Management of Pregnancy-Associated Acquired Haemophilia A: a Case Series from the Oxford Haemophilia and Thrombosis Centre, UK

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Introduction

Acquired haemophilia A (AHA) is a rare bleeding disorder caused by autoantibodies against factor VIII (FVIII) [1]. Fewer than 5% of all AHA cases are associated with pregnancy, affecting 1:350 000 births and typically occurring 1-4 months postpartum [2]. It is even rarer for AHA to present during pregnancy; the largest case series of post-partum AHA patients described only 1 case diagnosed in pregnancy (2% of cases in the EACH2 registry) [2]. We present a patient with AHA diagnosed in pregnancy and compare this with two women diagnosed postpartum presenting to a single haemophilia centre in a 6-month period.

Case 1: Intrapartum Acquired Haemophilia A

The first patient was a 24-year-old who had a prolonged APTT 2 months after the birth of her second child (74 seconds, normal 20-30 seconds). She had mild bruising. She fell pregnant with her third child and at 9 weeks gestation was referred to our haemophilia centre where she was found to have a chromogenic factor VIII <0.01iu/ml, anti-human FVIII inhibitor titre 2.2 Bethesda units (BU). Following discussion with obstetrics, she was started on intermediate dose prednisolone 40 mg daily (0.5 mg/kg) due to the potential risk of cleft lip/palate with the use of higher prednisolone doses in the first trimester. FVIII levels normalised 4 weeks after starting treatment (Figure 1). Her prednisolone was weaned from 20 weeks' gestation and she continued on this throughout pregnancy. She underwent emergency Caesarean section at 38 weeks due to fetal bradycardia. Her FVIII levels pre-surgery were 4.46IU/ml with an undetectable inhibitor level. She did not require any additional haemostatic support. The baby had no haemorrhagic complications and weighed 2.81 kg (9th centile). Cord blood confirmed the newborn's FVIII 1.22IU/ml with no detectable inhibitor.

	Case 1	Case 2	Case 3
Age (y)	24	36	35
PMH	nil	Osteopenia, limited scleroderma, multiple sclerosis	Nil
Timing of symptoms post-partum (weeks)	8	4	8
Parity	2	1	1
Symptoms	Bruising	Bruising	Bruising and haematuria
Presenting APTT (20-30 seconds)	47.4	47.1	75
FVIII (IU/ml) (0.5-2 IU/ml)	0.03	<0.01	<0.01
Anti-human FVIII inhibitor (BU)	1.6	12.9	7.1
Treatment	Prednisolone	Prednisolone Rituximab	Prednisolone, Rituximab, NovoSeven, MMF
Time to FVIII level normalisation (weeks)	4	8	22
Time to stopping IST (weeks)	30	12	50

