

Life Threatening and Occult Mediastinal Haemorrhage Secondary to Acquired Factor VIII Deficiency

Dear Editor,

Acquired Factor VIII (FVIII) deficiency is a rare disorder occurring at a rate of approximately 1 person per million each year.¹ It is due to the spontaneous development of auto-antibodies against FVIII. In 50% of the cases, no cause is identified, although it can be associated with pregnancy, autoimmune disease and malignancy.¹ Inhibition of FVIII occurs and patients may present with spontaneous ecchymoses, mucosal bleeding and muscular haematomas. Bleeding can sometimes be massive and potentially life-threatening, hence, acquired FVIII deficiency is an important differential diagnosis to consider in patients presenting with coagulopathy. We present a rare case of acquired haemophilia presenting with spontaneous and clinically occult mediastinal haemorrhage.

Case Report

A 67-year-old female with a history of type 2 diabetes mellitus and hypertension presented with swelling and bruising of both her legs for 3 days, following moxibustion (a traditional Chinese treatment that uses heat to stimulate acupuncture points) to her lower extremities. This was associated with exertional dyspnoea. Her medications include Glipizide 10 mg bd, Metformin 850 mg bd and Atenolol 100 mg OM. On physical examination, she was pale, with a heart rate of 120/min, a blood pressure of 100/70 mmHg, respiratory rate of 20/min and an oxygen saturation of 100% on 4 litres of oxygen intranasally. There were ecchymoses and swelling of both lower extremities, with the right larger than the left. An examination of the chest, heart and abdomen was normal. A rectal exam and aspiration of stomach contents through a nasogastric tube showed no evidence of bleeding of the gastrointestinal tract.

The haemoglobin concentration was 7.2 g/dL. The prothrombin time was normal, (12.3 seconds, normal 10.7-13.4) but the activated partial thromboplastin time (APTT) was prolonged, (49.6 seconds, normal 27.6-39.6). The electrocardiogram showed sinus tachycardia. The chest radiograph was normal. The provisional diagnosis was that of a bleeding diathesis with bleeding into the soft tissues of the lower extremities. We were also concerned about retroperitoneal bleeding in view of the profound anaemia. Computed tomography (CT) of the chest and abdomen revealed no retroperitoneal blood but the unexpected finding of a massive haematoma in the posterior mediastinum,

causing compression of the major airways (Fig. 1). No evidence of aortic dissection was seen. Further questioning of the patient did not reveal any excessive coughing, emesis or physical manipulations to the chest.

The patient underwent tracheal intubation for airway protection, as there were concerns that the haematoma will increase in size. Transfusions of packed-cells and fresh frozen plasma were initially administered. The prolonged APTT was not correctable with the 50:50 mix, indicative of the presence of an inhibitor. This was later identified as an inhibitor to FVIII, with a titre of 5 Bethesda Units (BU). As the patient was not known to be haemophilic, the diagnosis of acquired factor VIII deficiency was made. Because of evidence of ongoing bleeding despite very aggressive blood product support, 50 mg/kg of rFVIIa was administered as a single bolus dose daily for 7 days. This resulted in rapid haemostasis. At day 3, the haematoma had decreased in size. IV hydrocortisone 100 mg q6H and IV cyclophosphamide 50 mg qd was also started and the FVIII inhibitor levels had dropped to 1 BU by day 9. The patient was extubated on day 5 and discharged from the hospital on day 16. She remained on a combination of oral prednisolone and cyclophosphamide 6 months after discharge from hospital. Work-up for autoimmune disease, such as systemic lupus erythematosus, and malignancy was negative.

Discussion

Spontaneous mediastinal haemorrhage has previously been described in certain situations, such as the sudden increase in intrathoracic pressure due to sneezing or coughing,



Fig. 1. Contrast-enhanced computed tomography chest at the level of the aortic arch showing compression of the mid-trachea by the mediastinal haematoma.

coagulopathy due to uraemia or anti-coagulation therapy, enlarging mediastinal tumours and malignant hypertension.² To our knowledge, there has only been 1 other report of a spontaneous mediastinal haematoma secondary to an acquired FVIII inhibitor.³ In that case report, the patient was diagnosed with acquired FVIII deficiency after presenting with postpartum haemorrhage. She subsequently developed respiratory distress and mediastinal widening on chest radiograph. A CT Chest confirmed a mediastinal hematoma. Our patient, in contrast, had minimal respiratory symptoms and an examination of the chest was normal. Only an aggressive search for an occult source of bleeding led to the diagnosis of a mediastinal hematoma. As illustrated by our patient and the previous case,³ in addition to the retroperitoneum and the gastrointestinal tract, the mediastinum can also be a potential source of bleeding.

Treatment of acquired haemophilia involves arresting bleeding and immunomodulatory therapy to suppress or eliminate the anti-factor VIII antibody.⁴ In patients with high antibody titres (defined as more than 5 BU), fresh frozen plasma, cryoprecipitate and conventional doses of human Factor VIII are usually not useful, as they do not contain sufficient FVIII to overcome or neutralise the inhibitor. In these patients, porcine FVIII or rFVIIa have been used to secure haemostasis.⁴ Recombinant Factor VIIa, when given in high dose, promotes haemostasis by acting on activated platelets and exposed tissue factor to generate thrombin formation. As porcine Factor VIII is not available in Singapore, rFVIIa was used as a first line therapy in our patient with good response. Immunomodulatory therapy with glucocorticoids and cyclophosphamide was shown to be useful in the suppression of the anti-factor VIII antibody. This was used with success in our patient. Other options such as plasmapheresis, pooled human immunoglobulin and rituximab⁵ have also been used with variable success.

In conclusion, spontaneous mediastinal bleeding may occur in the setting of acquired haemophilia, and requires a high index of suspicion for the diagnosis to be made. In patients with ongoing bleeding due to an acquired haemophilia, rFVIIa is a reasonable option to arrest the bleeding.

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