

erulonephritis. Cardiac involvement is extremely rare. Since the discovery of the relationship of hepatitis C virus (HCV) to mixed cryoglobulinaemia, >90% of type 2 and type 3 cryoglobulinaemias have been attributed to this infectious agent [1–3]. Accordingly, interferon alpha (IFN- α) therapy has been used with promising results [4, 5]. Although the association between HCV-related cryoglobulinaemia and ischaemic disease, including coronary ischaemic disease, has been reported previously [6–9], our case is, to our knowledge, the first report of HCV-related cryoglobulinaemia with symptomatic coronary dissection.

A 27-yr-old female was admitted to our hospital with prolonged chest pain and a 5 yr history of intermittent arthralgia in the knees and hands. Pulmonary and cardiac auscultation were unremarkable. Slight hepatomegaly and splenomegaly were noted. Non-pruritic purpura was seen in the lower limbs with severe involvement around the malleoli (Fig. 1, upper right). The purpura developed 24 h prior to the chest pain. ECG showed a typical pattern of an acute lateral myocardial infarction.

Laboratory findings on admission were haematocrit 30%, platelet count 900 000 mm³, ASAT 174 U/l (normal: 5–40), ALAT 376 U/l (normal: 5–40), LDH 250 U/l (normal: 60–225), creatine clearance 55 ml/min. The creatinine kinase (CK) peak 6 h after the onset of the chest pain was 700 U/l (normal: 40–150). Immunological studies showed normal levels of IgG and IgA, and elevated levels of IgM (600 mg/dl; normal: 50–200). Complement study showed diminished levels of C3 (62 mg/dl; normal: 70–120) and C4 (4 mg/dl; normal: 15–25) and elevated levels of C3d (26 U/ml; normal: 0–20). Antinuclear antibodies and antineutrophil cytoplasmic antibodies were negative. Rheumatoid factor was positive (625 IU/ml; normal: 0–60) and anti-HCV antibodies (ELISA and immunoblot) were found. Cryoglobulins were discovered and immunoelectrophoresis confirmed a mixed type 2 cryoglobulinaemia (polyclonal IgG and monoclonal IgM kappa). HCV RNA was detected by polymerase chain reaction in both the cryoprecipitate and the serum.

Skin biopsy of purpuric lesions confirmed the presence of dermal vasculitis, with endothelial damage, extravasation of red blood corpuscles and leucocytoclasia (Fig. 1, bottom right). Immunofluorescence of the skin biopsy revealed the presence of immune reactants (IgM, IgG and C3) in the endothelium. The hepatic biopsy was consistent with chronic active hepatitis. Coronary angiography revealed an image of coronary dissection in the left anterior descending and first diagonal branch (Fig. 1, upper left).

Treatment with steroids, anticoagulants and nitrates was started. The possibility of plasmapheresis was considered, but eventually rejected due to the cardiac instability. Subcutaneous IFN- α was given; the treatment included 1 month at a dose of 2 million U/24 h and 6 months at 2 million U/48 h, and following 36 months of follow-up the patient is still on IFN- α at a dose of 2 million U/96 h. Three months after IFN- α was started,

Coronary dissection associated with hepatitis C virus-related cryoglobulinaemia

SIR, Mixed cryoglobulinaemia is a multisystemic disease, characterized by chronic angiitis, whose main symptoms are purpura, arthritis, peripheral neuropathy and glom-

