Autoimmune pancreatitis associated with skin granulocytic sarcoma: Case report and review of the literature

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Abstract
Autoimmune pancreatitis (AIP), also known as lympho-plasmacytic sclerosing pancreatitis (LPSP), is a rare disease and a unique form of pancreatitis in which the pathogenesis is suspected to involve autoimmune mechanisms that has distinct histological, immunological, serological and radiological findings. It is characterized histologically by lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis and presence of IgG4 positive plasma cells and lymphocytes. Elevated serum levels of IgG4 are also noted. It is usually misdiagnosed as pancreatic cancer. AIP frequently is associated with extra pancreatic manifestations and responds well to steroid therapy. Nonetheless, it is very rare condition for AIP accompany with skin Granulocytic sarcoma. In this report, we describe a patient AIP associated with skin Granulocytic sarcoma (GS).

Introduction
Autoimmune pancreatitis (AIP), also known as lympho-plasmacytic sclerosing pancreatitis (LPSP), is a rare disease and a unique form of pancreatitis in which the pathogenesis is suspected to involve autoimmune mechanisms. It’s a rare disease and often misdiagnosed as pancreatic cancer. Until now, the worldwide prevalence of AIP remains unknown. In patients who underwent pancreatic resection for suspected malignancy, 2.5%-8% were ultimately diagnosed with AIP without malignancy. There are no case reports in the literature of Skin Granulocytic Sarcoma with AIP. Here, we present a rare and interesting case of AIP associated with skin Granulocytic Sarcoma (GS).

Case report
A 76-year-old man was admitted to our department in November 2014 with a more than 4-month history of abdominal pain. He was healthy without any medical history. The patients had an anemic appearance. The physical examination was mild yellowing of the skin and sclera. Laboratory results revealed high levels of ALT (107 U/L, range: 15-40 U/L), AST (255 U/L, range: 9-50 U/L), γ-GGT (763.3 U/L, range: 10-60 U/L), ALP (473.6 U/L, range: 45-125 U/L), total bilirubin (48.4 µmol/L, range: 1.7-23 µmol/L), and direct serum bilirubin (25.8 µmol/L, range: 0-6.80 µmol/L). CA 199 was about 3 times the normal limit (111.85, range: 0-37 U/ml). Serum amylase and glucose were within normal ranges, as were CEA, and AFP. The ESR rate was elevated at 105 mm/h (range: 0-15 mm/h). Total IgG was elevated (38.8 g/L, range: 7.51-15.6 g/L), IgG4 was about 47 times the normal limit (40.52 g/L, range: 0.08-0.86 g/L), and γ-globulin was 43.4% (range: 11.1%-18.8%). Antinuclear antibody, anti-Jo-1 was positive anti-mitochondrial antibody, and smooth muscle antibody were all negative.

Radiographs of the chest were unremarkable. Computed tomography (CT) showed noncharacteristic sausage-like and low-density of pancreas and enlargement of the pancreas head (Figure 1A and Figure 1B). Magnetic resonance cholangiopancreatography (Figure 1C) and Endoscopic retrograde cholangiopancreatography (Figure 1D) depicted segmental narrowing of the distal common bile duct. Positron emission tomography (PET)/CT revealed increased uneven metabolism of the pancreatic head (Figure 1E). Other organs were normal.

The patient was diagnosed with AIP. And then, he was treated with prednisone at 40 mg/d for 2 wk, tapered by 5 mg/d every 1-2 wk with a maintenance dose of 5 mg/d over a period of 6 month. Total steroid administration lasted for 10 months.

During steroid administration, the patient was seen in our hospital in February 2015. Abdominal computed tomography showed reduced dilation of the pancreatic head (Figure 1F). Laboratory results revealed levels of IgG4 was about 8 times the normal limit (7.3 g/L, range: 0.08-0.86 g/L), AST (35.8 U/L, range: 9-50 U/L), ALT (31.1 U/L, range: 15-31 U/L), γ-GGT (763.3 U/L, range: 10-60 U/L), and total bilirubin (48.4 µmol/L, range: 1.7-23 µmol/L), and direct serum bilirubin (25.8 µmol/L, range: 0-6.80 µmol/L).

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40 U/L) γ-GGT (34.0 U/L, range: 10-60 U/L), ALP (61.4 U/L, range: 45-125 U/L), total bilirubin (20.3 μmol/L, range: 1.7-23 μmol/L), direct serum bilirubin (4.8 μmol/L, range: 0-6.80 μmol/L) and γ-globulin was reduced to 14.8% (range: 11.1%-18.8%). Serum IgG, amylase and glucose were within normal ranges, as were CA 199, CEA, and AFP. The ESR rate was reduced to 58 mm/h (range: 0-15 mm/h). Antinuclear antibody, anti-Jo-1 was positive and anti-mitochondrial antibody, and smooth muscle antibody were all negative.

In May 2015, it was first found that there was a small skin nodule presenting on the left leg with a diameter of approximately 0.5 cm, with smooth surface, no activity, and no tenderness (Figure 2A); after that its diameter enlarged progressively to more about 1.0 cm; after 1 month, more and more nodules and masses gradually appeared on double lower limbs. On physical examination, there were multiple scattered dark red and brown skin masses of various sizes (range, 0.5-1 cm) in the double lower limbs. The masses were with no tenderness, no activity, hard feeling, and did not fade with pressure. Then bone marrow puncture was performed. The result of bone marrow biopsy reveals no other hematologic malignancies. Pathological result of the bone marrow was that it was composed of round cell nodular hyperplasia. The pathogenesis is suspected to involve autoimmune mechanisms. The first description of what was later labeled “autoimmune pancreatitis (AIP)” may be credited to Sarles et al. [1], but the term autoimmune pancreatitis was first proposed in 1995 [2]. AIP is rare, with an estimated prevalence of <1 per 100,000 in the general population [3]. The pathogenetic mechanisms of AIP are incompletely understood.

