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Sjogren's syndrome complicating pancytopenia, cerebral hemorrhage, and damage in nervous system

A case report and literature review

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Abstract

Rationale: Sjogren's syndrome(SS) is a chronic autoimmune disease, which damages exocrine glands especially salivary and lacrimal glands, with xerostomia and xerophthalmia as common symptoms.

Patient concerns: We report a case of a 49-year-old woman presented with pancytopenia. Her laboratory examinations lead us diagnose her as Sjogren's syndrome complicating pancytopenia. She had neurological symptoms during her treatment, which represent only 4.5% of Sjogren's syndrome complicating damage in nervous system.

Diagnoses: Sjogren's syndrome complicating pancytopenia.

Interventions: Dexamethasone (40mg QD for 4 days) and immunoglobulin (25g QD for 2 days) were administered for intensive treatment followed by oral methylprednisolone 40mg QD as maintenance treatment. Total glucosides of paeony 0.6g TID and danazol 0.2g BID per os were given. We also gave her Piperacillin-tazobactam and moxifloxacin for anti-infection and Fluconazole for anti-fungal therapy, as well as other supportive treatments.

Outcomes: Follow-up of the patient observed the normalization of peripheral blood cell count, immunity indices and neurological examinations 6 months after discharge.

Lessons: For patients presented with blood system abnormalities unilineage or multiple-lineage cytopenia in particular, history investigations and relevant examinations should be considered to exclude the existence of autoimmune diseases like Sjogren's syndrome.

Abbreviations: ACD = anemia in chronic disease, CT = computed tomography, pSS = primary Sjogren's syndrome, SS = Sjogren's syndrome.

Keywords: cerebral hemorrhage, nervous system damage, pancytopenia, Sjogren's syndrome

1. Introduction

Sjogren's syndrome (SS) is a chronic autoimmune disease, characterized by lymphocytic infiltrates in the exocrine glands, specifically the salivary and lacrimal glands. Visceral damages and other clinical features can also occur in SS patients. SS affects 0.29% to 0.77% of the population in China.[1] Over 90% cases of primary SS demonstrate systemic damages.[2] Blood system involvement is 10% to 24% among which single lineage involvement is more common than 2 or 3 lineages involvements.[3] Here, we report a case of SS with pancytopenia, cerebral hemorrhage, and damage in the nervous system who presented to our hospital. Ethical clearance and approval was obtained from the Ethics Review Committee at the Yantai Affiliated Hospital of Binzhou Medical University (Yantai, Shandong, China) with a Project Reg. No: F-KY-0022–201706071-01.

2. Case presentation

A 49-year-old female was admitted on August 12th 2016 due to whole body ecchymosis for 2 weeks, headache for 2 days. Two weeks before admission, the patient complained ecchymosis on both legs with pain and discomfort in the whole body. These symptoms progressed and ecchymosis involved the hip and arms.

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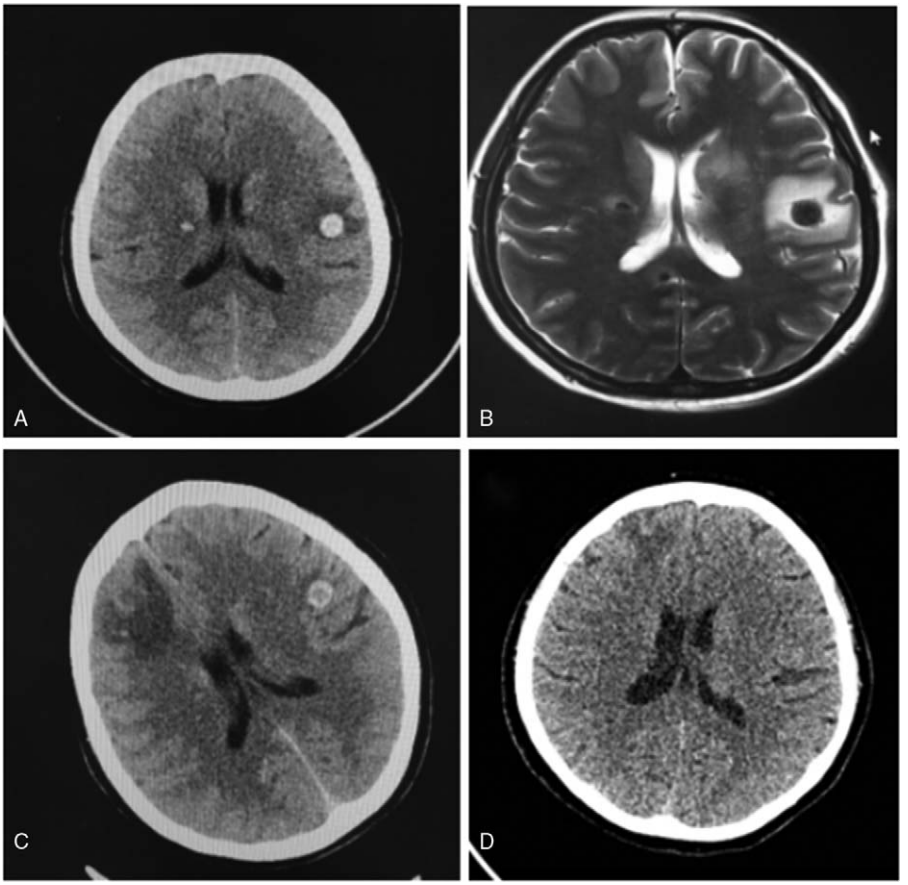

