Mendelian susceptibility to mycobacterial disease due to IL-12RB1 mutations in two siblings

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ABSTRACT

Background: Mendelian Susceptibility to Mycobacterial Disease (MSMD) is a rare genetic defect that interferes with the synthesis of IFN-γ. Eleven gene mutations (IL12B, IL12Rβ1, ISG15, TYK2, IRF8, SPPL2A, C4BB, IFNGR1, IFNGR2, STAT1, NEMO) has been recognised in MSMD. MSMD patients are at risk of tuberculous infection and less virulent non-tuberculous mycobacterium such as BCG vaccine substrains. Some patients are also susceptible to invasive Salmonella infections and mucocutaneous candida infection. Here, we report a case of siblings with IL12Rβ1 deficiency to investigate the spectrum of clinical presentation. **Methods:** Case notes of the patients were reviewed, and relevant clinical information were summarised and analysed. **Results:** An 8-year-old boy who received Bacille-Calmette-Guerin (BCG) at birth, presented twice at age 4 and 5 months with suppurative left axillary lymphadenitis which requiring surgical excision for the latter. He was subsequently treated with anti-tuberculosis (TB) therapy for 1 year. At age 4, he presented with a left inguinal abscess which was positive for *Salmonella sp.* And he was treated accordingly with no recurrence of illness thereafter. His 6-year-old younger sister, also vaccinated with BCG at birth, had a history of *Salmonella* meningitis at 2 weeks old and suppurative left axillary TB lymphadenitis at age 5 months, cervical TB lymphadenitis at age 9 months, and *Salmonella* septicaemia with disseminated BCG disease at age 21 months. Full blood counts, serum immunoglobulin and T and B cells enumeration were normal for both siblings. Whole exome sequencing results for both siblings showed homozygous mutations of the IL-12Rβ1 gene (missense mutation c.523C>T) consistent with autosomal recessive IL-12Rβ1 which causes MSMD. **Conclusion:** The disease spectrum of MSMD are highly variable from the most severe form of early onset, disseminated, recurrent and life-threatening mycobacterial disease to the least severe form of late onset or silent carrier due to incomplete penetration of the disease.