Reminder of important clinical lesson

Massive epistaxis in a patient with Eisenmenger syndrome: illustrating the clot-versus-bleed conundrum

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Summary

Eisenmenger syndrome (ES) causes polycythaemia and thrombocytopenia, thus rendering patients at risk from both thrombosis and haemorrhage. The clinical dilemma lies in how to treat one without precipitating the other. Our case demonstrates this important clinical problem. A 35-year-old lady with ES taking aspirin with clopidogrel for thrombo-prophylaxis presented with massive epistaxis. Blood tests showed polycythaemia, thrombocytopenia and normal clotting studies. A bone marrow biopsy ruled out leukaemia and normal imaging made pulmonary haemorrhage unlikely. Drug induced platelet dysfunction on a background of thrombocytopenia was the most likely cause of her epistaxis. Despite cessation of her dual anti-platelet therapy and multiple nasal packing, heavy epistaxis continued. She was given an infusion of platelets, and once her counts normalised, she was re-started on anti-platelet therapy.

BACKGROUND

Eisenmenger syndrome (ES) is a type of cyanotic heart disease first described in 1897 by Viktor Eisenmenger,¹ where a pre-existing left-to-right shunt (eg, a VSD) causes pulmonary vascular disease and pulmonary hypertension.² This leads to flow reversal in the shunt lesion or occasionally in a bi-directional shunt.² Like most cyanotic heart diseases, it renders the patient in a pro-thrombotic state either due to pulmonary vascular remodelling or secondary polycythaemia.³ Unlike its counterparts, ES patients are also prone to bleeding due to thrombocytopenia or clotting factor disturbances.³ With predispositions to these 'ying-yang' sequelae, managing ES patients presents a challenging dilemma: how can we prevent thromboses without causing haemorrhages?

CASE PRESENTATION

A 35-year-old lady of Indian origin with patent ductus arteriosus induced ES presented with sudden onset heavy epistaxis. Nasal packing was immediately implemented. There were no clear precipitants and she was otherwise well. Since she was chronically polycythaemic, she took Aspirin and Clopidogrel for thrombo-prophylaxis against hyperviscosity. Family history was unremarkable, and she was independent of activities of daily living. Physical examination showed finger clubbing, right parasternal heave and loud second heart sound, consistent with ES. Bleeding was visible from the nostrils bilaterally, which was packed in the emergency department. There were no bruises or any other sources of haemorrhage.

INVESTIGATIONS

Blood tests showed polycythaemia with a haemoglobin concentration of 18.7 g/dl and a haematocrit of 0.57. Her platelet count was $16 \times 10^9/l$ and clotting studies were normal (prothrombin time 11.7 s, partial thromboplastin

time 30 s). Thrombocytopenia was confirmed on blood film. This prompted a bone marrow aspiration and trephine, which did not show any dysplasia or metaplasia. Her repeated chest x-rays were normal and with the given history, significant pulmonary haemorrhage was deemed unlikely.

DIFFERENTIAL DIAGNOSIS

Antiplatelet drug induced platelet dysfunction.

TREATMENT

She was given a platelet infusion in the emergency department. Her aspirin and clopidogrel were temporarily stopped. Her epistaxis continued relentlessly for 2 days despite multiple nasal packing and balloon tamponade attempts to achieve haemostasis. With a further platelet infusion, her serial platelet counts started rising and her epistaxis gradually resolved.

OUTCOME AND FOLLOW-UP

Our patient was discharged once her platelet normalised and was followed up in the haematology outpatient clinic to re-start her thrombo-prophylactic treatments.

DISCUSSION

Patients with ES tend to be polycythaemic and are therefore at risk from thromboses.³ The use of thrombo-prophylaxis drugs in these patients is, however, controversial. According to the recent guidelines from the European Society of Cardiology, the use of antiplatelet agents and anticoagulants should be guided by the case history and risks of bleeding.⁴ These drugs can be considered in patients with atrial fibrillation, pulmonary artery thromboses (PAT) or low bleeding risk.⁴ However, the guidelines are unclear about whether antiplatelet drugs are indicated for

the prevention of thrombotic complications such as PAT. Indeed, conclusive evidence is lacking regarding the benefits of antiplatelet drugs in preventing thrombotic complications in ES.⁵ In light of her polycythaemia and lack of major bleeding risk factors, our patient was considered to be at low bleeding risk and dual-antiplatelet therapy was used as a form of thrombo-prophylaxis in the presence of haematological hyperviscosity. This was a case specific consideration.

Patients with ES are commonly thrombocytopenic, as demonstrated by Lill *et al* who studied 105 patients with cyanotic congenital heart disease. They found that 25% of these patients were thrombocytopenic and all of whom had ES.⁶ A possible mechanism is that megakaryocytes bypass the lungs due to the right-to-left shunt in ES and as a result cannot be converted into functional platelets.⁶ Therefore, when ES patients take anti-platelet drugs, the resulting platelet dysfunction can tip these patients over the edge and results in severe bleeds. This 'double-hit' of thrombocytopenia and platelet dysfunction is likely to be the mechanism of action in our patient, which is supported by the absence of other drugs with anti-platelet properties and alternative causes of epistaxis.

In the literature, bleeding complications of ES are well known. Woods presented 127 ES patients in 1958, all of whom reported haemoptysis.⁷ More recently, Broberg *et al*⁸ presented three patients with haemoptysis secondary to massive PAT. Jensen *et al*⁹ presented a similar case describing haemoptysis with PAT in 2007. Epistaxis has been mentioned in review articles^{10 11} but anti-platelet drug induced heavy epistaxis, although logically feasible, has not been reported.

Finally, ES is becoming rarer as cardiac shunts are diagnosed and closed before pulmonary hypertension develops.¹⁰ For this reason, clinicians are less likely to encounter it and may not be fully prepared in managing ES patients in the acute setting. It is therefore important to emphasise that patients with ES are prone to both thromboses and haemorrhages and treatment of one can precipitate the other.

Learning points

- ▶ Patients with ES are prone to both thromboses as well as haemorrhages.
- ▶ Antiplatelet drugs can cause platelet dysfunction in patients with pre-existing thrombocytopenia, resulting in severe haemorrhagic episodes.
- ▶ The use of antiplatelet drugs in ES is controversial and should be carefully considered.
- ▶ Epistaxis is an important presentation in ES and needs to be investigated carefully and treated promptly.

Competing interests None.

Patient consent Obtained.

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