
<td>-</td>
<td>negative (-)</td>
</tr>
<tr>
<td>White blood cells</td>
<td>6.73 * 10^9/l</td>
<td>19.09 * 10^9/l</td>
<td>4.00-10.00 * 10^9/l</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>4.44 * 10^9/l</td>
<td>11.66 * 10^9/l</td>
<td>2.00-7.00 * 10^9/l</td>
</tr>
<tr>
<td>Blood sedimentation for the first hour</td>
<td>24 mm/1 h</td>
<td>4 mm/1 h</td>
<td>0.00-20 mm/1 h</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>30.26 mg/l</td>
<td>2.62 mg/l</td>
<td>0.00-5.00 mg/l</td>
</tr>
<tr>
<td>Complement C3</td>
<td>0.36 g/l</td>
<td>0.21 g/l</td>
<td>0.90-1.50 g/l</td>
</tr>
<tr>
<td>Complement C4</td>
<td>0.06 g/l</td>
<td>0.16 g/l</td>
<td>0.20-0.40 g/l</td>
</tr>
<tr>
<td>Immunoglobulin IgG4</td>
<td>0.13 g/l</td>
<td>&lt; 0.06 g/l</td>
<td>0.03-2.01 g/l</td>
</tr>
<tr>
<td>Epstein-Barr virus (EBV) content</td>
<td>3.17 * 10^3 IU/ml</td>
<td>3.08 * 10^3 IU/ml</td>
<td>0.00 IU/ml</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>12.44 mmol/l</td>
<td>1.56 mmol/l</td>
<td>&lt; 1.7 mmol/l</td>
</tr>
<tr>
<td>Serum amylase</td>
<td>251 U/l</td>
<td>174 U/l</td>
<td>30-110 U/l</td>
</tr>
<tr>
<td>Serum lipase</td>
<td>1332 U/l</td>
<td>1602 U/l</td>
<td>23-300 U/l</td>
</tr>
<tr>
<td>Urinary amylase</td>
<td>1185 U/l</td>
<td>-</td>
<td>32-64 U/l</td>
</tr>
</tbody>
</table>

pANCA: Anti-neutrophil perinuclear antibody; ESR: Erythrocyte sedimentation rate.
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After her hospitalization, she was administered methylprednisolone, oral hydroxychloroquine, anti-infection drugs, liver protection, fasting water, and symptomatic treatment. Her facial rashes regressed, the bilateral parotid gland and submandibular gland were relieved, and her memory returned to normal. However, the double subcutaneous fat tissue on the side of her cheek was atrophied with mild atrophic scars. Despite these improvements, the patient’s serum amylase and lipase levels remained high. Methylprednisolone tablets were reduced to 20 mg at discharge and taken orally three times a day.

During the follow up period, the patient’s condition was stable and clinically asymptomatic. The patient’s blood sugar returned to normal following a gradual reduction of hormones. Methylprednisolone tablets were gradually reduced to 5 mg, three times a day; anti-double-stranded DNA antibodies were negative, but the serum amylase and lipase levels remained above the normal range (Figure 3).

Discussion

Systemic lupus erythematosus is a multi-systemic, connective tissue, autoimmune disease that affects multiple organ systems, including the skin, the cardiovascular system, the lungs, the kidneys, the joints, the digestive system, the blood, and the nervous system. We report a case wherein the patient developed pancreatic, salivary gland, central nervous system, skin, and thyroid involvement, and notably, showed a sustained elevation of serum amylase and lipase.

Serum amylase and lipase are criteria for the diagnosis of acute pancreatitis, but the in-
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Figure 3. The trend of serum amylase and lipase over time in the 162 days from the first admission to follow-up. It can be seen that the amylase is the highest on the 14th day, which is more than five times the normal range. A. It can be seen that the lipase is the highest on the 90th day, that is, when the patient's blood sugar rises, her blood glucose returned to normal, and the methylprednisolone was gradually reduced.

Figure 3. The trend of serum amylase and lipase over time in the 162 days from the first admission to follow-up. It can be seen that the amylase is the highest on the 14th day, which is more than five times the normal range. A. It can be seen that the lipase is the highest on the 90th day, that is, when the patient's blood sugar rises, her blood glucose returned to normal, and the methylprednisolone was gradually reduced.

crease can also be caused by damage to tissues such as the lungs, gallbladder, stomach, small intestine, skeletal muscle, fallopian tubes, uterus, and testes, and the disease can also be present in tumor tissues. In the current case, the patient's serum amylase and lipase were elevated, and we considered the following factors:

SLE: Hasselbacher et al. [1] reported an increase in serum amylase levels in patients with SLE without diseases of the pancreas or bile ducts, other abdominal diseases, or acute kidney disease, but they did not analyze the clear cause. We used the Web of Science and PubMed databases to search studies published in the past 35 years with the keywords “systemic lupus erythematosus” and “amylase” and/or “lipase” and “case report” (1984 to 2019). We excluded cases of lupus pancreatitis (patients with abdominal pain, nausea, and vomiting, and abnormal pancreatic imaging), a total of three related cases were retrieved (Table 2).

