Reminder of important clinical lesson

Life-threatening retro-pharyngeal bleed in a case of systemic lupus erythematosus – an uncommon but important evil of a common disease

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Summary

Acquired inhibitors of coagulation are antibodies that interfere with the coagulation system either by functional inhibition of the activity of clotting factors or by their increased clearance from the plasma. They can be idiopathic or seen in various physiologic (pregnancy and postpartum) or pathologic states (systemic lupus erythematosus (SLE), malignancies, rheumatoid arthritis) and can result in a variety of haemorrhagic sequelae. SLE can be associated with antibodies to multiple clotting factors and bleeding though rare can be an important haematologic manifestation with life-threatening consequences in these patients.

BACKGROUND

Though systemic lupus erythematosus (SLE) is well known to most clinicians, few may be aware of bleeding as a haematologic manifestation of this disease. Also since hypercoagulability due to antiphospholipid antibodies is a more frequent haematologic presentation in SLE, it can be easy to overlook the haematologic basis of bleeding diathesis in these patients. Since bleeding in lupus patients can sometimes be life-threatening, knowledge of this condition is extremely important in making an early correct diagnosis with prompt management of such cases. We therefore present a case of life-threatening bleed in a patient with SLE to highlight this complication.

CASE PRESENTATION

An older female with medical history of SLE presented with chest pain for 2–3 weeks and worsening dyspnoea to a local hospital. She also developed large haematoma of right upper extremity and small ecchymosis on lower extremities without any evidence of petechiae, mucosal, joint or intracerebral bleed. There was no improvement despite high dose steroids and eight units of blood transfusion and she was transferred to a tertiary care centre. On the second day after transfer, the patient developed tightness of throat and muffled ‘hot potato’ voice. There was evolving haematoma of right upper arm extending to anterior right neck and bruising of the floor of the right half of the mouth and oropharynx on examination.

INVESTIGATIONS

Initial investigation at the local hospital showed significant anaemia, evidence of intra vascular haemolysis and Coombs test positive for auto-pan-agglutinin and complement consistent with autoimmune haemolytic anaemia. At the tertiary centre, a CT scan of the neck was done and showed evidence of a large retro-pharyngeal bleed with impending

airway obstruction (figures 1 and 2). Coagulation profile showed high partial thromboplastin time (PTT) and normal prothrombin time (PT). Given the clinical evidence of bleeding in the setting of a medical history of SLE, it was suspected that patient might have an acquired inhibitor of coagulation. A PTT mixing study confirmed the presence of strong inhibitor. Specific coagulation factor assays revealed

Figure 1 Transverse section at the level of C3 showing a large retro-pharyngeal haematoma compressing over the posterior pharyngeal wall causing partial occlusion of the lumen.

Figure 2 Sagittal section of the head and neck showing a retro-pharyngeal haematoma extending for the most length of the pharynx.

an inhibitor to factor VIII. Bethesda assay was performed which showed inhibitor titre of 1:320. Antiphospholipid antibody investigation was negative for lupus anticoagulant and β -2 glycoprotein but positive for IgM anticardiolipin antibodies. Factor 7 levels and factor II activity were within normal limits.

DIFFERENTIAL DIAGNOSIS

Trauma can lead to haematomas but a history of this was absent in this patient. Qualitative or quantitative congenital defects of either coagulation factors or platelets can cause bleeding diathesis though these manifest much earlier in life. There was no history of any previous bleeding events in this patient.

TREATMENT

An ear, nose and throat consultation was requested. It was decided to hold off on intubation or surgical airway until absolutely necessary due to the potential for severe bleeding. Patient was started on recombinant factor VIIa at a loading dose of 270 μ g/kg followed by 180 μ g/kg every 8 h. High dose intravenous steroids were continued. Within 3 days, her right upper extremity swelling and pain and the discolouration at haematoma sites started improving. Factor VIIa transfusion was slowly tapered after 7 days of full dose therapy. She was started on rituximab 375 mg/m²

weekly for four doses, in addition to steroids to enhance inhibitor elimination.

OUTCOME AND FOLLOW-UP

After 4 weeks of treatment, the patient recovered with complete resolution of her bleeding diathesis and she was discharged home in a stable condition.

DISCUSSION

Bleeding as a haematological manifestation of SLE is quite uncommon and is attributed to inhibitors of clotting factors VIII, II, IX, XI, XII and XIII.^{1–4} Elevated PTT with a normal PT is the typical lab finding in patients with factor inhibitors. PTT mixing studies do not show correction and hence suggest antibody impairment of factor function rather than deficiency. Prothrombin inhibitors however cause an increased factor clearance and so correction on mixing studies is seen.⁴ Bethesda assays quantify antibody titres and are useful for monitoring various treatment modalities. Specific immunochemical measurement is required in case of prothrombin inhibitor. The spectrum of bleeding can range from mild to life-threatening bleed depending on the concentration of factor inhibitors and commonly manifests as ecchymosis, mucosal bleeds (gastrointestinal, epistaxis and haematuria) and soft tissue haematomas. A mortality of around 22–25% has been mentioned in different studies.^{5 6}

There are no specific therapeutic guidelines yet, but in general treatment consists of controlling the bleeding and elimination of the antibodies. Control of bleeding can be achieved using various agents depending on the severity⁶ of the bleed and the concentration of the factor inhibitor (expressed in Bethesda units). DDAVP and high dose human factor VIII concentrate may be helpful with low inhibitor titres (<10 Bethesda units) and recombinant human factor VIIa⁷ or activated prothrombin complexes are used when there are higher inhibitor titres. Several drugs can be used to eliminate the inhibitor including high dose steroids for a minimum of 3 weeks or immunosuppressive therapies like cyclophosphamide, rituximab. Intravenous immunoglobulin can be used in steroid refractory cases.⁸

Though some literature on acquired inhibitors of coagulation is available, very few cases of SLE with acquired inhibitors of coagulation have been published to date. A Medline search using the term ‘acquired inhibitors of coagulation’ generated 626 articles (in all languages) dating from 1962–2011, of which only eight articles^{9–16} referred to cases of acquired inhibitors in patients with SLE and only four^{10–13} of them mentioned cases with factor VIII inhibitors as in our case. These cases presented with hemarthrosis,¹⁰ metrorrhagia¹² and abdominal bleeding.^{11 13} Prompt diagnosis with immediate rightful management as in our case was the key to prevention of grave consequences from life-threatening bleeding in three of these cases. To our knowledge, a life-threatening retro-pharyngeal haematoma in a case of SLE with acquired factor VIII inhibitors has never been reported until now.

Learning points

- ▶ Though thrombotic sequelae due to antiphospholipid antibodies are common in patients with SLE, clinicians need to be aware of bleeding as an important haematologic manifestation in these patients and should have a low threshold to consider acquired inhibitors of coagulation among the differential diagnosis.
- ▶ Given the significant consequences of the bleeding diathesis due to acquired inhibitors of coagulation in SLE as well as in other associated conditions—which in some instances can be life-threatening, and the complexities associated with this diagnosis, an awareness of this possibility is very important to evaluate a haematologic basis of the bleeding, to differentiate it from congenital factor deficiency and for the early correct management.

Competing interests None.

Patient consent Obtained.

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