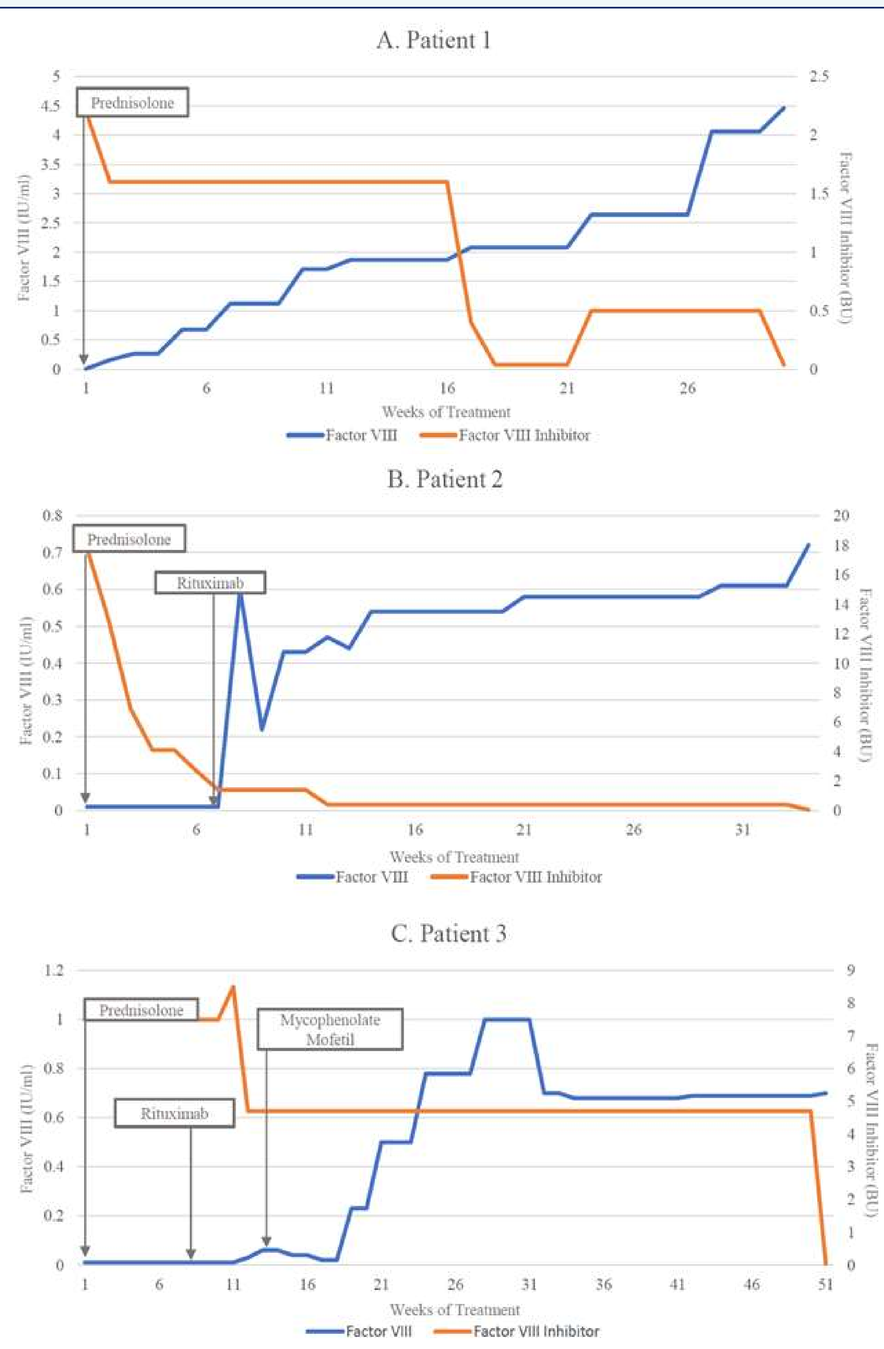

Figure 1 – Trends in Factor VIII (blue) and inhibitor (orange) for all three patients after initiation of treatment for pregnancy-associated acquired haemophilia A. Figure 1: The percentage change in factor VIII level (iu/mL) and corresponding inhibitor level (Bethesda Units BU), in relation to time is shown. Note prednisolone treatment and/or mycophenolate mofetil treatment were discontinued by weaning. Rituximab treatment was given over 4 weeks in all cases.

Case 2 and 3: Post-partum AHA

The second patient was a 36-year-old who gave birth to her 1st child by vaginal delivery after an uncomplicated pregnancy. She developed extensive bruising 4 weeks post-partum and her APTT was prolonged (47.1 seconds). FVIII level was <0.01iu/ml with anti-human FVIII inhibitor 17.8 BU and anti-porcine FVIII inhibitor 3.4 BU. She was started on prednisolone 1 mg/kg and, after 5 weeks, given 4 doses of 375mg/m^2 rituximab due to a poor response to steroids. Her FVIII levels increased to 0.54iu/ml 1 week after completing rituximab.

The third patient was a 35-year-old primigravid who presented with bruising 2 months post-partum. Blood tests showed a prolonged APTT (75 seconds), FVIII <0.01iu/ml, anti-human FVIII inhibitor titre 7.1 BU and anti-porcine FVIII inhibitor 0.5 BU. She commenced prednisolone 1mg/kg and, after 7 weeks of minimal response, was started on rituximab therapy with steroid weaning. Her FVIII levels remained low (0.02iu/ml), and she developed haematuria, and so was treated with NovoSeven 90mcg/kg. She was then started on mycophenolate mofetil (MMF) (initially 500 mg twice daily, increased to 1g twice daily). Two weeks after starting MMF her FVIII level improved to 0.23iu/ml and is now 1.00iu/ml, 7 months postpartum.

Discussion

These cases highlight the varied course of pregnancy-associated AHA. There is limited evidence on the management of AHA during pregnancy, with few reported cases in the literature. Careful patient counselling is essential as immunosuppressants can cross the placenta and into breastmilk, and so close liaison with the obstetric and pharmacy teams is vital in the management of these patients.

References

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