Haematopoietic Stem Cell Transplant for Wiskott-Aldrich Syndrome

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Abstract
We reviewed retrospectively 7 Chinese children diagnosed with Wiskott-Aldrich syndrome (WAS) and managed at the Department of Paediatrics & Adolescent Medicine of Queen Mary Hospital from 1988 to 2005. All patients presented with the classical triad of bleeding tendency, recurrent infections and infantile eczema from neonatal period to 2-3 months of age. The median lag time between diagnosis and presentation was 7 months. Thrombocytopenia and small platelet volume were consistent findings and present in all patients. Findings in immunoglobulin level, lymphocyte subset and lymphocyte proliferative studies were heterogeneous. Four mutations were found in 5 (2 cousins shared the same mutation). Haematopoietic stem cell transplant (HSCT) had been performed for all patients. All 7 had complete immune reconstitution with no major long-term complications in a median follow-up of 9.3 years. Early diagnosis and selection of appropriate donor for HSCT were important strategies for improved survival of patients with WAS.

Key words
Chinese; Haematopoietic stem cell transplant; Immunodeficiency; Wiskott-Aldrich syndrome

Introduction
Wiskott-Aldrich syndrome (WAS; MIM# 301000) is an X-linked recessive immunodeficiency characterised by thrombocytopenia and small platelet volume, eczema and recurrent infections due to combined cellular and humoral immunodeficiency. It is a rare disorder, occurring with a frequency of 4 per million male births.1,2 Phenotypic expression is highly variable. In some patients, they express the full triad of clinical manifestations, while others showed a milder phenotype which is known as X-linked thrombocytopenia. In a multi-institutional survey of 154 unselected patients with WAS, the classic triad was seen only in 27% of the study population, while 5% and 20% had only infectious manifestations and haematological manifestation (thrombocytopenia) before diagnosis.3 WAS is also associated with autoimmunity and malignancies.4,5 Major laboratory features of WAS, besides decreased platelet count and mean platelet volume, include progressive lymphopenia after 6 years of age, normal IgG, normal or low IgM, elevated IgA and elevated IgE, poor antibody response to polysaccharide antigens and diminished T cell response to a range of stimuli.5 The gene responsible for WAS, located on the short arm of chromosome X at Xp11.22-Xp11.23, was identified by positional cloning in 1994.6 The Wiskott-Aldrich Syndrome Protein (WASP) gene (GenBank NM_000377) consists of 12 exons, spanning 9 kb of genomic DNA, encoding a protein of 502 amino acids. Different researchers have looked into the function of WASP in the haematopoietic system. Recent evidence suggests that it belongs to the cytoplasmic scaffolding protein family and is functionally implicated in the regulation of the actin cytoskeleton.7 However, the mechanisms how mutations in WASP result...