Paroxysmal Cold Haemoglobinuria Following Measles Immunization

Immunization with live attenuated measles vaccine is generally considered to be a safe procedure, and though a mild measles-like illness may follow immunization, severe reactions are rare (Dudgeon, 1969). Paroxysmal cold haemoglobinuria has previously been reported in association with natural measles infection (Dacie, 1954; O’Neill and Marshall, 1967); we report here a case after measles immunization.

Case Report

Our patient was a 19-month-old girl who, 6 weeks before her admission, was immunized with live attenuated measles vaccine (Schwarz strain, Glaxo Laboratories Ltd.). 3 weeks later she developed a mild illness with a morbilliform rash, conjunctivitis, and rhinorrhea; this was complicated by bronchitis, and over the week before admission she became increasingly ill with anorexia, vomiting, and haemoglobinuria. There was no history of exposure to natural measles infection.

On admission she was pale and lethargic, but there was no lymphadenopathy, hepatosplenomegaly, or jaundice. Hb was 3.3 g/100 ml, WBC 33,000/μl (neutrophils 44%, lymphocytes 45%, metamyelocytes 11%), and platelets 498,000/μl. The reticulocyte count was 5%, and a blood film showed marked erythrocyte anisocytosis and polychromasia, and a moderate number of normoblasts. The direct antiglobulin and Donath-Landsteiner tests were both strongly positive, confirming the diagnosis of paroxysmal cold haemoglobinuria; spectroscopic examination of her urine, however, did not show any Hb pigments. Syphilis was excluded by negative Wassermann reactions and VDRL screening tests in the patient and both her parents. The measles complement-fixing antibody titre was 1 in 128.

Serological investigations. The positive direct antiglobulin and Donath-Landsteiner tests were obtained by standard methods. The patient’s serum contained a biphasic, complement-fixing IgG antibody, which had the specificity anti-P, typical of a Donath-Landsteiner antibody. The relation of anti-P to other antibodies of the P blood group system is shown in the Table.

The antibody differed from the syphilitic type of Donath-Landsteiner antibody only in its capacity to sensitize erythrocytes at relatively high temperatures. In this case we obtained laboratory evidence of sensitization up to 25 °C.

Clinical progress. The patient was kept warm with an electric blanket, and was given a transfusion of packed red cells, warmed to approximately 37 °C, which raised her Hb level to 14.2 g/100 ml. She has remained well for 4 months, with no recurrence of haemoglobinuria. The direct antiglobulin and Donath-Landsteiner tests were still positive on the day after transfusion, but became negative a week later.

Discussion

In its classical form, paroxysmal cold haemoglobinuria (PCH) is an uncommon, benign, autoimmune disorder, characterized by attacks of haemolysis with haemoglobinuria on exposure to cold, and is usually associated with congenital or acquired syphilis. The antibody is of IgG type, and binds with erythrocytes at low temperature; haemolysis occurs on subsequent warming of the blood (Donath and Landsteiner, 1904). Complement

<table>
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<td>Relation of Donath-Landsteiner Antibody to P Blood Group System</td>
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<table>
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<tr>
<th>Specificity</th>
<th>Remarks</th>
<th>P₁</th>
<th>P₂</th>
<th>P₁⁺⁻</th>
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<tr>
<td>Anti-P₁</td>
<td>Formerly anti-P</td>
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<tr>
<td>Anti-P</td>
<td>Donath-Landsteiner antibody</td>
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<tr>
<td>Anti-P + Pk</td>
<td>Formerly anti-Tj⁺</td>
<td>+</td>
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fractions C2, C3, and C4 are required in the warm phase, and fraction C1 is probably required in the cold phase (Hinz, Picken, and Lepow, 1961).

Since the introduction of penicillin treatment for syphilis, PCH has become much less common, and an increasing proportion of cases is now seen in association with acute viral infections (Dacie, 1962). In the majority of virus-associated cases the attack of haemolysis occurs either during the prodromal stage or shortly after the clinical appearance of the infection. One patient, however, developed PCH 5 weeks after an attack of mumps (Colley, 1964): our patient developed PCH 6 weeks after measles immunization. The possibility that her mild measles-like illness 3 weeks after immunization was in fact a coincidental natural measles infection cannot be excluded, though the absence of a positive history of contact and the frequency of such reactions after immunization with live measles vaccine make this unlikely.

An important difference between syphilitic and virus-associated PCH is the acute transitory nature of the latter (Dacie, 1962). The haemoglobinuria generally persists for only a few days, and may, as in our patient, have ceased before admission. The antibody disappears from the serum after a period ranging from a few days to several weeks, at which time the direct antiglobulin and Donath-Landsteiner tests become negative. However, the attack, while it lasts, may endanger life, and usually necessitates transfusion with ABO and Rhesus compatible cells, warmed to approximately 37 °C. The great rarity of P negative cells, which would be unaffected by the antibody, makes their use impracticable. The severity of haemolysis in these cases may be due to the antibody having a higher thermal range for erythrocyte sensitization (up to 25 °C in our patient) than in syphilitic cases (rarely as high as 20 °C) (Dacie, 1962; Schubote and Haenle, 1961; Colley, 1964).

**Summary**

A case of paroxysmal cold haemoglobinuria is described in a 19-month-old girl following measles immunization.

Haemoglobinuria occurred during the sixth week after immunization, and was associated with a raised measles antibody titre. The autohaemolsin was a typical Donath-Landsteiner antibody, having specificity within the P blood group system, but it showed the higher thermal range for erythrocyte sensitization characteristic of the acute transient variety of this disorder.

We are indebted to Dr. B. S. B. Wood, consultant paediatrician, for permission to publish details of his patient, and to Dr. J. Stuart, consultant haematologist, for his helpful encouragement and advice.

**References**


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**Intrahepatic Gas Shadows in Neonatal Duodenal Obstruction**

The presence of branching intrahepatic gas shadows extending to the liver edge in the neonate has been attributed to gas in the portal venous system, and has been considered a grave prognostic sign as it may be a feature of necrotizing enterocolitis (Touloukian et al., 1967; Wilson and Woolley, 1969), often with a Gram-negative bacteremia.

**Case Reports**

**Case 1.** A male child, 2,835g, was born by lower caesarian section for antepartum haemorrhage. Bile-stained vomiting started on the first day. Meconium was passed from the 1st to 3rd days. Continued vomiting led to transfer from the maternity hospital. Examination on admission on the 5th day showed visible epigastric peristalsis in a scaphoid abdomen. X-ray of the abdomen (Fig. 1), showed a branching pattern of gas shadows extending out nearly to the edge of the liver shadow. A little gas was seen in the intestines. Laparotomy revealed a severe stenosis of the duodenum distal to the common bile duct opening. The jejunum and ileum were normal and there was no evidence of ischaemic gut. A posterior duodenojunostomy was performed with good recovery.