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Case report-Olgu sunumu

Lymphocytic vasculitis developing after Hepatitis A vaccine and successful treatment with Nadroparin Calcium

Hepatit A aşısı sonrası gelişen Lenfositik vaskülit ve Nadroparin Kalsiyum ile başarılı tedavisi

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Abstract

Among the various types of vasculitis, the most common is small vessel vasculitis involving the post capillary venules. Etiological factors are drugs, infectious agents, blood disorders, malignancies and rheumatological disorders. In this report, a Hepatitis B virus (HBV) carrier patient who experienced lymphocytic vasculitis after vaccination for Hepatitis A is presented. On admission, the patient had desquamated red-purple rashes with the dimension of approximately 2-3cm, scattered on both arms and elbows. The lesions appeared 20 days after the Hepatitis A vaccine. Liver function tests, complete blood count, erythrocyte sedimentation rate, blood urea nitrogen and serum C-reactive protein levels were within normal ranges. Pathology of the skin biopsy taken from the dorsum of hand was consistent with lymphocytic vasculitis. With the subcutaneous Nadroparin calcium (2x0.4ml) treatment, the patient recovered completely in four weeks. In conclusion, physicians should also consider the adverse effect of hepatitis A vaccine in the differential diagnosis of lymphocytic vasculitis.

Keywords: Hepatitis A vaccine, vasculitis, heparin

Özet

Vaskülitlerin pek çok türü vardır, en yaygın olanı postkapiller venülleri tutan küçük damar vaskülitleridir. Etiyolojisinde ilaçlar, enfeksiyöz ajanlar, kan hastalıkları, neoplaziler ve romatoid hastalıklar yer almaktadır. Bu raporda inaktif Hepatit B taşıyıcısı olarak izlenen bir hastada Hepatit A aşısı sonrası gelişen lenfositik vaskülit vakası sunulmaktadır. Hasta, Hepatit A aşısı yapıldıktan yirmi gün sonra her iki kol ve dirsekte, dağınık yerleşimli, çok sayıda kırmızı-mor renkli lezyonlar nedeniyle polikliniğimize başvurdu. Hastanın karaciğer fonksiyon testleri, üresi, tam kan sayımı, sedimentasyon ve C-reaktif protein değerleri normaldi. Hastanın el dorsumundan alınan deri biyopsi örneğinin patoloji sonucu lenfositik vaskülit olarak tanımlandı. Nadroparin kalsiyum 2x0.4ml subkutan uygulama ile hastanın lezyonlarında 4 hafta içinde tam iyileşme sağlandı. Sonuç olarak lenfositik vaskülit ayırıcı tanısında hekimlerin Hepatit A aşısı yan etkisini de göz önünde bulundurması gerekmektedir.

Anahtar sözcükler: Hepatit A aşısı, vaskülit, heparin

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Introduction

Vasculitis is a condition characterized by inflammation of blood vessels. Its clinical manifestations are dependent on the localization and size of the involved vessels as well as on the nature of the inflammatory process. The primary vasculitides are idiopathic systemic diseases. Secondary vasculitides occur as a result of conditions such as connective tissue diseases, sarcoidosis, malignancies, hypersensitivity to drugs and substance abuse as well as infections [1]. Henoch-Schönlein purpura, essential mixed cryoglobulinemia and cutaneous leukocytoclastic angiitis are examples of small vessel vasculitis [2]. Cutaneous lymphocytic vasculitis is a clinicopathological process characterized by lymphocytic inflammation of and damage of the dermal blood vessels. It is accompanied by fibrin deposition in the blood vessel walls or lumens, or both [3]. This syndrome is presumed to be associated with an aberrant hypersensitivity reaction to an antigen such as an infectious agent, drug, or other foreign or endogenous substance. There have been multiple mechanisms implicated; such as circulating antigen-antibody complexes, type IV delayed hypersensitivity reactions and cell-mediated or endothelial attack by lymphocytes [3]. Different mechanisms may be operative in the induction of vasculitis by infectious agents [1]. Three mechanisms are most likely to be involved: a. Direct microbial invasion of endothelial cells; b. Participation in the immune-complex mediated damage of vessel walls; and c. Stimulation of (auto-reactive) B and/or T lymphocytes. Viruses generally have a role in vasculitis of the small and or medium vessels [1].