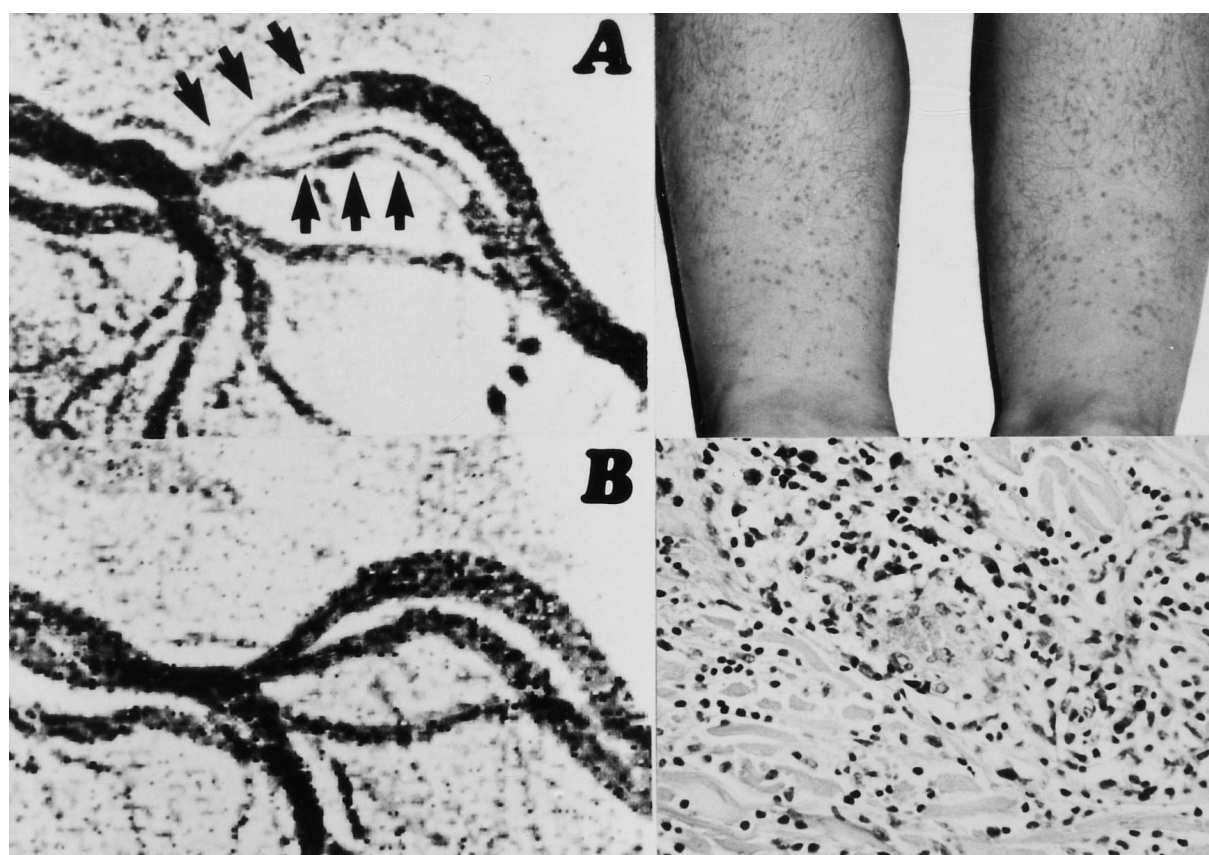


FIG. 1. Upper right: purpura in lower limbs. Bottom right: the photomicrograph shows a venule with endothelial necrosis and initial thrombus formation (haematoxylin–eosin, $\times 400$). Upper left (A): coronary angiogram revealing coronary dissection in the left anterior descending and diagonal branch (arrow). Bottom left (B): coronary angiogram performed 6 months later, revealing resolution of the previous image of coronary dissection.

there was a clear improvement in symptoms and purpura: hepatic enzymes returned to normal levels, and HCV-RNA as well as cryoglobulins were no longer detected. A new coronary angiogram was performed at 6 months, revealing resolution of the previous images of dissection (Fig. 1, bottom left).

Clinical presentation of mixed cryoglobulinaemia includes a multisystemic disease due to a vasculitic process induced by cryoprecipitable circulating immune complexes [3]. Cases of cardiac involvement are rarely reported and are usually due to myocardial infarction. Heart failure is often associated with coronary microcirculation damage in the course of systemic vasculitis and, not infrequently, is the cause of death [7]. Interestingly, endothelial damage in both skin and coronary vessels was demonstrated in our patient.

In viral vasculitis, the goal of therapy is to treat both the systemic condition and its cause at the same time. In this situation, conventional immunosuppressive therapy promotes perpetuation of the viral infection, exposing the patient to chronic lesions and to relapses. Antiviral therapy has demonstrated clear evidence of efficacy in vasculitis related to HBV and, to a lesser degree, HCV [3]. In our patient, after treatment with IFN- α , purpura disappeared and coronary dissection

was no longer present. These findings support the fact that IFN- α has been proven to be useful for patients with HCV-related cryoglobulinaemia, especially in those in whom HCV, RNA and cryoglobulins disappeared from the serum [8, 10].

In summary, our data suggested that HCV-related cryoglobulinaemia could be associated with endothelial damage and coronary dissection even in young patients. The endothelial injury could be accounted for by immune complex-mediated vasculitis. The successful treatment with IFN- α supports the use of antiviral therapy in vasculitis associated with viral infection.

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