Sjögren's syndrome presenting as thrombotic thrombocytopenic purpura in a male patient with previous Kikuchi-Fujimoto disease

Sirs,

Here we report a case of Sjögren's syndrome (SS) presenting as thrombotic thrombocytopenic purpura (TTP) in a male patient with previous diagnosis of Kikuchi Fujimoto disease (KFD).

A 28-year-old Caucasian man, with self-limiting cervical KFD 9 years before, presented with 5-day of fatigue, fever and mucocutaneous pallor. Two days later, he developed headache, right upper limb weakness, confusion and dysarthria. He had intravascular haemolytic anaemia (haemoglobin [Hb] 7.0 g/dL, total bilirubin 1.7 mg/dL, lactate dehydrogenase [LDH] 2363 IU/L, haptoglobin <10 mg/dL) with negative Coombs test and severe thrombocytopenia (platelets 8,000/mm^3). Blood smear revealed anisocytosis, poikilocytosis, schistocytes and polychromatic erythrocytes. Erythrocyte sedimentation rate was 94 mm/1sth, creatinine was 1.14mg/dL and general biochemistry and coagulation were unremarkable. Cultures and serology excluded infection. Cranial and thoraco-abdominal CT scans were normal. A diagnosis of TTP was suspected (PLASMIC score: 6) based on the combination of microangiopathic haemolytic anaemia, thrombocytopenia, fever, kidney injury and neurologic defects. The patient started daily plasma exchange therapy (PEX) with resolution of neurologic defects, increased Hb (9.4 g/dL) and platelet count (121,000/mm^3). TTP diagnosis was subsequently confirmed by a severe deficiency of a-disintegrin-like-metalloproteinase-with-thrombospondin-motif-type-1-member-13 (ADAMTS13) activity (<1%) and the presence of anti-ADAMTS13 IgG autoantibodies (>95UI). Disease worsening at day-7 (Hb 7.3 g/dL, platelets 11,000/mm^3 and haptoglobin <10mg/dL) prompted the addition of high-dose glucocorticoids (methylprednisolone 1g/day for 3 days followed by prednisolone 1mg/kg/d) and rituximab (375 mg/m^2/week). The patient was discharged after 30 days, 15 sessions of PEX and 4 weeks of rituximab, under prednisolone 100mg/day, without clinical manifestations of TTP, near-normalisation of blood tests (Fig. 1), normal ADAMTS13 activity (49%) and negative anti-ADAMTS13 auto-antibodies (6 UI). During the investigation, positive antinuclear antibodies (1:320 speckled), anti-Ro-52 (42 U/L) and anti-Ro-60 (7378 U/L) antibodies were detected. Other autoantibodies, including anti-dsDNA and antiphospholipid, were negative. Physical examination revealed severe oral dryness (clinical oral dryness score 7/10), extensive teeth absence and reduced unstimulated salivary flow (0.1 mL/min). Schirmer's test (15 mm/5'), ocular staining score (0) and tear break-up time were normal. Salivary gland ultrasound revealed moderate (grade 2) changes in parotids. Labial biopsy showed focal lymphocytic sialadenitis, focus score <1/4 mm^2. A diagnosis of SS was confirmed, fulfilling 2016 ACR/EULAR criteria.

Fig. 1. The change of Hb, PLT, LDH and treatment during hospital course and follow-up.
Hb: haemoglobin; PLT: platelets; LDH: lactic dehydrogenase; PEX: plasma exchange treatment; RTX: rituximab; MethylPDN: methylprednisolone; PDN: prednisolone.

At 2 months, Hb, platelets, LDH, ADAMTS13 activity normalised and anti-ADAMTS13 auto-antibodies were absent (Fig. 1). Steroids were discontinued at 6 months, and after one year the patient is off medication, without signs of TTP or SS extra-glandular activity.

TTP can co-occur with autoimmune diseases (AID) (1). A review identified 18 cases of concomitant SS and TTP (16 in primary SS) (2). Four cases were reported since (3-6). In these 20 primary SS patients, most were female (80%) and one-third (n=7/20) had SS diagnosed prior to TTP. Anaemia and thrombocytopenia were common, unlike fever, neurological and renal involvement (<50%). Older age and female sex are risk factors for TTP in patients with systemic lupus erythematosus (SLE), SS and other AIDs (2). Our case has interesting rare features, such as young age, male sex and a presentation including all 5 TTP clinical manifestations.

KFD is usually idiopathic, but has been associated with AID, namely SLE (7). A recent review identified 10 cases of KFD associated with primary SS (8), mostly in women (90%) and preceding SS onset (70%). Patients with KFD-SS have higher recurrence rates (70%) than idiopathic forms (3–4%). Our patient had atypical features of KFD-SS overlap, including male gender and lack of recurrence.

This is the first reported association between these three clinical entities, highlighting the possibility of atypical characteristics of TTP and KFD in patients with SS. It underscores the importance of screening for AID in patients with a history of TTP or KFD.

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