A rare cause of intrauterine growth restriction, respiratory insufficiency and cytopenia: hallmarks of Shwachman-Diamond syndrome in the neonate

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Case

- Term male newborn, from non consanguineous parents
- *Prenatal diagnosis:* intrauterine growth restriction (IUGR) and shortened long bones
- *Clinical examination at birth:* severe respiratory distress, narrow thorax and short limbs
- *Chest X-ray*: short, dysplastic ribs with enlarged metaphysis and small lung volumes
- *Blood count:* leucopenia, severe neutropenia (leucocytes 1.4 G/l, ANC 0.06 G/l), mild anemia (Hb 148 g/l) and thrombocytopenia (80G/l)
- *Initial evolution:*
  - CPAP started H2
  - Septic choc with paralytic ileus DOL 1, requiring intubation

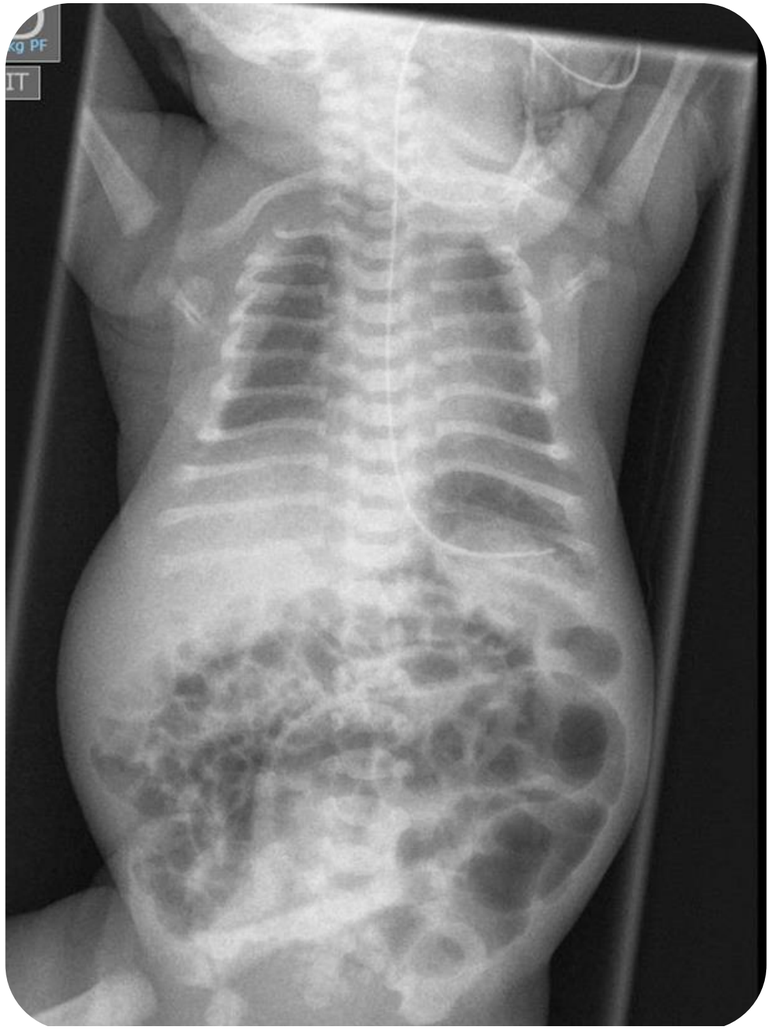

Image 1: The patient's chest and abdominal X-ray on DOL 1

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Case (continued)

- *Suspected diagnosis:* **Shwachman-Bodian-Diamond Syndrome** (SDS)
  - Exocrine pancreatic insufficiency searched and confirmed in this context
  - Genetic confirmation: compound heterozygous mutations SBDS gene (c.258+2T>C and c.183_184delinsCT)
- *Respiratory evolution:* respiratory insufficiency due to restrictive and hypoplastic lung disease
  - Extubation attempted after 14 days
  - Persistent need for NIPPV at 7M, hypercapnia
  - Mild pulmonary hypertension (resolved with O_2)
- *Growth evolution:*
  - Failure to thrive despite increased caloric intake and pancreas enzyme substitution
- *Hematological and infectiological evolution:*
  - Persisting anemia requiring 3 blood transfusions
  - Persisting severe neutropenia (isolation)
  - 3 episodes of febrile neutropenias treated with empiric ATB

