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Case Report

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Serratiopeptidase Induced Hemorrhage in a Patient with Behçet's Disease

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Abstract

Behcet's disease is a multisystemic chronic inflammatory disease which is presented as recurrent oral ulcers, genital ulcers, uveitis, arthritis, and vascular disease. Venous thrombosis is the most common vascular complication. Venous thrombosis could be the result of endothelial inflammation. Rather than giving primary anticoagulation, by controling systemic inflammation the venous thrombotic events can be prevented. Serratiopeptidase is a proteolytic enzyme which is against fibrin build up. We report Serratiopeptidase induced diffuse ecchymotic hemorrhage of a patient with Behçet's disease.

Key Words: Behcet's disease, Serratiopeptidase, diffuse ecchymotic hemorrhage.

Introduction

Behcet's disease is a multisystemic chronic inflammatory disease. It was first described by in 1937 as a characteristic clinical triad of recurrent oral aphthous ulcers, genital ulcers, and uveitis (1). Later additional manifestations were described, including joints, skin, vessels, brain, lungs, genitourinary, and gastrointestinal disorders (2). The disease has vascular manifestations which depends on the type and location of the vessel involved (3,4). Systemic vasculitis is an important pathological finding in Behcet's disease. Blood vessels of all sizes may be effected, both in venous and arterial systems (5). In Behcet's disease, venous involvement is usually causes vascular complications. It may result in superficial thrombophlebitis and deep venous thrombosis (6). Venous thrombosis can be seen in the early stage of Behçet's disease (7). Venous thrombosis could be the result of endothelial inflammation (8). Rather than giving primary anticoagulation, by controling systemic inflammation the venous thrombotic events can be prevented (9,10). Actually primary anticoagulation is not recommended (11).

Serratiopeptidase is a product of enterobacterium Serratia sp which is acting as a proteolytic enzyme. Enterobacterium Serratia sp is isolated from the intestine of silkworm. Serratiopeptidase is called by several names like serralysin, serratia peptidase, serratiapeptase, serratio peptidase, or serrapeptidase. Main work of Serratiopeptidase is purifying products of inflammatory process and eliminating pus, cysts, arterial plaque, blood clots, scar tissue and hematoma. It is against fibrin build up. Serratiopeptidase can prevent swelling and fluid retention as an anti-edemic drug. Common side effects are gastric discomfort, nausea, pneumonitis, allergic reaction, and there is increased risk of bleeding when taken the drug with garlic, fish oil and turmeric and other herbal supplements (12,13).

Diffuse ecchymotic hemorrhage is extremly rare in Behçet's disease. We report Serratiopeptidase induced diffuse ecchymotic hemorrhage of a patient with Behçet's disease.

Case Report

A 28-year old Syrian woman with Behçet's Disease was admitted to emergency department with a large number of ecchymotic foci on her body surface. She had a history of Behçet's Disease for 4 years. The patient explained that she had experienced venous thrombosis one year ago, and she also had this disorder edema develoloped in her legs right after having the venous thrombosis. The patient also said that she was recommended to use Serratiopeptidase constinously to prevent the development of some kind of thrombosis as well as to prevent from having the edema in her legs.

She had a previous history of using azathioprin 100 mg/day, omeprazole 20 mg/day, serratiopeptidase 20 mg/day as medication. The patient had no prior history of surgical operation, and she denied smoking, alcohol, and any illicit drug use. On physical examination, her blood pressure was 120/80 mmHg, heart rate 89 beats per minute and regular, respiratory rate 18 per minute, body tempreture was 36.2 °C. Her cardio-respiratory system was normal, abdomen was soft and non-tender and there was no organomegaly, and other systems were also normal. She had ecchymosis varying diameter 3 to 10 cm along her back, abdomen, upper and lower extremities. Those had occurred within 24 hours as mentioned on her history. There was no evidence of gastrointestinal and genitourinary bleeding in patient. On laboratory examination, her blood analysis were as follows: APTT 90 second, PT undetecteable, platelet

523.000/µL, hemoglobin 12 gr/dL, leukocyte 18.300/µL, creatinin 0.4 mg/dL, BUN 14 mg/dL, sodium139 mEq/L, potassium 4.1 mEq/L, AST 15 U/L, ALT 15 U/L, total protein 6.5 gr/dL, albumine 4.2 gr/dL, glucose 84 mg/dl, calcium 9.4 mg/dL, phosphorus 3.8 mg/dL, LDH 152 U/L. The peripheral blood smear was evaluated as a normal. In addition, urine and stool microscopy, C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor, serum iron, serum iron binding capacity, ferritin, vitamin B12, folic acid levels were normal. Fecal occult blood was negative. The patient's chest radiography, electrocardiography, and abdominopelvic ultrasonography were normal.

Discussion

Behcet's disease is a multisystemic chronic inflammatory disease. It was first described as a triple complex of recurrent oral ulcers, genital ulcers and uveitis. Our patient’s history fulfilled the proposed criteria of the international study group for Behcet's disease (14).

The pathogenesis of thrombotic tendency in patients with Behcet’s disease is not well known. Venous thrombosis could be the result of endothelial inflammation (15) but also endothelial cell ischemia or disruption that leads to enhancement of platelet aggregation is accused (16). Other possible causes of thrombotic process are the anti phospholipid antibodies and elevated von Willebrand factor antigen levels have been demonstrated (17).

Thromboses of the large vessels are related to a poor prognosis. Arterial occlusions and aneurysms are associated with the presence of venous thromboses (18). Studies showed that anti-coagulant treatment is not effective in preventing venous thrombosis (19,20). Rather than giving primary anticoagulation, by controling systemic inflammation the venous thrombotic

events can be prevented (9,10). Anticoagulants, antiplatelet or antifibrinolytic agents are not recommended in management of deep vein thrombosis associated with Behcet's disease (11). Our patient was receiving a proteolytic enzyme called serratiopeptidase which was against fibrin build up. She was receiving this proteolytic enzyme uncontrolled. This drug has no specific follow up laboratory test and it might increase the likelihood of bleeding. Her coagulation parameters were deteriorated and she also had diffuse ecchymotic bleeding. Since diffuse ecchymotic hemorrhage is extremely rare in Behçet's disease, we believe that her bleeding situation was because of the serratiopeptidase intake. We have given fresh frozen plasma and vitamin-K in order to control the bleeding. Repeated controls of coagulation parameters had indicated that the coagulation tests became normal. During follow-up ecchymosis had been resolved.

In conclusion, vascular thrombosis is a serious issue and it might accompany to the course of Behçet's disease. In controlling vascular thrombosis, anticoagulants, antiplatelet or antifibrinolytic agents were not recommended because of the high bleeding risk. While taking these drugs or proteolytic herbal drugs to prevent thrombosis, bleeding risk should be taken into consideration.

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