Unusual manifestations of type II cryoglobulinaemia associated with Waldenström’s macroglobulinaemia

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Abstract
Cryoglobulinaemia in association with Waldenström’s macroglobulinaemia is relatively common, ranging from 8% to 18% of cases; however, < 5% have symptoms or complications. We describe a patient with a history of cutaneous, peritoneal, and fallopian tube vasculitis related to type II cryoglobulinaemia associated with Waldenström’s macroglobulinaemia. Cytotoxic treatment was initiated (cyclophosphamide, vincristine, and prednisone) and had a good initial response. However, after the third course of chemotherapy, the patient presented with septic shock and died. Even though cryoglobulinaemia is a model of systemic vasculitis, peritoneal and fallopian tube vasculitis associated with type II cryoglobulinaemia has not been described previously.

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Case report
A 57 year old white woman was referred to hospital because of a two week history of intermittent fever, fatigue, 5 kg weight loss, several nodular purpuric cutaneous lesions, arthralgias of her ankles, wrists, metacarpophalangeal joints and shoulders, abdominal pain with diarrhoea and vomiting. On physical examination, she was pale and pyrexial (39°C). There was a palpable nodular purpura of the legs and no arthritis. A splenomegaly was present with a diffuse abdominal tenderness but no contracture. There was no peripheral lymphadenopathy and neurological examination was normal. Routine haematological tests revealed: haemoglobin, 99 g/litre; white blood cell count, 4.4 × 10⁹/litre; platelets, 289 × 10⁹/litre, erythrocyte sedimentation rate, 107 mm in the first hour; and C reactive protein, 107 mg/litre (normal, < 10). Results of blood chemical tests were unremarkable (serum electrolytes, urea, creatinine). Serum protein was 50 g/litre and immunoelectrophoresis disclosed an IgM k paraprotein. Bence-Jones protein was detected in the urine and serum immunoglobulin values were as follows: IgG, 0.24 g/litre; IgM, 1.09 g/litre; IgA, 0.28 g/litre. Immunological studies (antinuclear antibodies, antineutrophil cytoplasm antibodies) were negative except for the presence of rheumatoid factors. C4 concentrations were dramatically low (0.07 g/litre; normal range, 0.2–0.4 g/litre). Serological tests for virus infection were negative (Epstein-Barr virus, cytomegalovirus, hepatitis B and C virus, human immunodeficiency virus 1 and 2). There was a mixed cryoglobulinaemia (35 mg/litre) with an IgM monoclonal component. The IgM was an autoantibody with rheumatoid factor activity. Culture of blood and urine specimens yielded no microorganism. A bone marrow aspirate demonstrated infiltration with lymphocytoid plasma cells and mature plasma cells. Chest and abdominal computed tomography (CT) disclosed mediastinal, paraatraheal, and retroperitoneal lymphadenopathies and a splenomegaly. In addition, there was an irregular nodular mass (7 × 8 cm) involving the right ovary and a mild ascites with slightly increased peritoneal enhancement. The skin biopsy showed leucocytoclastic vasculitis with IgM deposits on immunofluorescence study. A coelioscopy disclosed multiple purpuric lesions on the peritoneum, ovaries, and fallopian tubes. The ovarian mass was resected and biopsies of the peritoneum and fallopian tubes were performed. They revealed leucocytoclastic vasculitis with fibrinoid necrosis (figs 1 and 2). Pathological study of the ovarian mass revealed a benign tumour.

The patient was diagnosed as having Waldenström’s macroglobulinaemia with mixed cryoglobulinaemia and systemic vasculitis (peritoneal, fallopian tubes, and cutaneous). Cytotoxic treatment was initiated (cyclophosphamide, vincristine, and prednisone) resulting in a good initial response. Abdominal symptoms decreased, and arthralgias and purpura of the legs were absent after two courses of...
III cryoglobulinaemia is mainly noted as the presence in the serum of one or more immunoglobulin complexes that activate inflammatory effectors and complement factors to induce vascular lesions characterised by neutrophil infiltration, deposition of immune complexes, and necrosis of the vessel wall.11  

In conclusion, our case suggests that cryoglobulinaemia could be taken into consideration among the aetiologies of peritoneal and fallopian tube vasculitis. Clinicians should be aware of this uncommon complication, particularly in patients with associated lymphoid malignancy.