**LESSON OF THE MONTH**

Unable to see the wood for the trees

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**Case history**

A 48 year old man with 17 year history of primary Sjögren syndrome (pSS) presented with a sudden swelling of the left lower limb without pain, fever or any other symptom. The diagnosis of pSS was based on xerophthalmia, xerostomia, and swelling of the parotid glands in the presence of positive antinuclear antibodies (ANA), rheumatoid factor (RF), anti-Ro (85 IU ELISA, normal range <25 IU), anti-La (37 IU ELISA, normal range < 25 IU), and typical pathological findings in a minor salivary gland biopsy specimen. During 17 years, the clinical course was characterised by recurrent swelling of the parotid glands without evidence of extraglandular disease or significant changes in his laboratory profile.

On admission, diffuse non-tender swelling of the whole limb was observed without lymphadenopathy. The rest of the physical examination was normal. He was admitted to hospital with suspected deep vein thrombosis (DVT) and treatment with intravenous heparin was started. An ultrasound Doppler examination up to the left inguinal area could not confirm DVT, but in view of the suggestive clinical picture, intravenous heparin was continued. Table 1 summarises laboratory tests on admission. A chest radiograph was normal.

Two days after admission, the patient became anuric with progressive dyspnoea. Physical examination was suggestive of pleural effusion, confirmed on chest radiograph and thoracocentesis, which revealed a transudate without malignant cells. Electrocardiogram was normal. Central vein pressure was found to be high (24 mm Hg). Blood tests showed renal deterioration with blood urea nitrogen 83 mg/dl and serum creatinine of 4.3 mg/dl. The patient was treated with diuretics, dopamine, and haemodialysis—with a significant improvement in his dyspnoea but none in his renal function. He developed fever with a temperature of 39°C. Ultrasound of the abdomen was normal and there was no evidence of hydronephrosis or a space occupying lesion. Doppler ultrasonography of the renal arteries and veins was normal.

Five days after admission, in view of the urinary sediment, increased erythrocyte sedimentation rate (ESR), cryoglobulaemia and low C4 concentrations (table 1), it was assumed that the acute renal failure was caused by cryoglobulinaemic vasculitis. Pulses of intravenous methylprednisolone (1 g/day × 3) followed by oral prednisone (80 mg/day) and a single pulse of 750 mg cyclophosphamide were given but, although becoming afebrile, no improvement in his renal function was observed.

Nine days after admission, the patient experienced sudden faintness and pain in the left lower abdominal quadrant. He looked pale and sweaty. Blood pressure was 90/60, pulse 112/min, the abdomen was tender, mainly in the lower abdominal quadrant, rectal examination was normal. The haemoglobin decreased to 7.2 g/dl. Although partial thromboplastin time was not excessively prolonged and platelet count was above 100 000/mm³, an acute internal haemorrhage was suspected. Heparin was stopped and packed blood cells were given. Computed tomography of the abdomen demonstrated thickening of the iliopsoas and moderate amount of peritoneal fluid, suggestive of a retroperitoneal haematoma (fig 1). The patient was stabilised haemodynamically and the haemoglobin concentration increased to 9.5 g/dl.

In view of the persisting renal failure and cryoglobulinaemia, plasmapheresis was added. Eleven days after admission, an improvement in urinary output was observed at first and the renal function slowly returned to normal. Repeated abdominal computed tomography showed disappearance of the peritoneal effusion, but findings consistent with retroperitoneal haematoma were still present.

Twenty one days after admission, the patient was feeling well and released from hospital without any pathological findings on physical examination except for the dry mucosal membranes. The oedema of the left limb was completely resolved. Renal function tests,
Unable to see the wood for the trees

confirmed diagnosis of large cell lymphoma, (keratin positive). Pathological studies although its origin could not be defined. A fine needle aspiration of the mass that seemed to be a primary tumour in the lower abdomen disclosed a 8×5×7 cm solid mass that was resected under anticoagulant therapy. Repeat ultrasound imaging showed a further increase in the dimensions of the mass, which was in part responsible for the delay in the correct diagnosis, probably reflected a heparin induced bleeding within the lymphoma. True retroperitoneal haematoma is a rare complication of anticoagulant treatment.

Patients with an abdominal mass other than a palpable liver or spleen should undergo early laparotomy as multiple imaging procedures seldom bypass accidental biopsy, and frequently delay definitive histological diagnosis. This is especially true in a patient who is prone to lymphoma. Most patients with retroperitoneal non-Hodgkin’s lymphoma need laparotomy to confirm the diagnosis.

The lesson
- The unexplained presenting symptom—in this case, the mysterious limb oedema—should never be neglected. Diluted but not solved by other medical emergencies, each treated successfully, it remained the clue to the correct, alas delayed, diagnosis.
- The potential development of lymphoma in patients with pSS must always be remembered, especially in the context of unusual or unexplained clinical manifestations, or both, for example, cryoglobulinaemic vasculitis. The latter may prove to be clues to the evolution from pSS, an exocrine disease with polyclonal B cell activation, to more systemic disease with polyclonal, oligoclonal, and monoclonal B cell activation, thus potentially heralding lymphoproliferative disease with monoclonal activation.
- Aggressive immunosuppression may mask not only inflammatory signs but also partially suppressed lymphoproliferative disorders.

Figure 1 Computed tomography of the upper pelvic region demonstrating a mass anterior to the left iliopsoas muscle (arrow) with free fluid level, suggestive of retroperitoneal haematoma.

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