Chronic hepatitis C with mixed cryoglobulinemia: A case report

Kronik C hepatitli bir olguda mikst kriyoglobulinemi

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ÖZET: *Bu olgu bildirisinde 2 yıldan beri alt ekstremitelerinde palpable purpura hikayesi olan ve dermatopatolojik olarak lökositoklastik vaskülit tanısı alan 54 yaşında bir kadın hasta sunulmuştur. Etyolojik araştırmalarda kryoglobulinemi, hipokomplementemi, romatoid faktör pozitifliği, anti-HCV ve HCV-RNA pozitifliği, diffüz hepatomegali ve karaciğer iğne biyopsisinde kronik aktif hepatit saptanmıştır. Olguda, vaskülitin HCV infeksiyonuna bağlı olarak ortaya çıkan ve immun kompleks oluşumunda rol oynayan kryoglobulinemi sonucu geliştiği düşünülmüştür.*

Anahtar kelimeler: **Lökositoklastik vaskülit, kriyoglobulinemi, hepatit C virus infeksiyonu**

SUMMARY: *In this case report, a 54 years old woman with a 2 years history of palpable purpura on lower extremities with the dermatopathological diagnosis of leukocytoclastic vasculitis is presented. Etiological investigations showed cryogolobulinemia, hypocomplementemia, rheumatoid factor positivity, anti-HCV positivity, HCV-RNA positivity, diffuse hepatomegaly and chronic active hepatitis on liver biopsy. In this case, vasculitis was linked to hepatitis C virus infection as the cause for the production of cryoglobulins.*

Key words: **Leukocytoclastic vasculitis, cryoglobulinemia, hepatitis C virus infection**

HEPATITIS C virus (HCV), a single stranded RNA virus, identified in 1988, accounts for most cases of Non A-Non B hepatitis. HCV infection frequently causes chronic hepatitis and cirrhosis. Anti HCV antibodies have been found in up to 67 percent of patients with a history of intravenous drug use, and in 10 to 30 percent of patients receiving chronic hemodialysis (1,2). Although HCV is most efficiently transmitted primarily by the parenteral route, a large number of sporadic cases have no obvious risk factor (3,4).

Many dermatological diseases including lichen planus, cryoglobulinemia related vasculitis, porpyhria cutanea tarda, erythema multiforme, urticaria, polyarteritis nodosa and Behçet's Syndrome are known to be possibly associated with HCV-induced chronic active hepatitis (1,5-11).

We report a case of mixed cryoglobulinemia associated with HCV induced chronic active hepatitis.

CASE REPORT

The patient is a 54 years old white woman with a two years history of palpable purpura on lower extremities and arthralgias.

Physical examinations revealed sparse palpable purpura accompanied by diffuse reticular hyperpigmentation over both legs (Fig. 1).

Light microscopy of the skin biopsy specimen from her leg showed leukocytoclastic vasculitis (Fig. 2).

There was a history of myomectomy operation six years ago but there was no obvious history of transfusion. She denied intravenous drugs usage, sexual promiscuity and homosexuality.

Investigations showed the following results: Erythrocyte sedimentation rate was 30 mm/h; the bilirubin, ALT and AST levels were within normal range; gamma glutamyl transferase 80 IU/L (normal: 7-64 IU/L); rheumatoid factor (+++) (normal negative); cryoglobuline (+): antinuclear antibody negative (normal negative); anti smooth muscle antibody mild positive (normal negative); Complement 4 level was 0.08 g/L (normal 0.10-0.40); complement 3 level was normal; results of serum protein electrophoresis was normal. Hepatitis B surface antigen and antibody for hepatitis B surface antigen were not detected. Anti HCV

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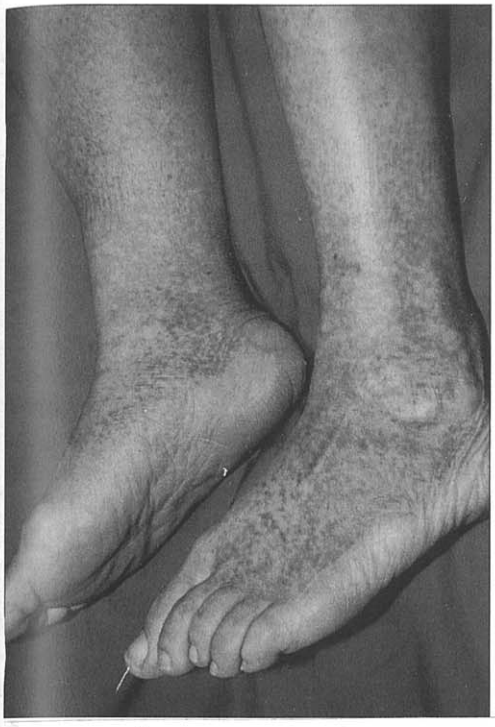

Figure 1. *Diffuse reticular hyperpigmentation over both legs.*

antibody was found positive by second generation ELISA (Abbott) and HCV-RNA was detected in the serum by a "nested" polymerase chain reaction procedure using primers located in the highly conserved sequence from the 5' non-coding region of the HCV genome. Findings of ultrasound examination of the abdomen showed diffuse hepatomegaly. Examination of liver biopsy specimen revealed chronic active hepatitis.

