LETTERS TO THE EDITOR

WILEY

Persistent coagulopathy during *Streptococcus pneumoniae* sepsis and left foot abscess in a previously healthy infant revealed tyrosinemia

To the editor:

A 2-month-old boy presenting with left foot swollen for four days was admitted to our hospital. The temperature was normal. There was no vomit, seizure or diarrhea. Left foot abscess incision drainage was given 2 days prior to presentation. He had no history of skin rash or joint swelling. His birth weight was 3.7 kg with born full-term. The perinatal period was normal. The weight was 5.2 kg and height was 61 cm on initial assessment. Physical examination revealed mild jaundice and left foot abscess drainage incision. The other evaluation was normal.

After laboratory examination, complete blood count showed hemoglobin 6.8 g/dL, white blood cell count 25.9×10^9/L (neutrophils 60.7%, lymphocytes 32.3%, monocytes 6.3%) and platelets 133×10^9/L, and biochemistry revealed abnormal liver function (elevated indirect bilirubin and normal liver enzyme). The coagulation profile was prominently disturbed (prothrombin time 106 s and International Normalized Ratio 9.3). Initial assessment of immune function was normal. Two sets of blood cultures on admission were positive for penicillin-sensitive *Streptococcus pneumoniae* (SP) (serotype 6B). Left foot abscess culture was also positive for penicillin-sensitive SP (serotype 6B). A next generation sequencing analysis for left foot abscess was also suggestive of SP infection. Anti-pneumococcal therapy was adjusted to ceftriaxone over 14 days with good recovery of foot abscess. A magnetic resonance imaging (MRI) showed lesions in the shrunken liver and no enhancement in abnormal signals of liver (Figure 1A). Liver stiffness measurement was 19.8 Kpa. The presence of specific antibodies (positive IgM and IgG), blood cytomegalovirus (CMV) load (500 copies/mL) and urine CMV viral load (7000 copies/mL) confirmed the diagnosis of CMV infection. Then he was treated with intravenous ganciclovir.

High serum methionine (109 μmol/L) and tyrosine (724 μmol/L) with the α-fetoprotein level (45 389 ng/mL) and persistent coagulopathy despite treatment with fresh frozen plasma and vitamin K, suggested tyrosinaemia. Whole-exome sequencing identified compound heterozygous variants in fumarylacetoacetate hydrolase (*FAH*, NM_000137), including a known pathogenic maternal nonsense variant c.520C>T (p.R174*) and a paternal missense variant c.742G>A (p.G248R) in the proband (Figure 1B). The paternal missense variant was predicted to be likely pathogenic by SIFT and Polyphen. Mutations in the *FAH* gene have been attributed to hereditary tyrosinemia type 1 (HT1). So this patient was diagnosed as HT1. Fortunately, his sister did not carry these variants (Figure 1B).

In the 3rd month of life the patient was discharged from hospital with liver function and coagulation function improved, having been on a diet restricted in

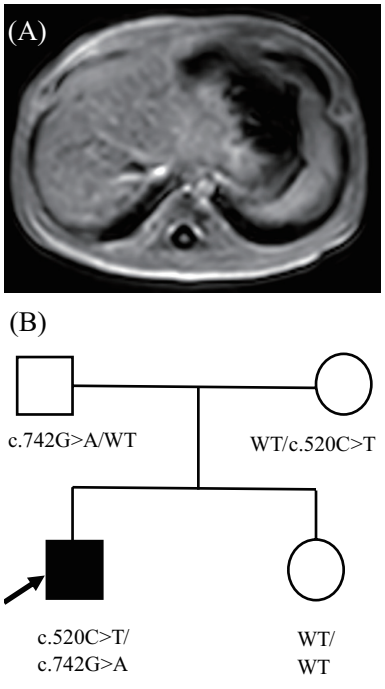

FIGURE 1 MRI and genetic analysis of the proband. (A) Axial gadolinium-enhanced T1-weighted MRI showed lesions in the shrink liver. (B) Pedigree of the patient.

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phenylalanine, methionine and tyrosine. The patient died a year after discharge because of severe liver damage without compliance to dietary restrictions.

HT1 is an autosomal recessive disorder of tyrosine metabolism and is caused by deficiency FAH, resulting in accumulation of the intermediate toxic metabolite fumarylacetoacetate released into the circulation and thus can be measured for diagnosis.[1] These are several reports of invasive pneumococcal disease (IPD) with HT1. Wabitsch et al[2] reported a severely ill 2-month-old female infant with meningitis and septicaemia caused by SP and HT1. Gill and Lipscomb[3] reported a 3-month-old, previously healthy girl diagnosed with primary pneumococcal peritonitis associated with HT1. At present, no study has been conducted on the correlation between the pathogenesis of IPD and HT1. Georgouli et al[4] reported a 5-month-old boy with HT1 presented with *Escherichia coli* sepsis and severe coagulopathy due to liver dysfunction. To our knowledge, this is the first reported case of SP sepsis and left foot abscess with CMV infection and HT1. For our patient, persistent coagulopathy during SP sepsis and foot abscess is indicative of tyrosinemia, especially with abnormal liver function.

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CONSENT FOR PUBLICATION

Consent was obtained from the patient's parents.

CONFLICT OF INTEREST

The authors declare no competing interests.

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