Case Report

A rare case of intravascular coagulation after honey bee sting

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Summary
A patient presented with coagulation problems a few days after honeybee sting. The purpuric skin changes developed on the legs and buttocks. She manifested signs of hypotension with disturbance of consciousness. Allergen-specific IgE serum levels against honey bee venom antigens reached >17.5 kU/l. The platelet count was 33,000/ml . The prothrombin index decreased to 28%, prothrombine time was prolonged to 34". Fibrin degradation products were present in serum. After 10 day treatment the girl improved, but necrotic skin changes required further plastic surgery. Honeybee sting problems should be taken into account as a cause of coagulation problems.

Key words: insect venom allergy, unusual reaction, intravascular coagulation

Introduction

Insect venom induced allergic reaction is a life threatening disorder. Insect stings can cause severe effects, lead to cardiovascular collapse and death. The mortality rate is estimated to be approximately 1-5% in different countries. Pathogenesis of that disease is closely linked to the immunologic mechanisms. Besides the usual, immediate type reactions, in a very few cases of insect stings symptoms may appear after several days (i.e serum sickness) [1]. No case of localized IC (intravascular coagulation) as a result of bee sting has been reported to date.

Case report

A 17-year-old girl presented for evaluation of sudden weakness, septic fever (40°C), and joint and muscular pain that made her body movements nearly impossible. All these symptoms began 10 days after a bee sting that resulted only in local reaction on the arm. She developed purpuric skin lesions with necrotic center and a characteristic distribution on the legs (mainly on the crural region), and the buttocks. Initially they could have been described as punctured and tiny purpuric spots, but their size and number increased rapidly. The patient manifested signs of hypotension with disturbance of consciousness. She complained of abdominal pain. Four days after occurrence of those severe symptoms the patient was transferred from the local hospital to our medical center.

Her past medical history was unremarkable. She was in excellent health, had no history of immune-mediated diseases and reported no history of respiratory illnesses as a child.

On examination the patient appeared very weak and unable to ambulate because of the muscle and joint pain. Purpuric maculae were seen on the skin and concentrated on the distal parts of the lower extremities. No lymphoadenopathy was found. The mucous membranes of the throat and tonsils were normal, without inflammatory changes. Lungs were clear to auscultation . Cardiovascular examination revealed a loud holosystolic murmur at the base of the heart. Abdominal examination was unremarkable. Bilateral knee, ankle and metatarsus – phalangeal joints were swollen and tender. Neurologic examination showed no deficits although motor exam was difficult because of severe pain.

The hematocrit was 40 percent, the white cell count was 16,800/ml with 64 percent neutrophils. The platelet count was 33,000/ml and erythrocyte sedimentation 60 mm/hr. Peripheral blood smear was normal. The

prothrombin index decreased to 28%, prothrombin time was prolonged to 34"(normal value:11-16 sec.) and coagulation time was 8'15" (normal value). Fibrinogen level was decreased to 0.82 g/l (>1,0 g/l). The alanine aminotransferase activity reached 58 U/l(3-26 U/l), and the aspartate aminotransferase 77 U/l (6-18 U/l). Serum creatinine level was 1.52 mg/dl (<1.5 mg/dl). C-reactive protein level was 269 mg/l (normal value <5 mg/l). Fibrin degradation products were present in serum. Urinanalysis was normal. An electrocardiogram, chest radiographs and ultrasonographic examination of the abdomen were normal. Because of the suspicion of endocarditis an ultracardiographic examination was performed. It revealed no abnormalities (valve surfaces were free of vegetations). Cultures obtained from the blood, nasal and pharyngeal specimens were negative. Serum level of total IgE was 474 IU/l. Allergen-specific IgE serum levels against tree, grass, cereals, pollens, against the majority of food allergens and against honey bee venom antigens reached the 4-6 class (>17.5 kU/l)(Pharmacia CAP System, Sweden). Concentration of IgE/ IgG immune complexes containing IgG anti-IgE estimated by use of monoclonal anti-IgE antibodies (Pharmacia –LKB,Sweden) was above the refence range at 1740U/ml. Repeated estimation of IC after following two months were 340 U/ml.

Immune complexes assay has been described previously [2].