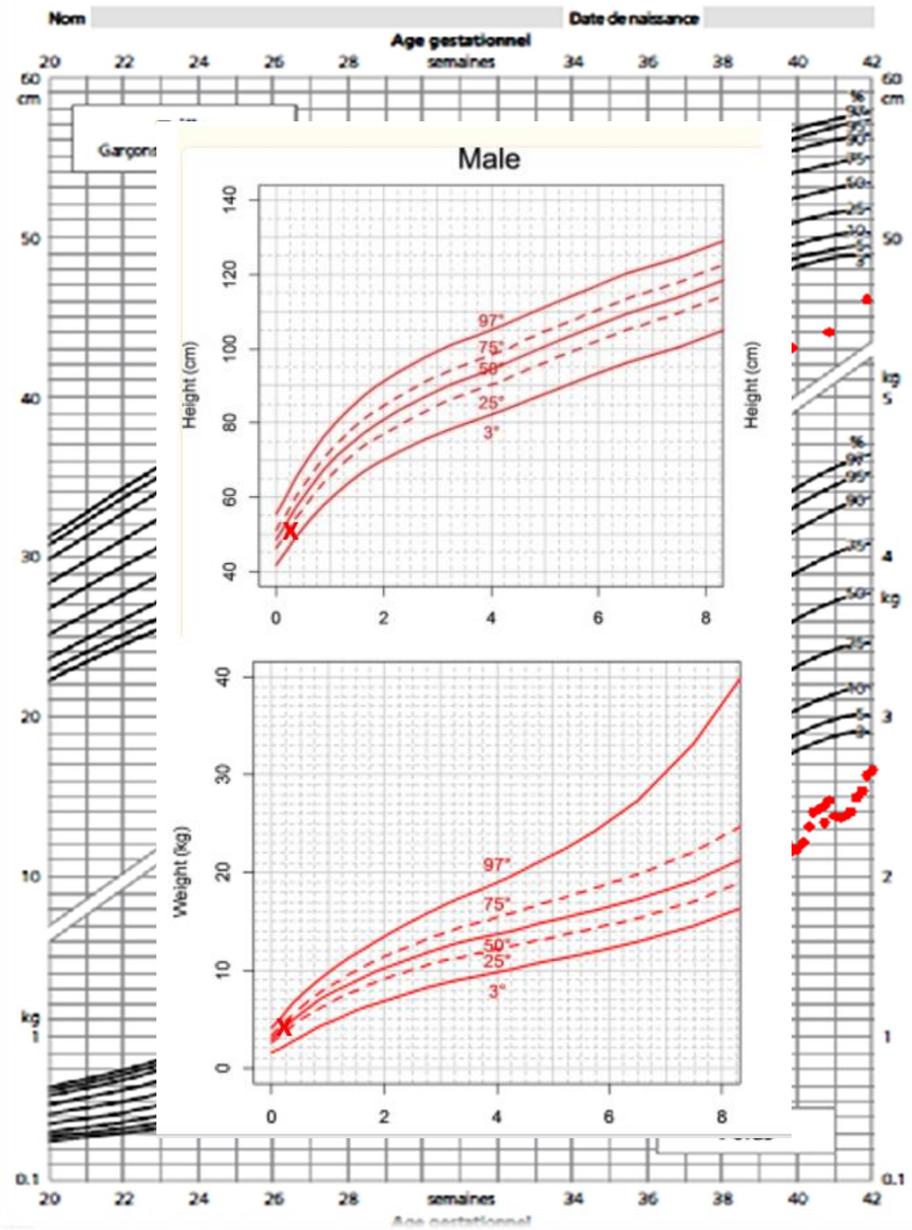

Image 2: The patient's growth chart for height (top) and weight (bottom)

Discussion

- **SDS syndrome** (MIM#617941): rare AR disease (≈1:160,000 live births)
  - essential role in **ribosome biogenesis**

  ➔Triad: **cytopenia (neutropenia), exocrine pancreatic ins. and skeletal dysplasia**
- In our patient: **severe phenotype** with early **neonatal onset due to skeletal dysplasia**
- Rib cage abnormalities seen in up to 50% of cases
- Prognosis uncertain with >50% mortality because:
  - Increased risk of myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML)
  - Hematopoietic stem cell transplantation (HSCT) is curative for SDS-associated BMF and/or MDS or AML
  - Eligibility for HSCT limited by our patient's respiratory situation (which may evolve)

Conclusion

- The association of **SD** with **cytopenia** (neutropenia), must raise SDS
- Search and treat exocrine pancreatic insufficiency
- Presentation with **severe thoracic dysplasia, respiratory failure and severe neutropenia** at birth is rare and poses therapeutic and ethical challenges that must be taken into consideration

Video 3 : Patient's respiratory distress at 3 months (consent from the mother was obtained)

Authors & Affiliation

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