Case report

A 22 year-old male patient with a diagnosis of inactive hepatitis B infection (carrier state) since March 2008, got vaccinated for Hepatitis A virus (HAV) in January 2009. Twenty days after the vaccination, the patient was admitted to our clinic with the complaints of red-purple colored, purpuric and papular rashes on both arms and elbows (figure 1). He had no recent history of drug use. He had no photosensitivity relevant to connective tissue diseases, no urticarial lesions or itching. Liver function tests, urea, complete blood count, sedimentation and C-reactive protein levels of the patient were within normal range. Among viral hepatitis markers, HBsAg was positive while HBeAg, HBV DNA, Hepatitis C virus antibody (Anti-HCV) and anti-HAV lg G were negative by ELISA. Ig M antibodies to Cytomegalovirus (CMV), Epstein Barr Virus (EBV) and Rubella were absent, but lg G antibodies were found to be positive by ELISA. To rule out some connective tissue diseases which may be the underlying condition, anti-nuclear antibody (ANA) and anti-dsDNA tests were carried out, both were found to be negative. Complement 3 and 4 levels were also found to be within normal range and nephelometric method was used for detection. Bilateral, scattered, erythematous purpuric papules, sometimes vesicules or nodules were observed in the distal ends of upper extremities at the dermatological examination. Findings consistent with lymphocytic vasculitis were observed in the histology of skin biopsy samples taken from the hand dorsum. The patient had been using topical clobetasol propionate pomade for his lesions when he came to our clinic and he reported that he had got partial benefit from the treatment. Since he was a hepatitis B carrier, systemic steroid or immunosuppressive agent was not considered for the treatment of vasculitic rash. Topical steroid treatment was stopped and Nadroparin calcium (Fraxiparine, Glaxo Smith Kline, TR) (0.4 ml=3800 IU) twice daily was started. Patient's lesions showed complete regression within 4 weeks, and the treatment was stopped upon completion of 8 weeks (figure 2). Relapse in the lesions was not observed during the follow-up period of two weeks after treatment discontinuation. Trombocyte count, liver and kidney function tests of the patient proceeded at normal levels during the treatment. No adverse effects associated with the treatment was observed

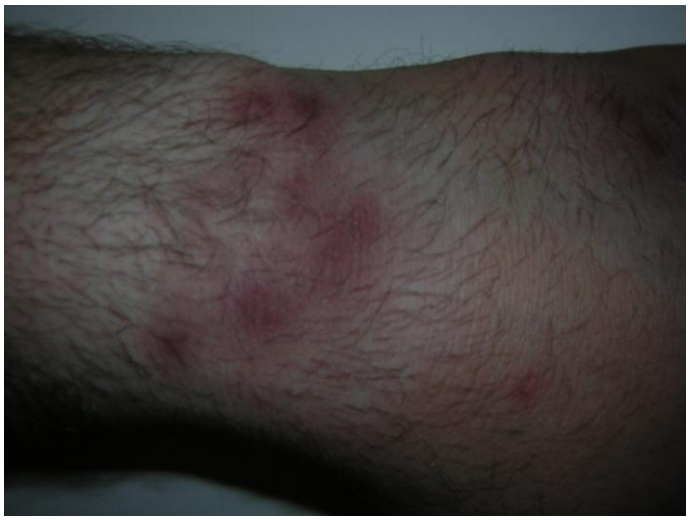

Figure 1: Erythematous, purpuric, papulonodular lesions on hand dorsum before treatment.

