Severe combined immunodeficiency: A tale of two brothers

A male infant presented at five months of age with eventually fatal respiratory syncytial virus infection, and a history of chronic oral candidiasis and failure to thrive. A blood count to investigate neonatal jaundice had demonstrated lymphopenia (0.9×10^9/L), but this was not followed up in the newborn period. The clinical diagnosis of severe combined immunodeficiency (SCID) was confirmed by hypogammaglobulinemia and a deficiency of T cell numbers and function. X-linked SCID was suspected from the infant's family history, which showed that three maternal uncles died in infancy, and it was confirmed by mutation analysis (1).

The mother became pregnant again. Genetic testing on a chorionic villous sample showed an affected fetus. Chorionic villous sample human leukocyte antigen tissue typing results submitted to the bone marrow registry found a stem cell donor. The baby was delivered expectantly into conditions that were kept as sterile as possible, was treated with prophylactic antibiotics against *Pneumocystis jiroveci*, previously known as *Pneumocystis carinii* (a common pathogen in severe immunodeficiency), and was kept in protective isolation until he underwent a transplant two weeks after delivery. He was discharged home after three weeks, with early signs of bone marrow engraftment. He has had a full recovery, with a normally functioning immune system. He requires no ongoing therapy and should enjoy a normal life.

LEARNING POINTS

- SCID is a rare disorder in which babies are essentially born with little or no immune system, leaving them unable to defend themselves from potentially life-threatening infections. SCID has a high morbidity and mortality, unless treated early. Infants with SCID who receive bone marrow transplant before developing serious infections have an excellent prognosis, with 95% survival reported for infants undergoing bone marrow transplant in the first month of life.
- A general estimate of SCID incidence is one in 75,000 to 1,000,000 live births. The SCID study of the Canadian Paediatric Surveillance Program confirmed 19 cases between April 2004 and December 2007. Three deaths were confirmed at the time of yearly summaries.
- The key to improving the survival chances of a baby with SCID lies in early detection. Nearly all SCID cases have lymphopenia that is detectable at birth.
- Live-attenuated vaccines are contraindicated for infants and children with severe immunodeficiency diseases. Bacille Calmette-Guérin (BCG) vaccination is also contraindicated because of the risk for disseminated BCG infection.
- Great advances have been made in identifying a variety of molecular genetic defects causing SCID. Molecular diagnosis allows accurate genetic counselling and prenatal screening. Nine forms of SCID have been identified over the past 10 years. The two most common forms are:
  - X-linked SCID (approximately 50% of all cases), and
  - Adenosine deaminase deficiency (approximately 15% to 25% of cases).
- Effective therapeutic interventions, including bone marrow and stem cell transplantations, are now available for SCID patients. Gene therapy is also available for some cases of SCID. It involves introducing a normal copy of the defective gene through a virus vector into the patient's bone marrow cells.
- Canadian Blood Services' OneMatch is a member of an international network of registries, and can search more than 11 million donors on over 50 registries in other countries. By agreeing to make their donor data available worldwide, international registries have significantly increased the chances of being able to find a matching donor for any patient, anywhere in the world.

REFERENCES

1. Cohen L, Hirschfeld AF, Junker AK, Davis J, Turvey SE. Detection of a novel nonsense mutation in the interleukin 2 receptor gamma gene causing X-linked severe combined immunodeficiency. Ann Allergy Asthma Immunol 2006;96:632.

The Canadian Paediatric Surveillance Program (CPSP) is a joint project of the Canadian Paediatric Society and the Public Health Agency of Canada, which undertakes the surveillance of rare diseases and conditions in children and youth. For more information, visit our Web site at <www.cps.ca/cpsp>.

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