



Autoimmune Neutropenia with Functional Hyposplenia and Dextro Isomerism

Y Singh, G C Rastogi

The association of dextro isomerism with functional hyposplenia or asplenia is well recognised (1), but the association of dextro isomerism, hyposplenia / asplenia with autoimmune neutropenia (AIH) has not previously been reported. This case with an unusual association of autoimmune neutropenia, functional hyposplenia and dextro isomerism is being presented.

This infant presented with an asymptomatic heart murmur at the age 11 weeks. Echocardiography showed laevo-cardia with abdominal aorta to the right of the spine and inferior vena cava to the left of the spine, uninterrupted.

There was a total anomalous pulmonary venous drainage to the lower part of the right superior vena cava, possibly via the azygos, with no significant obstruction. There was a complete atrio ventricular defect and, in addition, a large superior sinus venous atrial septal defect, and a common atrio ventricular valve with no incompetence. Abdominal ultrasound confirmed the presence of a spleen. However the peripheral smear showed Howell Jolly bodies, suggesting functional asplenia. Full blood count showed neutropenia, which varied between 0.1×10^9 and 0.4×10^9 , and was not cyclical. An iso immune type of neutropenia was excluded, as maternal blood was negative for neutrophil antibodies. Anti IgG and anti IgM type anti-granulocyte antibodies were detected in the infant's blood. Anti-lymphocyte antibodies were not found. The presence of granulocyte specific IgG and IgM antibodies in the infant serum confirmed the diagnosis of autoimmune neutropenia. In view of the functional hyposplenia and neutropenia this infant has been kept on prophylactic

antibiotic. At the age of 11 months this infant's neutrophil count spontaneously recovered to 1.7×10^9 .

The definition of neutropenia in infants is different from that in adults (2). In infants aged 2 weeks to 1 year, the lower limit of normal neutrophil count is $1.0 \times 10^9/L$. After the first year of life, the lower limit is $1.5 \times 10^9/L$, as in adults. Neutropenia can be acute or chronic, when lasting >6 months. Chronic benign neutropenia can be regarded as a synonym of autoimmune neutropenia (AIN) in children. AIN of infancy is a very rare condition and its estimated incidence in the Scottish population is approximately 1 in 100,000 children per year. AIN has a slight preponderance in girls (3-4). Howell-Jolly bodies in the presence of anatomically normal spleen confirm functional hyposplenia (2,5).

Primary AIN is caused by granulocyte-specific autoantibodies and occurs predominantly in infancy. Clinical presentation and diagnosis have not been well established, resulting in burdening diagnostic investigations and unnecessary treatment with granulocyte colony-stimulating factor (G-CSF) (6).

AIN is either primary or secondary. In primary AIN, neutropenia is the only abnormality. In secondary AIN, other primary pathologies occur, including systemic autoimmune disease, infections, and malignancy. In infants, secondary AIN is extremely rare (6).

Diagnosis is serological. The most commonly detected antibodies are immunoglobulin G (IgG) antibodies against specific neutrophil antigens, most commonly against anti-neutralizing antibody (NA)1 and anti-NA2, but also against other neutrophil antibodies (7-8). In one study by Lalezari and colleagues, neutrophil

From the Departments of Paediatrics, Wycombe Hospital, United Kingdom.

Correspondence to : Dr. Y. Singh, 28 Bryn Morfa, Bodelwyddan Rhyll LL18 5TP, United Kingdom.



antibodies were demonstrated in 119 cases out of 121 infants with chronic neutropenia, thereby establishing the autoimmune nature of the disease(8).

In one study of 240 cases, primary AIN was mainly diagnosed at the age of 5 to 15 months but was observed as early as day 33 of life. In 90% of the cases, AIN was associated with benign infections despite severe neutropenia(3).

Spontaneous remission, shown by 95% of the patients, usually occurred within 7 to 24 months. Though 89% of the patients received antibiotics for prophylaxis of infections, symptomatic treatment with antibiotics was sufficient in most patients. For severe infections or for surgical preparation, G-CSF, corticosteroids, and intravenous IgG were administered, resulting in increased neutrophil counts in 100%, 75%, and 50% of the patients treated, respectively. In another two studies, all cases of AIN followed the classic benign course of the condition and all children eventually attained a normal absolute neutrophil count (4-9). In the presented case of AIN with functional hyposplenism, the clinical course has been benign, although this infant has been given prophylactic amoxicillin for functional hyposplenism. In conclusion, we believe this is the first case of AIN with functional hyposplenism and dextro isomerism. Despite functional hyposplenism, the clinical course of AIN has been benign in our case. We

recommend that after a confirmed serological diagnosis of AIN, these children should not be burdened with further diagnostic investigations, even in the presence of functional hyposplenism.

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