The cases reported by Goyal et al. [2] and Cutlan et al. [3] differ from our patient's case in that our patient did not have lower extremity skin nodules caused by pancreatic panniculitis, nor did our patient demonstrate abnormal renal function. The case reported by Goto et al. [4] is similar to our patient in that our patient, although the follow-up time was relatively short, had been taking oral steroids; however, the patient in the previous study also had dyslipidemia, elevated blood sugar, parotid gland inflammation, lupus panniculitis, and central nervous system and thyroid involvement, which may have had an effect on the elevation of serum amylase and lipase. SLE is a disease characterized by a variety of autoantibodies, and it is possible that many antibodies to different serum enzymes exist. At present, there are limited large-scale studies on systemic lupus erythematosus patients with an increase in serum amylase and lipase with no abnormalities in pancreatic imaging.

Pancreas: 1.) Acute pancreatitis: The diagnostic criteria for acute pancreatitis usually requires two of the following three criteria: Typical abdominal pain; amylase and/or lipase levels that are three or more times the upper limit of normal; and typical abdominal ultrasound, an abdominal CT scan, or magnetic resonance imaging of acute pancreatitis. In typical patients with acute pancreatitis the serum amylase rises rapidly in the first 12 hours after the onset of symptoms, peaks at 48 hours, and returns to normal within 3-5 days. Serum lipase usually rises within 4-8 hours and peaks at 24 hours; this activity lasts for a long time, up to 8-14 days [5]. Abdominal ultrasound, abdominal CT scan, or magnetic resonance imaging manifes-
Table 2. List of related cases

<table>
<thead>
<tr>
<th>Author (year) references</th>
<th>Age (yr)/Sex</th>
<th>Disease diagnosis</th>
<th>Disease course</th>
<th>Main symptoms</th>
<th>Abdominal imaging</th>
<th>Amylase and lipase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current case</td>
<td>24/F</td>
<td>systemic lupus erythematosus, hypertriglyceridemia, steroid diabetes, mumps, lupus panniculitis (unconfirmed by pathology), neuropsychiatric SLE</td>
<td>13 years</td>
<td>no abdominal pain, nausea, vomiting</td>
<td>normal</td>
<td>serum amylase 251 U/l (reference range: 30-110), serum lipase 1332 U/l (reference range: 23-300), continued to rise 162 days</td>
</tr>
<tr>
<td>Goyal et al. (2019) [2]</td>
<td>62/F</td>
<td>systemic lupus erythematosus with chronic membranoproliferative glomerulonephritis, pancreatic panniculitis</td>
<td>newly diagnosed</td>
<td>erythematous nodules on the bilateral anterior shins</td>
<td>normal</td>
<td>serum lipase was 585 U/l (reference range: 8-78) and decreased to 358 U/l after 14 days</td>
</tr>
</tbody>
</table>
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tations may not be obvious at the early stages, and may even be normal [6, 7]. In the current case, after treatment with fasting and acid suppression, the amylase and lipase levels were still high. Although we considered the possibility of acute pancreatitis to be small, we did not rule out subclinical pancreas involvement and negative imaging findings. 2.) Autoimmune pancreatitis (AIP): A special type of chronic pancreatitis mediated by autoimmunity. The common clinical manifestations are abdominal discomfort, obstructive jaundice, weight loss, and endogenous and/or exocrine pancreatic insufficiency [8]. Laboratory tests often show elevated autoantibodies and/or IgG, especially IgG4. In terms of imaging, autoimmune pancreatitis often manifests as diffuse or focal changes in the pancreatic parenchyma, and also shows stenosis of the pancreatic duct. Histopathology shows the infiltration of lymphocytes and plasma cells, and steroid therapy is generally effective. In the current case, the patient had no obvious abdominal pain, no symptoms of jaundice, her IgG4 levels were not elevated, and the abdominal imaging was normal. Although we considered the possibility of autoimmune pancreatitis to be low, a histopathological examination is required in order to confirm. 3.) Benign pancreatic hyperenzymemia (BPH): Gullo described the disease in 1996, and the pathogenesis is still unclear [9]. It is found to be familial and sporadic in adults and children without any pancreatic or systemic disease [10]. Pancreatic division has also been reported in patients with BPH [11]. The main feature is a chronic increase in serum amylase, lipase, and trypsin, which are more than 2-4 times the normal range, and sometimes as much as 15 times. After initial findings, BPH should only be considered after at least 2 years of follow-up, and all imaging findings must be negative during this period. The serum amylase and lipase levels continued to rise in our patient, up to 5 times the normal range. There were no abnormalities in the two pancreatic CT scans, but magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS) were not performed. The patient should be followed up for a long time, and if necessary, she should have further relevant examinations.