The patient was treated with antibiotics (Amoxicillin/ clavulanic acid before admission to our department, Cefuroxime sodium, Gentamicin sulphate), corticosteroids (Prednisone 60 mg per day in slowly tapered doses), kalium supplementation, vitamin K, etamsylate, proton pump inhibitor (pantoprazole). In 10 days the patient improved noticeably, although the necrotic skin lesions involved large portions of the lower limbs (Figure 1). Changes on the upper limbs and buttocks slowly healed leaving crusts revealing epithelium with signs of granulation. The patient was released in good condition, but plastic surgery was advised.

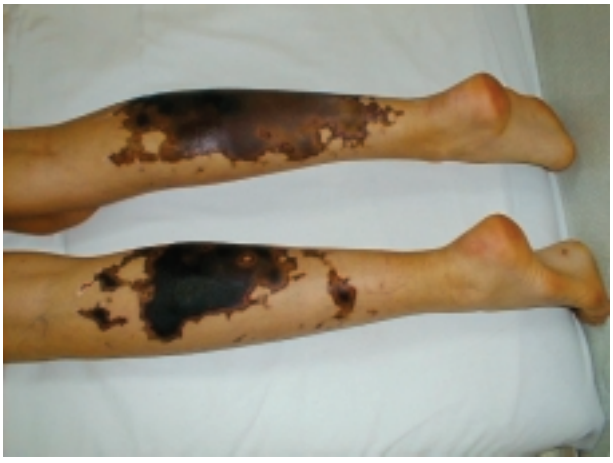

Figure 1. Necrotic changes on the posterior side of the cruris two weeks after sting.

Discussion

This case shows atypical, unusual reactions after insect sting. Some of them occur a few hours or even a few days after the sting. An injection of hymenoptera antigen can cause a wide range of severe late effects: serum sickness, severe neurological disturbances, i.e. polyradiculomyelitis (Guillain-Barre syndrome), seizures, acute renal failure, hemolysis, thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC), myocardial infarction, or cardiac arrhythmias [1,3]. In certain clinical syndromes the stimulus to intravascular coagulation appears to be localized yet the haematologic changes are obvious throughout the circulating blood.

In the base of insect venom induced allergic response lays the type I acc. to Gell-Coombs reaction where IgE plays a pivotal role. The hypothetic role of IgG and type III reaction is still an object of investigation.

Mesothelium damage, thrombocyte and macrophage activation, cytokine, leucotriene release, bradykinin and PAF play the key role in the pathogenesis of DIC. Deposition of immune complexes in the basement membrane of small blood vessels and activation of the complement system may also contribute to the pathogenesis of the disease. That mechanism could develope symptoms of glomerulonephritis or lymphadenitis.

Fogel et al. described a case of a 12-year old boy, who was bitten by a wasp 7 days after an upper airways infection and on the next day after the bite developed into severe, generalized necrotizing vasculitis. Despite intensive care measures and high doses of corticosteroids, the patient died after 2 months [4].

Descriptions of blood coagulation disturbances due to anaphylactic reaction after a wasp sting given by Rathoff suggest the leading role of antithrombin in their pathogenesis [5].

Monzon et al. reported hemolytic anemia as a result of a wasp sting [6]. The same agent was recognized as responsible for Schoenlein-Henoch disease manifestation in a child [7]. Smith et al. described DIC in two subjects with severe anaphylaxis after insect sting [8]. Both of them presented decrease of serum fibrinogen, Factor V, Factor VIII and high-molecular-weight-kininogen concentration.

Clinical features presented by the patient in response to insect venom suggest the involvement of immune complexes and this may explain the delayed manifestation of symptoms and their character. Activation of tissue thromboplastin enhanced the coagulation cascade. The shock observed was accompanied by haemorrhagic lesions concentrated particularly on the lower extremities and signs of widespread thrombosis of skin capillaries and venules

with centers of necrosis. Fortunately, in contrast to observations made by Fogel et al. this pathology did not involve seriously affect internal organs besides temporarily increased creatinine level. Activation of serum kinin-forming system plays the key role in initiating the clotting cascade [8]. Bradykinine is certainly capable of causing hypotension and cleavage of high-molecular-weight-kininogen concomitantly with changes in blood coagulation and fibrinolitic parameters of disseminated intravascular coagulation [9]. The uncommon case of localized IC caused by honey bee sting presented here illustrates the possibility of insect sting- induced serious coagulation disturbances. The severity of clinical manifestations vary among patients, even when the disorder is produced by the same agent. The reasons for this variability are not apparent.

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