The result of these examinations confirmed the diagnosis of cutaneous leukocytoclastic vasculitis which is connected with the chronic hepatitis C virus infection causing cryoglobulinemia.

DISCUSSION

Leukocytoclastic vasculitis is a condition that results from destruction of the blood vessel wall, and is most often caused by the deposition of immuncomplexes in postcapillary venules. Skin lesions are characterized by palpable purpura especially on the legs. Many patients have arthralgia, malaise and fever. Can be found in ref (12).

After the availability of HCV antibody test, the hepatitis C virus is now thought to be responsible for the majority of cases of cutaneous leukocytoclastic vasculitis associated with nonA-nonB hepatitis (2). The possible role of immune factors in

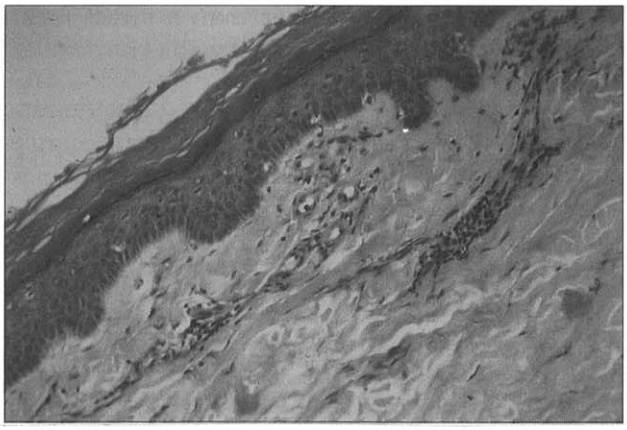

Figure 2. *Findings of a skin biopsy specimen showed late stage leukocytoclastic vasculitis: The superficial perivascular infiltrate consists mainly of mononuclear cells and there is not considerable nuclear dust and deposits of fibrin within or around vessels wall. (Hematoxylin-eosin stain; X100).*

the patho-genesis of HCV-associated vasculitis was reported (6). A high prevalence of immunologic abnormalities has been reported in patients with chronic HCV infection: Anti GOR autoantibodies; anti liver kidney microsomal type 1 antibodies, antinuclear and anti smooth muscle antibodies (9). The immune response to HCV may also be implicated in essential mixed cryoglobulinemia (6). Cryglobulunemia may be seen in a number of the various vasculitic syndromes. Essential mixed cryoglobulinemia may present as a typical hypersensitivity vasculitis confined to the skin (13,14). The association between HCV infection and cryoglobulinemia type II has been suggested by Pascaul et al (15). Cases of cryglobulinemia and cutaneuos leukocytoclastic vasculitis associated with hepatitis C virus infection were reported by Duran et al. and Pakulo et al. (1,6). Palpable purpura is more frequent in essential mixed cryglobulinemia when patients are HCV infected. The HCV infected group had higher serum cryoglobulin level (16).

Karesberg et al suggested that rheumatoid factor was a sensitive serologic marker for mixed cryglobulinemia in HCV-infected patients (14). The cryoglobulins usually consist of cryoprecipitable IgM rheumatoid factor directed against endogenous IgG (13). The emergence of a monoclonal rheumatoid factor has been linked to chronic viral infection (Epstein Barr Virus, HBV), which might participate in the activation process leading to the uncontrolled proliferation of a B cell clone. Hepatitis C virus may have a similar effect (15).

The vasculitis in HCV infections is probably the

result of cryglobulins rather than a direct result of virus deposition in the vessel wall (1).

In our case, investigations showed rheumatoid factor positivity, cryoglobulinemia, hypocomplementemia (especially C4), anti HCV antibody positivity, HCV-RNA positivity, diffuse hepatomegaly and chronic active hepatitis on liver biopsy and so vasculitis is connected with the HCV infection causing production of cryglobulinemia that play role in the formation of immuncomplexes.

Finally, in this case report, we wanted to emphasize the importance of searching for HCV infection in cutaneous vasculitis for an early diagnosis of HCV infection.

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