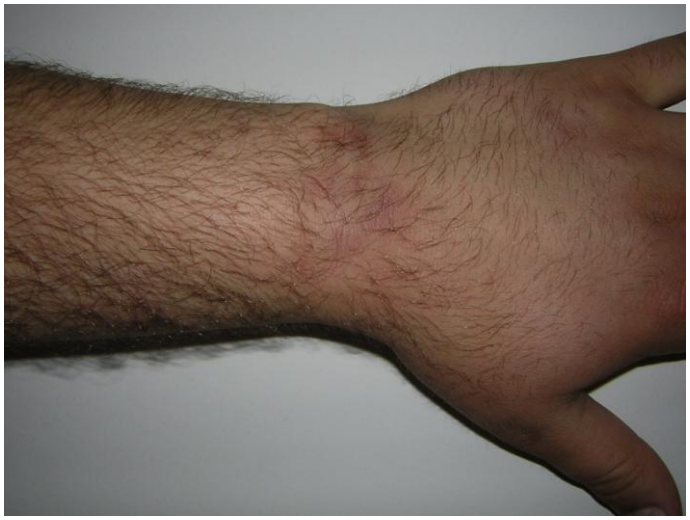

Figure 2: View of hand dorsum after treatment.

Discussion

HBV is associated with 2 types of vasculitic syndromes. Firstly, an immune complex mediated small-vessel vasculitis, affecting mainly the skin, and secondly, a polyarteritis nodosa like vasculitis with multisystem involvement. The first form of vasculitis typically occurs in around 10% of the patients prior to the onset of jaundice or other symptoms of hepatitis. Clinical findings are fever, arthralgias, and rashes due to vasculitis. In the circulation, HBsAg, HBeAg and HBV DNA are detected [1]. There were not clinical symptoms of Hepatitis B infection in our patient and HBeAg and HBV DNA were found to be negative. HAV infection is rarely associated with extrahepatic manifestations. Some cases of cutaneous vasculitis, cholestatic hepatitis, and cryoglobulinemia that were associated with HAV infection have been reported [4]. Mild local reactions have been reported in 20-60% of individuals who received Hepatitis A vaccine. These reactions include pain, swelling, or erythema at the injection site. Mild fever, malaise, headache, or fatigue, occur in 4-15% of recipients. Anaphylaxis and Guillain-Barre syndrome can be

associated with hepatitis A vaccines, but the occurrence of each is extremely rare [5]. The national vaccine adverse event reporting system (VEARS) followed 428 people who had HAV vaccine between the years 1995-1997 and reported less serious adverse affects such as frequently seen mild fever, myalgia, headache, pruritis and nausea. In spite of appearing rarely, it was reported that serious adverse effects such as fever, elevated liver enzymes, infection, abdominal pain and headache were seen. Again in the same report, more rarely adverse effects such as vasculitis, thrombocytopenia and diabetes mellitus were also noted [6]. Since live HAV can provoke leukocytoclastic vasculitis, inactivated HAV antigen could have similar immunogenicity and could thus induce the same pathogenic immune dysregulation [4]. Nadroparin calcium is a form of low molecular weight of heparin. It is obtained via depolymerisation of standard heparin. Anti Xa/ anti thrombin (anti II a) activity ratio is high, its antithrombic effect begins rapid and continue for a long time. It is approved for use to prevent post-operative thrombosis, and to treat venous and arterial thrombosis [7]. It is known that low molecular weight of heparin has been a successful treatment in patients with livedoid vasculitis. Livedoid vasculitis is a minor-vessel vasculitis and often occurs as purpuric macules, papules and painful ulcers of the lower extremities [8]. Since there is a great similarity between histopathological features of lymphocytic vasculitis and that of livedoid vasculitis, and since our patient gave poor response to the topical steroids and we could not use systemic glucocorticoids (he is a Hepatitis B carrier), we decided to give Nadroparin calcium in the treatment and the outcome was good.

In the English literature three cases with lymphocytic vasculitis were reported to be associated with Anthrax, Hepatitis B, Influenza vaccination [3, 9, 10]. To the best of our knowledge this is the first case with a diagnosis of lymphocytic vasculitis, for whom, low molecular weight of heparin has been used for the first time in the treatment.

Finally, lymphocytic vasculitis can rarely be seen after the Hepatitis A vaccination. In the conditions (diabetes mellitus, hypertension, Hepatitis B, C) in which systemic glucocorticoids and immunosuppressive therapy can not be used, low molecular weight of heparin could be an effective choice.

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