## HCV-related cryoglobulinemic syndrome beginning as isolated gynaecologic vasculitis

Sirs,

Isolated or single-organ vasculitis (SOV) is known to occur in the breast, testes, single abdominal organs, or limited segments of the aorta and other arteries. Vascular inflammation has usually been an incidental finding in this setting, identified when surgical resection was indicated for other presumed diagnoses (1). SOV may also be the first manifestation of a systemic process (1). Histologic patterns may vary from granulomatous to non-granulomatous vasculitis, affecting small-sized, medium-sized or large-sized vessels (1), and a classification for SOV, based on histology and organs affected, has been proposed (2).

Gynaecologic vasculitis (GynV), or vasculitis involving the female genital tract, has been reported as SOV, and less frequently in the context of a systemic vasculitis (1, 3). In a recent review on this topic (3), only one case out of 163 cases of GynV occurred in the course of mixed cryoglobulinemia vasculitis (4). In this case, the onset of systemic features, *i.e.* fever and mononeuritis multiplex, was concomitant to the development of vasculitis of the adnexa and greater omentum (4). The patient was infected by the hepatitis C virus (HCV) and underwent surgical resection because of suspected mechanical ileus. Histopatological analyses of the adhesions, both the adnexa and greater omentum revealed a necrotising small and medium-sized vessel vasculitis (4).

We describe a case of a 56-year-old woman presenting with isolated GynV two years before the onset of a full blown, systemic cryoglobulinemic syndrome.

The patient was admitted in July 2006 to the gynaecology department of the "Santa Maria della Misericordia" Hospital of Udine, Italy, because of chronic pelvic pain that had started 3 years before and that had been rapidly worsening for 2 months. She underwent pelvic ultrasound and computer tomography scan studies without any significant findings. Due to the worsening of the symptoms, a diagnostic laparoscopy was performed showing multiple adhesions due to a pelvic inflammatory disease, and bilateral hydrosalpinx. A bilateral salpingo-oopherectomy was then performed together with a hysterectomy. Histopatologic findings were consistent with non-granulomatous necrotising vasculitis of the small arteries of the cervix and of both ovaries and with bilateral hydrosalpinx and uterine adenomyosis.

The patient was known to have chronic HCV infection (genotype 1b, HCV-RNA 1,500,000U/ml) without transaminase elevation. She had never been given antiviral therapy. After surgery, she was evaluated in our Rheumatology Clinic. She denied previous episodes of purpura or history of skin ulcers, and no evidence of other organ involvement was clinically found. Laboratory analysis revealed the presence of the rheumatoid factor (300U/L) and type II cryoglobulins (249ml/L) in the serum; C3 and C4 complement levels, the inflammatory markers (ESR, CRP), anti-nuclear antibodies (ANA), anti-neutrophil cytoplasmic autoantibodies (ANCA) and antibodies to extractable nuclear antigen (ENA) were all normal or negative. White blood cell count, haemoglobin level and platelet count were within the normal range. Urinary sediment was negative, as well as 24-h proteinuria. The patient underwent an electromyography study because of a history of recurrent leg cramps, but it did not show any signs of peripheral neuropathy. A diagnosis of SOV related to HCV-positive mixed cryoglobulinemia was formulated. The patient was then followed every year at our Clinic. In 2008, two years later, the patient developed a full-blown cryoglobulinemic syndrome characterised by mild purpuric poussès of the lower limbs, arthralgias and paresthesia at both the legs. The rheumatoid factor increased (643.6 U/L), while complement levels and inflammatory markers remained in the normal range. Electromyography documented a moderate axonal sensitive polyneuropathy. The involvement of other organs was excluded. Therapy with colchicine and gabapentin was started.

This is the first reported case of isolated gynaecologic-onset, biopsy-proven SOV, antedating a classic crioglobulinemic syndrome in the long-term follow-up. The course of the disease strengthens the concept of a careful evaluation in the presence of SOV, as stated (1, 3, 5). Furthermore, it highlights the occurrence of different immunological responses to the same presumed viral trigger, *i.e.* HCV (6-8), leading to different disease phenotypes over time. The possibility that a systemic vasculitis was already present at the time of SOV diagnosis cannot be definitely excluded, since mixed cryoglobulinemia was already present at that time. However, no other organ was clinically involved, and complement levels and inflammatory markers were normal. Thus, from a clinical point of view, the diagnosis of SOV was supported at disease onset, as usually observed in gynaecologic vasculitis (1, 3).

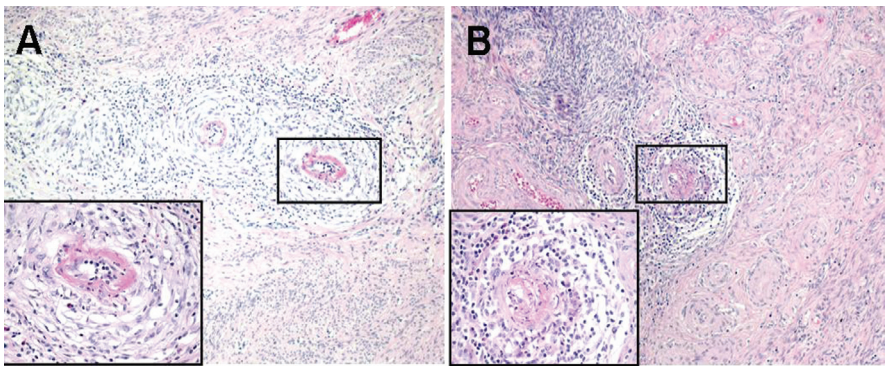


**Fig. 1**. Arteritis affecting small-sized vessels of the cervix (**A**) and ovaries (**B**) is shown (original magnification x 10, haematoxylin-eosin staining), with non-granulomatous inflammation and fibrinoid necrosis disclosed by higher magnification (x 40).

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