

Introduction

Congenital thrombotic thrombocytopenic purpura (cTTP) is an autosomal recessive disorder with mutations in the ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) protease. This protease breaks down von Willebrand factor (VWF). When impaired, excess VWF causes platelets to aggregate in the microvasculature, this is known as a thrombotic microangiopathy (TMA). In pregnancy, thrombi disrupt the uteroplacental circulation, causing placental and uterine infarction, reducing blood supply to the fetus [4].

Diagnosis in pregnancy is difficult due to symptom overlap with other TMAs, including haemolysis elevated liver enzymes low platelet (HELLP) syndrome, pre-eclampsia (PET) and acquired TTP (aTTP). These conditions often require termination of the pregnancy, whereas cTTP can be managed antenatally with fresh frozen plasma (FFP) [5]. FFP works by replacing the ADAMTS13 enzyme.

We describe the outcomes of four pregnancies in three women with cTTP.

ADAMTS13 Mutation	
Pt1	Homozygous for c.2260T>C p.(Cys754Arg)
Pt2	Homozygous for c.3178C>T p.(Arg1060Trp)
Pt3	Compound heterozygous for c.330+1G>A, p.(?) and 3178C>T, p.(Arg1060Trp)

Figure 1: ADAMTS13 Mutations in Our Patients

Case 1

Pt1, a 17-year-old, was diagnosed as an infant with cTTP. She presented at **6+0 gestation** and treatment included:

- 10ml/kg SD-FFP alternate weeks until 20 weeks, followed by weekly until 37 weeks.
- 5mg folate daily in the 1st trimester.
- 75mg aspirin daily until 35 weeks.
- Uterine artery dopplers at 24 weeks and growth scans at 28, 32 and 36 weeks.

Pt1 remained asymptomatic and induction at 37+3 weeks resulted in a healthy baby girl. She continued with 15ml/kg SD-FFP weekly until eight weeks postpartum.

Case 2

Pt2, a 33-year-old, presented at **21+2 gestation** with hypertension, haemolytic anaemia and thrombocytopenia. Two days later she developed an eclamptic seizure and was admitted to ITU for magnesium sulphate and FFP. Her condition stabilised however, intrauterine death was confirmed on 21+5. A fetal autopsy detected severe growth restriction and placental infarction. Low ADAMTS13 levels (13.3%) identified TTP as the likely cause. Treatment with plasma exchange (PEX) and prednisolone was commenced but Pt2 continued deteriorating. Genetic screening later confirmed cTTP rather than aTTP, therefore treatment was switched to FFP.

Pt2 declined treatment outside of pregnancy and remained asymptomatic. The following year, she fell pregnant and was commenced on the same treatment plan as Pt1, with the addition of dalteparin daily until six weeks after delivery. At 30+2 weeks an emergency caesarean section was performed due to growth restriction and abnormal CTGs. The baby was taken to the NICU and survived.

Case 3

Pt3, a 25-year-old, presented at **32+0 gestation** with diarrhoea, vomiting and a rash. Blood tests revealed haemolytic anaemia and thrombocytopenia. ADAMTS13 activity of 1.8% and antibody inhibitor levels of 3 confirmed the diagnosis of TTP. Treatment for aTTP was commenced with daily PEX, prednisolone, dalteparin and aspirin, and she was discharged after eight days. At 34+0, she developed severe peripheral oedema and PET, meaning a caesarean section was needed. Pt3’s baby showed no signs of growth restriction. Postnatal genetic screening identified cTTP as the cause.

