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Congenital Tuberculosis (TB) – use of second line medication and therapeutic drug monitoring (TDM)

Background: Diagnosis and treatment of congenital TB in premature infants are challenging due to limited data on medication management and extremely high mortality.
Case: A male infant was born at 33 weeks of gestational age to a mother admitted with progressive respiratory illness, who died soon after delivery from disseminated TB. The infant's symptoms were slowly progressive over the first month of life. The presence of mycobacteria in the placenta prompted the initiation of anti-TB treatment in the neonate, and the diagnosis was confirmed by positive MTB PCR in gastric and tracheal aspirate; and growth of MTB from gastric aspirate and bronchoalveolar lavage cultures. Initial treatment included Isoniazid (INH) 10mg/kg/day, Rifampin (RIF) 15mg/kg/day, Pyrazinamide (PZA) 35mg/kg/day, and Ethambutol 20mg/kg/day. The clinical course was complicated with worsening respiratory distress and abdominal distention raising the possibilities of drug resistance (sensitivity to INH, RIF, and PZA later confirmed), malabsorption in the context of abdominal TB, or the natural progression of the disease. Initially, INH and Rifampin serum levels were low and INH dose was increased to 15mg/kg/day and RIF to 20mg/kg/day. Repeat serum levels were still low for RIF due to RIF-induced vomiting but increased after treating nausea. Ethambutol was replaced by Levofloxacin 15mg/kg/day, due to concerns about Ethambutol toxicity and unreliable therapeutic levels in this age group. Because of lack of clinical improvement, a paradoxical hyperinflammatory reaction to TB treatment was suspected, prednisone was prescribed for 4 weeks. From age 2 months the patient improved progressively.
Learning point: In premature neonates, therapeutic drug monitoring may be necessary to optimize therapy, and the use or addition of second-line medications should be considered due to limited dosing information for some first-line drugs and the aggressive nature of congenital TB.

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