Hypogammaglobulinaemia in a patient with ring chromosome 21

Shouichi Ohga, Futoshi Nakao, Osamu Narazaki, Naoki Fusazaki, Tomonobu Aoki, Kenji Kamesaki, Toshio Hara

Abstract
An 8 year old boy with ring chromosome 21 who was susceptible to sinorespiratory infections due to hypogammaglobulinaemia is reported. He presented with the characteristic features of monosomy 21 syndrome, such as psychomotor retardation, hypertonia, large saccular ears, prominent nasal bridge, micrognathia, thrombocytopenia, and patent ductus arteriosus. His serum IgG concentration was less than 1.5 g/l at 3 years and 6 months of age after repeated hospitalisations with pneumonia, otitis media, and convulsions. Regular replacement of intravenous gammaglobulin effectively reduced such infectious episodes. A predisposition to infection in patients with ring chromosome 21 may be explained by hypogammaglobulinaemia and merit treatment with gammaglobulin.

Keywords: gammaglobulin treatment; hypogammaglobulinaemia; monosomy 21 syndrome; ring chromosome 21

Monosomy 21 syndrome (21q− or 21-deletion syndrome) is a rare congenital anomaly characterised by such clinical features as intrauterine growth retardation (IUGR), psychomotor retardation, hypertonia, antimongoloid slant, prominent nasal bridge, large and saccular low set ears, and micrognathia.1 2 Despite there having been several reports dealing with this syndrome, increased susceptibility to infections and associated immunological defects have not been clearly described.3–6 The World Health Organisation classification of primary immunodeficiency disease’ lists trisomy 21 (Down’s syndrome), deletions or rings of chromosome 18 (18p− or 18q−), and Turner’s syndrome (XO), but not monosomy 21 as constitutional chromosomal defects associated with immunodeficiency.

We describe a case of ring chromosome 21, where there was the characteristic manifestation of monosomy 21 syndrome together with hypogammaglobulinaemia, and where the infection was successfully controlled with gammaglobulin treatment. The clinical significance of hypogammaglobulinaemia in monosomy 21 is discussed.

Case report
A Japanese boy aged 3 years 6 months was referred to our hospital for investigation into the cause of recurrent infections. His parents were cousins, and a 2 year old male sibling was healthy. There was no immunological disease or chromosomal abnormality among relatives. He had been born to a healthy mother with no history of medication or infection during the pregnancy at 42 weeks’ gestation and weighed 2098 g at birth. IUGR was diagnosed antenatally. At 47 days, patent ductus arteriosus and mild aortic stenosis were found. Cytogenetic study of peripheral lymphocytes revealed a karyotype of 46,XY,r(21)(p11q22) in all 20 cells examined. High resolution analysis showed the fusion site of a ring chromosome 21 (fig 1). Heart failure resolved after ligation of the patent ductus arteriosus at 12 months of age. Convulsions emerged at 19 months of age and he suffered from acute hepatitis of an unknown cause at 24 months of age. Thereafter, he was hospitalised seven times during a period of 18 months because of pneumonia, otitis media, and convulsions.

On admission, physical examination revealed an alert short, skinny boy of 89 cm in height (−6.1 SD) weighing 8629 g (−3.9 SD) with high fever (39°C), tachycardia, and tachypnoea due to pneumonia. Antimongoloid slant, prominent and broad nasal bridge, large saccular low set ears, high arched palate, micrognathia, and cryptorchidism were noted, but there was no anaemia, jaundice, skin eruption, purpura, lymphadenopathy, or hepatosplenomegaly. Auscultation revealed...
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respiratory moist rales and an ejection systolic heart murmur (Levine 3/6) at the left sternal border. Neurological examination demonstrated general hypertonicity, hyperactive reflexes, and psychomotor retardation. He was able to roll over, but could not crawl or sit up by himself. Peripheral blood counts showed a white cell count 15.4 × 10^9/l with 3% metamyelocytes, 12% bands and 38% segmented neutrophils, 26% lymphocytes, 20% monocytes, and 1% eosinophils, red cell count 4140 × 10^12/l, haemoglobin 123 g/l, and a platelet count of 45 × 10^12/l. Blood chemistry indicated normal liver and kidney function. Analysis of the serum protein fraction before the first administration of gammaglobulin showed a total protein level of 41 g/l (normal range 67–83), with 63.7% albumin (59.7–70.8), 7.0% alpha1- (1.6–2.9), 17.3% alpha2- (5.8–67–83), with 63.7% albumin (59.7–70.8), total protein level of 41 g/l (normal range before the first monosomy; the first description was of an syndrome was originally defined as group G and recurrent infections. Monosomy 21 syndrome is due to 21q deletion or other accompanying defects. The examination of Btk genes to exclude the chance association of X linked agammaglobulinaemia with this syndrome showed no abnormality. No excessive protein loss was evident. These indicate a congenital defect in immunoglobulin production in this syndrome, but do not confirm a specific intrinsic abnormality within the B cells. Our observation may provide helpful information in
elucidating the basic mechanism of B cell maturation, as well as in the further mapping of chromosome 21.

We are grateful to Shoji Hashimoto, MD and Satoshi Tsukada, MD (Third Department of Internal Medicine, Osaka University Medical School, Osaka) for the analyses of Btk kinase activity and the Btk gene. The English was revised by Miss K Miller (Royal English Language Centre, Fukuoka, Japan). This work was supported in part by a grant from the Ministry of Health and Welfare for Primary Immunodeficiency Diseases.

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Arch Dis Child 1997 77: 252-254
doi: 10.1136/adc.77.3.252

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