Figure 1. The imaging findings of this patient. (A) Many quasi-circular high density nodes on both cerebral hemispheres can be seen using brain computed tomography (CT). (B) Brain magnetic resonance images (MRI) (plain and enhance scan) revealed multiple lesions in the brain. (C) Brain MRI showed the nodes were low density inside whereas high density outside. (D) Brain CT examined on October 18th 2016 showed that focal intracerebral hemorrhage was absorbed. CT = computed tomography, MRI = magnetic resonance images.

She had headache with nausea and vomiting 2 days before hospitalization. Her past clinical history was unremarkable, except for cephalalgia for many years without treatment. Investigations regarding autoimmune diseases and hematological diseases were performed.

The patient was found to be positive for SSA and Ro-52. ANA core particle type 320+ and cytoplasm particle type 1:80. Blood routine revealed pancytopenia (WBC 2.6×10^9/L, Hb 59 g/L, Plt 1×10^9/L), C3, C4, ds-DNA normal. Brain computed tomography (CT) revealed many quasi-circular high-density nodes on both cerebral hemispheres (Fig. 1A). Brain magnetic resonance images (MRI) (plain and enhance scan) revealed multiple lesions in the brain, suggesting focal cerebral hemorrhage (Fig. 1B). Two bone marrow morphologies all showed few megakaryocytes. Iron stain of bone marrow smear revealed iron-deficiency anemia. Bone marrow biopsy and karyotype were normal. The patient had dry mouth and dry eye before so we tested her breakup time of tear film. The breakup time of eyes was 4 seconds and 5 seconds, respectively. Schirmer's test: 5 mm/5 min. The following diagnosis was given: Sjogren's syndrome, secondary pancytopenia, iron-deficiency anemia, and hematencephalon. Dexamethasone (40 mg QD for 4 days) and immunoglobulin (25 g QD for 2 days) were administered for intensive treatment followed by oral methylprednisolone 40 mg QD as maintenance treatment. Total glucosides of paeony 0.6 g TID and danazol 0.2 g BID per os were given. Because the patient still had fever while using glucogorticoid and her white blood cell (WBC) count was low, which indicated she might have infection, we gave her Piperacillin-tazobactam and moxifloxacin for anti-infection. The patient had fever for at least 7 days so fluconazole was used as prophylactic antifungal therapy. Mannitol was used to reduce intracranial pressure. RBC, PLT, plasma, and cryoprecipitate infusion and other supportive cares were also given. Blood routine on September 7th 2016 showed WBC 6.0×10^9/L, Hb 103 g/L, PLT 157×10^9/L. The patient had convulsion with no inducement on September 3rd 2016. Brain CT revealed quasi-circular high-density nodes on both cerebral hemispheres and basal ganglia. The nodes were low density inside whereas high density outside (Fig. 1C). She undertook brain MRI later, which showed many nonintensified lesions. The outcomes of lumbar puncture were all normal except for increased nucleated cells number at 0.004×10^9/L. The patient was given depressant and intracranial pressure reduction and the symptoms of convulsion, ecchymosis, fever, and headache relieved gradually. The patient was discharged from hospital on September 17th 2016. During follow-up, her headache gradually disappeared and blood routine became normal. Her brain CT on October 18th 2016 showed that the focal intracerebral hemorrhage had been absorbed (Fig. 1D). Intracranial metastatic tumor was excluded based on the results of treatment and follow-up.