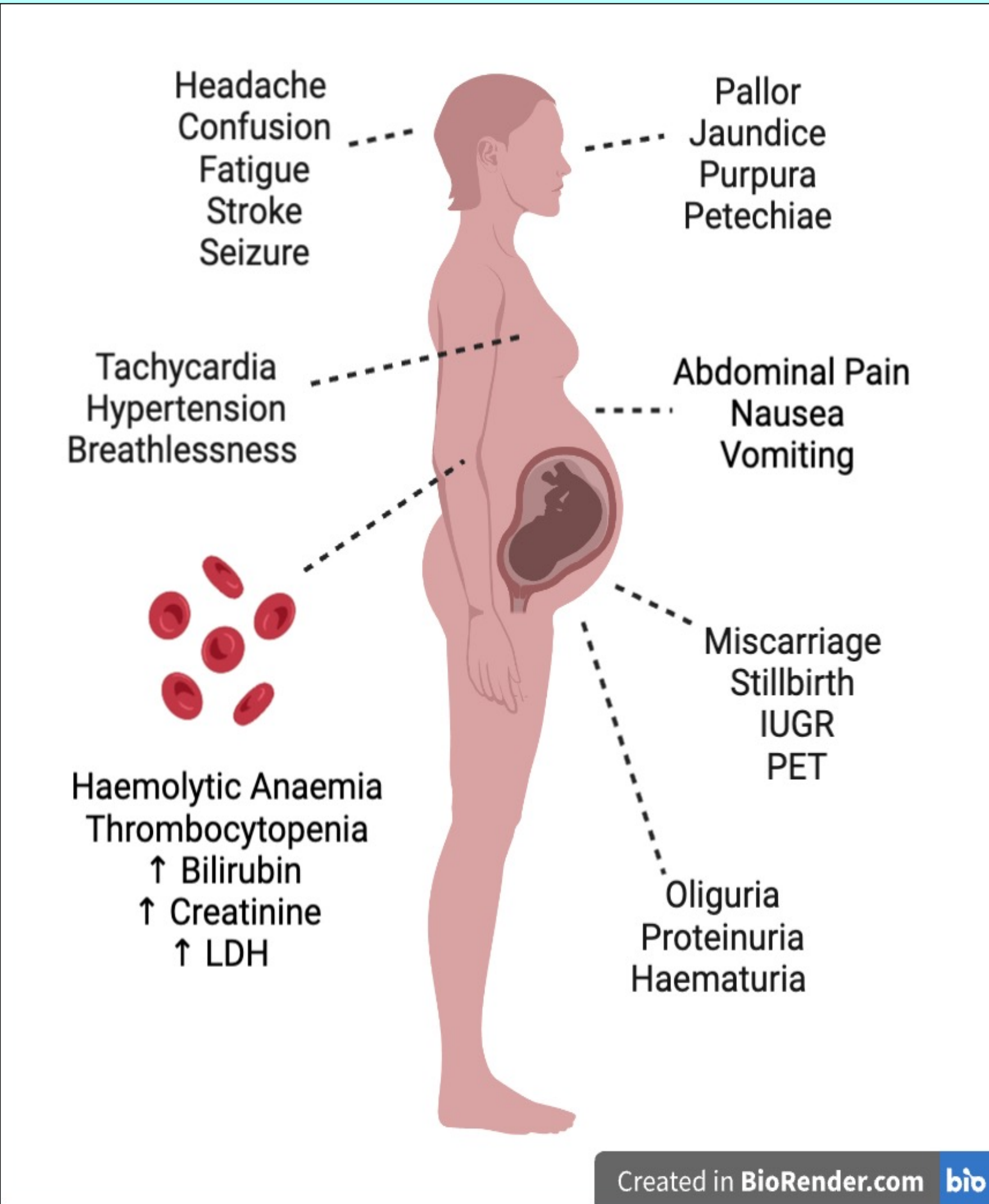


Figure 2: Features of cTTP in Pregnancy [8]

Discussion

Outcomes of cTTP in pregnancy are linked to:

Gestation of presentation

- Prenatal diagnoses improve outcomes [5].
- Presentations between 20 and 30 weeks are associated with severe fetal growth restriction and fetal death [7].
- Reaching 30 weeks without an acute episode of cTTP is associated with fewer sequelae of disease [5,7].

Speed and accuracy of treatment

- Early ADAMTS13 screening is required to differentiate TTP from other TMAs.
- cTTP must be differentiated from aTTP, which is more common. The need for aggressive early treatment means patients are treated for aTTP initially [3], as seen in both Pt2 and Pt3. Antibody testing and genetic screening are options for this.

Type of mutation

- The c.2260T>C, p.(Cys754Arg) mutation seen in Pt1 has previously been linked to childhood presentations of cTTP [2].
- The c.3178C>T, p.(Arg1060Trp) mutation seen in Pt2 and Pt3 is associated with adult and pregnancy onset cTTP [1,6,7].

Conclusion

cTTP is a life-threatening condition that mimics other TMAs; thus, diagnosis is both difficult and urgent. These cases highlight the differing ways in which this disease presents and continues conversations into the factors which influence outcomes. Increasing the database of such cases is how we facilitate more research into this fascinating disease.

References

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