Interleukin-2 receptor β deficiency: First reported case in an infant born to non-consanguineous parents, presenting with failure to thrive and enteropathy

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Introduction
We present a rare cause of immune deficiency, the first reported case attributable to this genetic abnormality in the absence of consanguinity.

Presentation
- Female infant born at term, birthweight 2.5kg, first child
- Exclusively breastfed for four months, meeting milestones and gaining weight along 9th centile
- Bronchiolitis at five months and found to be on the 0.4th centile
- At seven months of age weight static <<04th centile despite amino acid formula feeds via nasogastric tube (NGT)
- By nine months she had a chronic wet cough, significant rhinorrhea and an ongoing oxygen requirement

Assessment
- GI: Poor feeding, oral and perianal inflammation, chronic diarrhoea
- Rheum: Polyarticular swelling with sterile aspirations
- ID: Recurrent fevers, widespread lymphadenopathy – histology of tonsillar tissue showed numerous microbial pathogens
- Derm: Hyperpigmented lesions to the lower legs, umbilical rash, widespread eczema
- Ophthalmology: Chronic bilateral uveitis
- Developmental delay & soft dysmorphic features

Investigations
- Microcytic anaemia, thrombocytopenia, leucopenia
- CMV IgG positive, IgM negative
- Elevated ALT
- Fluctuating inflammatory markers
- Raised double negative T cells
- Hypergammaglobulinaemia: raised IgG & IgA
- Positive autoantibodies including: anti-cardiolipin, anti-B2G1, anti-MCV, Anti-GBM
- Faecal calprotectin – 777.1 (post-steroids)
- Bone marrow aspirate - No obvious infiltrate seen

Figure 1: Patient’s growth chart illustrating faltering growth from 16 weeks, improvement at nine months following NGT feeds, and continuation of growth following initiation of PN

Figure 2: D1 acute on chronic inflammation, lymphoid hyperplasia, villous blunting. Focal degenerative vacuolisation of the surface epithelial cells, D2 acute on chronic inflammation, focal villous blunting

Discussion
Interleukin-2 is involved in building protection against autoimmune disease by stimulating T-cell differentiation. Genetic mutations in its receptor are exceptionally rare, with only four homozygous defects identified in seven infants, one neonate, and two fetuses, all conceived to consanguineous marriage partners. Common clinical manifestations amongst the seven surviving the neonatal period reflect the underlying immune dysregulation with enteropathy, arthritis, uveitis, dermatitis and hypergammaglobulinaemia, together with a susceptibility to respiratory and herpesvirus infections.

Our patient initially presented with failure to thrive accompanied by recurrent infective episodes, eventually evolving into an inflammatory picture with little infective pathology after the first six months. Prior to HSCT, however, she did become symptomatic of reactivated CMV.

This case illustrates the complex interrelationship of autoimmunity, inflammation and susceptibility to infections associated with an underlying immune dysregulation and the MDT approach to the management of such patients.

Progress
- PN along with significant dietetic and speech and language involvement whilst inpatient
  - Weight at 13 months of age on the 5th centile
  - 24th centile at 15 months
  - Managing small amount of food orally
  - Pulsed Methylprednisolone followed by oral prednisolone
  - Systemic inflammatory symptoms improved significantly
  - Achieving developmental milestones
  - Haematopoietic stem cell transplant (HSCT) at 17 months of age

References

No conflicts of interest to declare. Katherine.Cornelius@wales.nhs.uk