3. Discussion

3.1. Blood system damage caused by Sjogren's syndrome

Most reports state that anemia is the most common characteristic in primary Sjogren's syndrome (pSS) and most cases are moderate anemic. Zhou et al[4] found that the percentage of pSS patients who had secondary anemia was 34.1% of which 69% were anemia in chronic disease (ACD), 18% were autoimmune hemolytic anemia (AIHA), 9% were iron-deficiency anemia and leukopenia were commonly antibody-mediated. Hara et al[5] and Shinoda et al[6] reported that erythropoiesis was inhibited in antibody-mediated pathways. However, Qing et al[7] had the opinion that the deficient erythropoiesis in pSS is due to disorder of iron metabolism. Cheng et al[8] attributed the anemia to the decreased release of RBC to the circulating pool. The iron stain of bone marrow smear of this patient showed IDA, and the polysaccharide-iron complex was given for treatment. Around 5% to 15% of SS cases also complicate thrombocytopenia. Previous studies showed SS with thrombocytopenia demonstrate higher rates of autoantibodies than that with normal platelet count suggesting a role of autoantibodies in the pathogenesis of thrombocytopenia probably through directly inhibiting maturation of megakaryocytes or interrupting the function of thrombopoietin.[9] Li et al[10] found that abnormally activated CD4+ T cells mediate the production of autoantibodies by B cells which bind to and accelerate the subsequent clearance of RBC and platelet from circulation; studies show that splenomegaly and the presence of SSB in SS patients are likely to be the reasons for thrombocytopenia. Our patient demonstrated pancytopenia and megakaryophthisis, which may be due to the autoantibodies production. Zhao et al[11] showed that SS patients younger than 35 years old are more likely to have pancytopenia and low alexin C3. So, we should use C3 as a follow-up index in these patients.

3.2. Nervous system damage caused by Sjogren's syndrome

Nervous system damage caused by Sjogren's syndrome is not rare. About 10% to 30% SS patients have peripheral nerve damage and 4.5% have central nervous system damage.[12] The onset of nervous system damage is usually hidden and the clinical manifestations are variable. The lesions can complicate brain (focal lesion and diffuse lesion), spinal cord, as well as optic nerves.[12,13] The dry mouth and eyes of these patients are usually ignored by doctors. So, a doctor should take overall consideration and careful analysis when he has patients with above symptoms. If the patients have symptoms in central nervous system, he should differentiate with nervous system damage caused by multiple sclerosis(MS).[14] Tjensvoll et al[15] reported that pSS patients are more likely to develop chronic headache as well as depression and fatigue than non-pSS patients. Our patient was diagnosed cerebral hemorrhage with normal platelet count and cerebrospinal fluid examination; thus, the convulsion was very likely due to the cerebral hemorrhage and the protopathy as well. Furthermore, the patient complained intermittent headache throughout the year before admission and demonstrated hypertension at admission. We therefore cannot exclude the possibility of tension-type headache caused by Sjogren's syndrome.

3.3. Treatment and prognosis

The first-line treatment for SS with hematologic abnormities is glucocorticoids. Plasmapheresis can be used for severe cases. As cytopenia is mainly mediated by immunological disorder, immunosuppressants like cyclosporin A can also be considered. It was also suggested that autoimmune disease is caused by hematopoietic stem cells abnormalities.[16] So, hematopoietic stem cell transplantation can cure the disease fundamentally by rebuilding the normal immune system. According to 2016 pSS ACR/EULAR standard of classification,[17] the diagnosis of pSS of our patient was fulfilled. Intravenous glucocorticoid and immunoglobulin were administered as induction treatment followed by oral glucocorticoid, danazol, and total glucosides of paeonia as maintenance treatment. The disease improved after 4 days of treatment and the blood cell counts recovered subsequently.

4. Conclusion

Blood system damage caused by Sjogren's syndrome is closely related to immune disorder which can obscure the clinical manifestations of Sjogren's syndrome and thus complicate the diagnosis. For patients presented with blood system abnormalities unilineage or multiple-lineage cytopenia in particular, history investigations and relevant examinations should be considered to exclude the existence of autoimmune diseases such as Sjogren's syndrome.

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