Case Report on a Child with Paroxysmal Cold Haemoglobinuria

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Abstract PCH is one of the most common causes of acute AIHA in young children, although it affects patients of all ages. In children it is commonly seen following a viral illness or after immunization. Donath Landsteiner test is the diagnostic test. This is a case report of a child who presented with features of haemolysis and was diagnosed as PCH.

Keywords Paroxysmal cold haemoglobinuria (PCH) · Autoimmune haemolytic anaemia (AIHA) · Donath Landsteiner (D-L)

Introduction

PCH is a rare syndrome, which is mediated by a biphasic antibody causing direct intravascular haemolysis [1]. In children it results in an acute life threatening haemolytic process, that primarily occurs after an infection and in adults it tends to occur either as a polyclonal syndrome following an infection or associated with a monoclonal IgM protein where a high proportion may have a lymphoproliferative disorder [2].

We report a case of a child presented with evidence of intravascular haemolysis, and diagnosed as PCH with mild renal impairment.

Case Report

A 3 year old previously healthy girl was admitted to the paediatric unit of with a 3 day history of fever associated with cough and cold. On admission she passed dark red-to-black coloured urine. The following day she was found to be very pale and mildly icteric with a mild hepatomegaly.

The initial investigations revealed a Hb of 4.5 g/dl, with normal white cell and platelet count. The blood smear showed red cell agglutination with moderate number of spherocytes. The reticulocyte count was normal initially. Serum bilirubin was 56 µmol/l with the direct fraction of 9 µmol/l. Urine examination revealed weakly positive haemosiderin, indicating intravascular haemolysis, with absent bile and no red cells were seen under microscope. Renal function was deranged with a high blood urea and serum creatinine. These results pointed towards an intravascular haemolysis with mild renal impairment.

Due to the low Hb, she was transfused with packed cells and the post-transfusion Hb was 9.1 g/dl. She was transferred to the high dependency unit for further management. Subsequently the direct coomb's test was performed which became positive with C3d specificity and IgG was negative. The cold agglutinin titre was not significant with adult cells, cord cells and patient's cells, which could have been due to multiple transfusions. However, the Donath Landsteiner test was positive which directed towards the diagnosis of PCH. As the Hb dropped further to 6.5 g/dl while in the high dependency unit where the temperature is less than 20°C, the patient was transferred back to the general paediatric ward where she made an uneventful recovery following blood transfusion. This fact further emphasized the diagnosis of PCH. On discharge the renal functions were normal.

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In view of finding of an underlying cause, serological investigations were performed for mycoplasma and EBV infection, which were negative. However, tests for other viral infections were not performed.

Discussion

PCH was first recognized as a distinct clinical entity in 1872 and the hemolytic antibody was described by Donath and Landsteiner. The antibody was first observed as a cross-reacting antibody to an antigen on *Treponema pallidum*. Obviously this is now rare [2]. It is commonly encountered in children with postviral illness [3] or after immunization [3, 4]. Some episodes occur in patients with lympho-proliferative disorders and collagen vascular disease [2]. Acute PCH typically occur in young children and the median age of presentation is 5 years although it affects patients of all ages [5]. Currently, chronic PCH is very rare and almost all cases are of acute and transient type [5]. Acute attacks are frequently severe but the illness resolves spontaneously within a few days to several weeks after onset [5]. The incidence of PCH according to the data available vary from 5.1 to 10% and the boy-to-girl ratio is 2.1:1 [5].

The child usually presents with a history of an upper respiratory infection. Pallor, jaundice and haemoglobinuria are the most common clinical findings and abdominal pain, fever are also common. 25% of cases present with hepatosplenomegaly [5, 7] as a reactive process [6]. The presence of P antigen on skin fibroblasts is thought to give rise to urticaria.

Severe and rapidly progressive anaemia occur with relative reticulocytopenia in some at the time of presentation as that occurred in this patient. Reticulocytopenia represents an ineffective marrow response either to viral haemopoietic suppression or preferential destruction of red cells by D-L antibodies [6]. Spherocytosis is particularly common in peripheral blood. Other features are anisopoikilocytosis, fragmented red cells, basophilic stippling, polychromatophilia, autoagglutination, erythrophagocytosis and nucleated erythrocytes [5].

In this patient urine haemosiderin positivity confirmed intravascular haemolysis and the C3d specificity supported immune-mediated haemolysis. As PCH is one of the most common causes of acute AIHA in the young children [5], the Donath Landsteiner test, which is the diagnostic test [5], was performed together with a control and it was positive. However, the cold agglutinin titre was also performed and it was not significant. The autoantibody associated with PCH is termed a biphasic hemolysin as it

sensitizes red blood cells in the cold but only haemolyses them when the red blood cells reach 37°C [5, 8]. The thermal amplitude range up to 15–24°C [8]. Rare patients have been described when the DL test is positive when the incubation phase is as high as 32°C [5].

Once D-L positivity is obtained in the DL test, determination of the specificity of the autoantibody is indicated though it was not performed in this patient. Almost all cases of PCH are associated with anti-P specificity, although other specificities associated with PCH have been rarely reported [5]. Commonly, the titre and thermal range of the antibody fall rapidly, so that 2 to 3 months later it is no longer detectable [5].

Though acute attacks are frequently severe it characteristically resolves spontaneously within a few days to several weeks after onset and rarely recurs [5]. This patient required only supportive care which included blood transfusion and warming. The great rarity of P negative cells, which would be unaffected by antibody, makes their use impracticable [4].

Corticosteroids are often given although their effectiveness is difficult to evaluate because of the transient nature of haemolysis [5]. In adults it is treated with cyclophosphamide. Rituximab was used successfully in rare refractory cases [7]. Clearance of the antibody may be possible with plasma exchange [2].

In our patient we could not find the causative agent. However, the prognosis of acute PCH is excellent, although deaths have been reported [5].

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