Mumps: Patients with mumps and systemic lupus erythematosus are rare [12-14]. Mumps is more common with viral infections, especially those infected with the EB virus [15], and an EB virus infection may also be associated with SLE [16]. In patients with mumps, it has been reported that the serum amylase level remains elevated at the fourth week [17]. The serum amylase and lipase levels of the patient in the current case had been elevated for 162 days. Hypertriglyceridemia: The mechanism of severe hypertriglyceridemia (triglycerides > 10 mmol/L), which accounts for 1%-7% of all acute pancreatitis cases [18], remains unclear. Studies have shown that triglycerides are hydrolyzed by trypsin to produce free fatty acids, leading to a release of inflammatory mediators and free radicals, thereby damaging acinar cells and pancreatic blood vessels and causing ischemia and inflammation [19, 20]. In this case, the patient’s triglyceride level was elevated, which was related to the oral steroids and her eating habits. We believe that the increase in serum amylase and lipase is closely related to hyperlipidemia. Diabetes: An increased glucose concentration could affect the activity of amylase and lipase [21]. The patient’s blood glucose was normal during the first hospitalization, but this increased after using steroids; thus, elevated serum amylase and lipase may be related to the effects of serum glucose. Drug-induced pancreatic enzyme elevation: It has been reported that the long-term use of steroid hormones can also induce pancreatitis [22], and that lupus pancreatitis may be related to the use of glucocorticoids [23]; this suggests that there may be subclinical damage to the pancreatic acinar cells [24]. In our case, the elevation of serum amylase and lipase may not have been caused by glucocorticoids, as the levels of serum amylase and lipase decreased after the intravenous methylprednisolone treatment. The etiological relationship between corticosteroids and pancreatitis is not yet known. For this patient, other factors cannot be ruled out at the moment, but steroid hormones may be a trigger.

In addition to having bilateral facial rashes, the patient also demonstrated skin depressions, atrophy, and scarring of the subcutaneous adipose tissue on both of her cheeks, as well as swelling of the submandibular gland; we considered that lupus panniculitis may be the reason. The clinical manifestations of lupus panniculitis are characterized by nodules and
hardened subcutaneous plaques, which can cause atrophy of the skin and subcutaneous tissue. These nodules and plaques are usually located on the forehead, cheeks, proximal limbs, buttocks, eyelids, and salivary glands [25, 26]. However, the final diagnosis of the disease must be confirmed by pathology. In addition, when systemic lupus erythematosus affects the nervous system, it can cause a series of central and peripheral clinical symptoms; we term this as neuropsychiatric SLE (NPSLE). A common change demonstrated by MRI is white-matter hyperintensities (WMH) and brain atrophy [27-29]. The current case is a young woman whose cognitive impairment is mainly memory loss, with bilateral thalamic changes and brain atrophy in imaging; her memory returned to normal after steroid therapy. In addition to the pancreas, salivary glands, skin, and central nervous system, the patient also experienced other organ system involvement. Furthermore, the patient’s white blood cells and neutrophils were high, which we consider to be caused by steroids. Thyroid involvement occurred after the EB virus infection, and a thyroid color ultrasound showed thyroid parenchymal changes, but normal thyroid function. Infection with EB acts as a triggering factor, stimulating the patient’s existing immune abnormalities, leading to a worsening of the condition and multiple organ involvement. The clinical manifestations of patients with systemic lupus erythematosus are diverse. The patient we report had pancreatic, salivary gland, central nervous system, skin, and thyroid involvement, and according to a comprehensive literature analysis, patients who have elevated serum amylase and lipase levels may have no clear symptoms and clear pancreatic imaging. There are currently only a few studies on elevated serum amylase and lipase levels in patients with systemic lupus erythematosus, and further clinical studies are warranted. When the clinician encounters such a situation, it is necessary to carefully consider the cause and perform a comprehensive analysis, further examination, and a clear, dynamic observation of the patient’s condition, accompanied by regular follow-ups. When patients with systemic lupus erythematosus have multiple organ system involvement, we should fully grasp the patients’ conditions and perform comprehensive management to improve the patients’ quality of life.

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This study was carried out in accordance with the recommendations of the Ethics Committee of the China-Japan Union Hospital of Jilin University with written informed consent from all subjects. Written informed consent was obtained from the participants for the publication of this case report.

Disclosure of conflict of interest

None.

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References


