

Case Report




Factor-V-Leiden mutation in a neonate presenting with arterial ischemia

Abstract

Factor V Leiden mutation is a rare cause of familial thrombophilia, more commonly seen in Caucasians. It is associated with thromboembolism in the neonatal population.¹ We report a case of a term female infant who developed an arterial ischaemic right thumb and the dorsum of the right hand several hours after birth and as part of the work up the baby was found to have Factor V Leiden Mutation (Heterozygous). Parents who are of Middle Eastern origin had no family history of thrombophilia. The baby was born in good condition and the only significant perinatal history was gestational diabetes which is another known risk factor for neonatal thromboembolism. The neonate was successfully managed with subcutaneous low molecular weight heparin and hyperbaric topical oxygen. We think the presence of factor V Leiden associated with gestational diabetes predisposed to this rare presentation.

Case

We report a case of a term, female infant born by ventouse assisted delivery at 38 weeks gestation. She was born in good condition with Apgar scores were 9 at 1 minute and 10 at 5 minutes. The baby weighed 3290 grams. Both parents were of Middle Eastern origin and non-consanguineous. Mother is a primigravida; perinatal history was insignificant apart from gestational diabetes controlled by diet alone. She was not on any medications during pregnancy, and there were no risk factors for infection. The antenatal antibody screen was negative, and antenatal scans were all reported as normal. There was no significant family history and specifically no history of thrombophilia or thromboembolic disease. However no laboratory testing was carried out for the parents.

When the baby was examined at birth, there were no obvious abnormalities detected. The father took a photograph of her at birth, and the right thumb looked healthy. However at 12 hours of age, the mother noted a bluish-black discolouration of the baby's right thumb. There were also scattered bluish-black skin lesions over the dorsum of the right hand. The lesions were consistent with localised skin ischaemia. The distribution of the ischaemic skin lesion was consistent with occlusion of the first right dorsal metacarpal artery. The rest of the skin examination was normal. The baby was pink, well perfused. No dysmorphic features were noted. She had a good cry, tone, suck and activity. Cardiovascular, respiratory, abdominal and central nervous system examination revealed no abnormalities. All peripheral pulses were palpable and of good volume.

Management

The baby was admitted to the neonatal intensive care unit for further management and evaluation of the lesion. The management included wrapping the hand in a plastic bag with 6 litres of 100% oxygen delivered directly to the affected area. The baby received subcutaneous Clexane injections twice daily for five days. She was also given intravenous antibiotics (Flucloxacillin and Gentamicin), due to a slight rise in the C-reactive protein to 8 mg/dl; antibiotics were discontinued after 48 hours when the blood culture revealed no growth. She also received vitamin K and multivitamins as per standard practice. We referred the baby to the vascular surgeons and plastic surgeons to evaluate the viability of the thumb. The working diagnosis at that point was ischemic lesion secondary to a thromboembolic phenomenon or local vasculitis. The aim was to rescue the thumb and prevent amputation.

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Investigations

Imaging

The following radiological investigations were done: Doppler ultrasound of the right upper limb, X-ray of the right hand, Echocardiography, Abdominal ultrasound of the kidney, ureter and bladder and cranial ultrasound. These were all normal.

Eye examination

Indirect Ophthalmoscopy was normal with no evidence of retinal haemorrhage or infarction.

Bloods tests

Full blood count revealed normal haemoglobin and platelets, white cell count was high on the first day, but then normalized. C-reactive protein increased from 3.9 to 8 mg/dl. Blood culture showed no growth after 48 hours. Clotting was normal (Partial thromboplastin time was 52.8 seconds, Partial Thrombin time was 14.5 s and INR 1.24).

Thrombophilia Screening revealed :Thrombin Time-Normal, Protein S Free-70% (Normal 56-124), Antithrombin Activity- 71% (Normal 70-122), Protein C-25.8%, Factor V Leiden Mutation- Single R506Q Mutation identified (Heterozygous).

Progress

- There was a dramatic improvement of the ischemic lesions. The lesions changed from black to blue and then to purplish pink over the next few days.
- Baby was discharged and followed up in the clinic. No prophylaxis was offered to the baby.
- We did not offer long-term prophylaxis in the form of heparin.
- However baby was referred to the paediatric Haematology team for further assessment and management.

Diagnosis

The diagnosis is ischaemic lesions of the right thumb and multiple ischaemic skin gangrene over the dorsum of the right hand. The distribution of the skin lesion was consistent with occlusion of the first dorsal metacarpal artery. Risk factors for thromboembolism included factor V Leiden mutation and maternal gestational diabetes.

Discussion

Factor V Leiden thrombophilia is a rare genetic disorder caused by a single gene mutation. Factor V Leiden is the most common inherited form of thrombophilia. The major clinical manifestation of the heterozygous Factor V Leiden mutation is venous thromboembolism. An association between the FVL mutation and arterial thromboembolism in older children and adults remains controversial though evident in our case. Factor v Leiden thrombophilia plays a significant role in venous and arterial thromboembolism in neonates.¹

Factor v Leiden is the commonest cause of thromboembolism in the Caucasian population but there is no available data for Middle Eastern origin as in our case. The debate about whether to screen for thrombophilia with a positive family history is unsettled. In our case, there was no significant family history. However, studies have shown that family history in children, unlike adults, perpetuates no increase in risk, and thus, studies suggested not to test children less than 15 years with a family history.² However there is a universal consensus to screen those with clinical presentation.

The presence of gestational diabetes mellitus (GDM) is a risk factor for thromboembolism in neonates. However the commonest thromboembolism associated with GDM is renal vein thrombosis which was not present in our case. The presence of other risk factors for thromboembolism with the presence of factor V Leiden mutation can increase that risk of developing a thromboembolism. In our case, gestational diabetes (GDM) could be an extra trigger. Factor v Leiden thrombophilia is also associated with increased risk of abdominal thromboembolism. Studies have shown increases in renal vein thrombosis (OR 10.9 95% CI: 3.85–31.1; P < 0.0001), Portal Vein Thrombosis (OR 5.47 95% CI 1.7–17.6; P < 0.0007) and Hepatic Vein thrombosis (OR 3.3 95% CI 0.58–18.7; P = 0.18).³

The presence of factor V Leiden mutation increases the risk of developing stroke in children odds ratio of 3.26 (95% CI, 2.59 to 4.10).⁴ In our case there were no clinical signs of stroke and the

cranial ultrasound scan was normal. Prophylaxis was not given in our case because recurrent thromboembolism in children with factor V Leiden is rare.⁵ This is a rare case of spontaneous neonatal ischaemia that has been successfully treated with low molecular weight heparin. We hope our case will add to the literature in neonatal thromboembolism, its causes and management.

Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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