Recent histological and clinical studies have suggested the existence of 2 subtypes of AIP: type 1 and type 2. Type 1 AIP is more prevalent in elderly Asian males and is characterized by lymphoplasmacytic sclerosing pancreatitis, obliterative phlebitis and infiltration of large numbers of IgG4(+) plasma cells. Type 2 AIP is more prevalent in Caucasians and is characterized by granulocyte epithelial lesions. Most patients with type 1 AIP have a significantly elevated serum IgG4 concentration, which is an important feature for diagnosis and for differentiating between AIP and other conditions such as pancreatic cancer [4].

Diagnosis is based on imaging, biochemical, histological and clinical criteria. With increased awareness of this condition and better diagnostic algorithms, patients with AIP can be effectively treated with steroids, obviating the need for surgical resection. In 2001, elevation of the serum immunoglobulin G4 (IgG4) level was identified as a crucial diagnostic feature of AIP. Increased serum IgG4 levels (≥ 135 mg/dl) are frequently detected in patients with AIP, and serum IgG4 levels are closely associated with disease activity [5]. Tissue infiltration by an increased number of IgG4+ plasma cells in patients with AIP was also recognized.

As this case presented with elevated serum IgG4, and had pathological results consistent with the diagnosis of AIP which met the Asia and International Consensus Diagnostic Criteria for AIP [6,7]. An important clinical feature of the disease is its dramatic response and rapid resolution with steroid therapy. Misdiagnosis of carcinoma can possibly lead to unnecessary surgery. In this case, abdominal CT showing the nonotypical sausage-like pancreas, but after diagnosed with AIP and with the steroid administration, the dilation of the pancreatic head had reduced, which also met the Asia and International
Consensus Diagnostic Criteria for AIP [6,7]. Magnetic resonance cholangiopancreatography (Figure 1C) and Endoscopic retrograde cholangiopancreatography (Figure 1D) depicted segmental narrowing of the distal common bile duct. Whole-body 18F-fluorodeoxyglucose (FDG)-PET showing pathologic FDG uptake in the pancreatic head. During the latest follow-up, the laboratory results indicated that the tumor maker Carbohydrate antigen 199 (CA199) were normal and serum IgG4 was about 6 times the normal limit (5.47 g/L, range: 0.08-0.86 g/L). Antinuclear antibody was positive and other antibodies were all negative. The patient was very responsive to steroid therapy and didn’t show any sign of pancreatic tumor, so cancer of the pancreas and bile duct was excluded.

As all the guidelines for AIP treatment, this patient was also treated with oral steroid. Follow up imaging from abdominal CT and laboratory tests showed the restoration of normal pancreatic morphology and normal serum index.

After the steroids were administered for 6 months, the patient developed small skin nodule presenting on the left leg with a diameter of approximately 0.5 cm, with smooth surface, no tenderness and no activity; after its diameter enlarged progressively to more about 1.0 cm; after 1 month, more and more nodules and masses gradually appeared on double lower limbs. Based on the pathological findings of skin biopsy specimen, the diagnosis of primary granulocytic sarcoma (GS) without hematologic involvement was established.

Granulocytic sarcoma (GS) also called myeloid sarcoma (MS) is an extramedullary tumor of immature granulocytic cells. GS is a rare disease with an incidence of 2/100000 in adults [8] and occurs at any age both in pediatric and elderly patients. It can be find at any site of the body, but the most common locations are soft tissues, bone, peritoneum, lymph nodes, and gastrointestinal system [9,10]. The skin lesions of GS are generally manifested as papules, nodules, tumors, or plaque. It is a rare entity, and mostly accompanied by acute myeloid leukemia (AML) [10]. It is also observed during the course of myeloproliferative disorders especially in chronic myeloid leukemia and myelodysplastic syndromes. In some rare circumstances, it is detected before clinical signs of leukemia or other diseases. When the bone marrow biopsy reveals no other hematologic malignancies, the granulocytic sarcoma is described as nonleukemic, primary or isolated. Primary GS without hematologic disorders is commonly misdiagnosed as lymphoma or histiocytic, lymphoblastic, or lymphocytic leukemia. Therefore, immunohistochemically analysis should be performed to arrive at a correct diagnosis. MPO is the marker of myeloid lineage and is a useful marker of GS. CD68 positivity of the tumor cells indicates that they are monocytic and of granulocytic lineage. The prognosis of GS is poor, especially when associated with AML [11]. Byrd et al. [12] stated that 97% of all primary GS patients who did not receive systemic chemotherapy later developed AML.

AIP frequently is associated with extra pancreatic manifestations such as sclerosing cholangitis, Sjögren’s syndrome, ulcerative colitis, psoriasis, siladenitis, rheumatoid arthritis, tubulointerstitial nephritis, and retroperitoneal fibrosis [13]. The incidence of malignancies in patients with autoimmune pancreatitis is still unknown. However, there is no report of autoimmune pancreatitis associated with skin granulocytic sarcoma. Here, we report a case of skin granulocytic sarcoma associated with AIP. Granulocytic sarcoma
(GS) is a rare disease with an incidence of 2/1000000 in adults. The most common locations include the skin, soft tissue, bone, periosteum, and lymph nodes [14]. However, numerous sites have been described. It is a rare entity, and mostly accompanied by acute myeloid leukemia (AML). In this case, bone marrow biopsy reveals no other hematologic malignancies. Granulocytic sarcoma, which is AIP associated extra pancreatic lesions, is reported to respond well to systemic chemotherapy and radiotherapy [15].

References

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