

# Erythema Nodosum Following Hepavax-Gene Hepatitis B Vaccine Inoculation

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## Abstract

Erythema nodosum (EN), a cutaneous reaction with sudden onset, consists of inflammatory, tender, warm nodular lesions, usually located bilaterally on the anterior aspects of the lower extremities. The nodules have bright red color initially, however, they become livid red or purplish within a few days, and finally they exhibit a yellow or greenish appearance. The lesions show spontaneous regression within 3-6 weeks, without ulceration or scarring and recurrent episodes are uncommon. Usually acute episodes of erythema nodosum are associated with fever, malaise, arthralgia, headache, abdominal pain, vomiting, cough and diarrhea (1).

EN is a cutaneous reactive process that may be triggered by a wide variety of possible stimuli such as infectious diseases, sarcoidosis, rheumatologic disorders, inflammatory bowel diseases, malignancies and medications (1).

We report a 35 year-old, non-pregnant woman with chief complaint of fever, chills and skin lesions following first hepatitis B vaccine injection was hospitalized at a teaching hospital in Tehran, Iran in November 2005.

Twenty-four hour after vaccine administration, skin lesions appeared. Lesions began as several warm, red tender nodules. EN is discussed in this case report.

## CASE REPORT

A 35 year-old, non-pregnant woman with chief complaint of fever, chills and skin lesions following first hepatitis B vaccine injection (Hepavax-Gene; manufactured by Green Cross Vaccine Corp; Korea) was hospitalized at a teaching hospital in Tehran, Iran in November 2005.

Her symptoms started 4 days before admission, 8h after hepatitis B vaccine inoculation, and included fever and chills; body pain added after about 12h of injection. Twenty-four hour after vaccine administration, skin lesions appeared. Lesions began as several warm, red tender nodules, with poorly defined borders located bilaterally on the both legs and vary from 2-6 cm (Figure 1).

## Figure 1

Figure 1: Patients skin lesions on the legs.



Vital signs at admission were: BP: 130/90; PR: 95; RR: 28; T(axillary): 38.2 °C Lab tests include: WBC: 8200/mm<sup>3</sup> (PMN=75%, L=22%) Hemoglobin: 14.2 g/dL Platelet: 133000/mm<sup>3</sup> Prothrombin time: 13S; INR=1 Blood Sugar: 146mg/dL Urea: 19mg/dL Serum creatinine: 1mg/dL

Bilirubin: Total=1, Direct=0.1 ESR: 44mm/h LDH=420IU/L CPK=96IU/L AST=20IU/L ALT=30IU/L Wright and comb's wright: negative HBs antigen: negative HBc antibody: negative HCV antibody: negative HIV: negative Blood culture: negative Urine culture: negative VDRL: negative Antistreptolysin-O: 50IU Throat culture: negative Tuberculin skin test: negative Rheumatoid factor: negative Blood smear (malaria and borrelia): negative Urinalysis: inactive Chest X-Ray: negative Past Medical History: negative for any diseases Drug History: negative Family History: negative

### INTRODUCTION

Erythema nodosum (EN), a cutaneous reaction with sudden onset, consists of inflammatory, tender, warm nodular lesions, usually located bilaterally on the anterior aspects of the lower extremities. The nodules have bright red color initially, however, they become livid red or purplish within a few days, and finally they exhibit a yellow or greenish appearance. The lesions show spontaneous regression within 3-6 weeks, without ulceration or scarring and recurrent episodes are uncommon. Usually acute episodes of erythema nodosum are associated with fever, malaise, arthralgia, headache, abdominal pain, vomiting, cough and diarrhea (1).

EN is a cutaneous reactive process that may be triggered by a wide variety of possible stimuli such as infectious diseases, sarcoidosis, rheumatologic disorders, inflammatory bowel diseases, malignancies and medications (1).

Although this process can occur at any age, however, most cases appear between the second and fourth decades of the life (1). It is suggested that EN occurs three to six times more frequent in women than in men (2).

A complete clinical history should be elicited in all patients, with reference of previous diseases, medications, foreign travel, pets and hobbies, as well as familial cases (1).

Bed rest is often sufficient treatment. Aspirin and non-steroidal anti-inflammatory drugs may be helpful to enhance analgesia and resolution. Systemic corticosteroids are rarely indicated in EN (1).

### DISCUSSION

Group A  $\beta$ -hemolytic streptococcus has well-known relationship with EN. The cutaneous lesions appear 2-3 weeks after the throat infection and are accompanied by an antistreptolysin-O (ASO) titer rising (1). Our patient had no history of sore throat or any sign of previous upper

respiratory tract infection and had negative ASO test and throat culture. Since Iran is considered an endemic country for tuberculosis, the subject underwent tuberculin skin test that showed negative result. Another common etiologic disease for EN is sarcoidosis which was ruled out in this patient with normal chest X-ray. The subject had no history of malignancy or rheumatologic disorder. Her rheumatic factor test was negative that is compatible with EN laboratory findings reported by other investigators (1). Other possible infectious etiologies were ruled out in this subject by normal leukocyte count, negative blood and urine culture tests, blood smear evaluation for malaria and borrelia, VDRL, wright and comb's wright tests, HBs antigen, HBc antibody, HCV antibody and HIV.

The erythrocyte sedimentation (ESR) rate is often very high in EN cases, however, it returns to normal when the eruptions subside (1). It is supposed that ESR elevation in children shows significant correlation with the number of lesions (3). Our patient with 4 lesions had slightly increment in ESR (44mm/h).

The patient had no history of foreign travel, pets contact or familial case of any skin disorder.

Drugs are considered as the frequent cause of EN. Sulfonamides and oral contraceptive pills are the most common causative medications for EN. The patient had no history of using any drug including oral contraceptives and antibiotics during the past several days.

Our patient was treated with indomethacin 150mg per day. The skin lesions regressed after about 30days without any scarring in our patient.

We searched Medline from 1970 to 2006 and found 4 case reports of EN associated with hepatitis B vaccine inoculation (4,5,6,7).

The authors believe that the most possible etiology of EN in this subject is hepatitis B vaccine inoculation due to the chronological relationship between skin lesion appearance and the vaccine injection and ruling out other probable causative conditions.

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