Paroxysmal cold haemoglobinuria in syphilis patients

Paroxysmal cold haemoglobinuria (PCH) was first described by Donath and Landsteiner in 1904 and is one of the rarest autoimmune haemolytic anaemias. Acute intermittent attacks of intravascular haemolysis following exposure to cold and the presence of a biphasic haemolysin, the Donath-Landsteiner (DL) antibody, are the classical clinical manifestation and pathognomonic laboratory finding of PCH. The autoantibody is typically IgG, usually showing anti-P specificity. The antibody is described as biphasic because it sensitises red cells at 0-4°C and causes complement-mediated haemolysis when the temperature is raised to 37°C.

The association of PCH with syphilis, particularly the congenital form, has been described earlier. Although there has been a decline in the prevalence of syphilis subsequent to the advent of antibiotics, there are still certain regions in India with a high prevalence of the disease.

We undertook a study on 26 patients with syphilis (four primary and 22 secondary syphilis) over a period of six months. The study of the incidence of PCH in syphilis patients and to seek a correlation between DL antibody and evidence of haemolysis. The patients were aged 12 to 36 years and 18 of them were males. Twenty five healthy controls were also studied. The diagnosis of syphilis was based on clinical and serological findings. All patients were given penicillin therapy 10-20 million units over a period of 21 to 28 days. The environmental temperature to which the patients were exposed varied from 10-36°C.

A complete haematological profile was obtained, along with urine tests for the presence of haemoglobin and haemosiderin, together with VDRL test for evidence of syphilis. To demonstrate paroxysmal cold haemoglobinuria direct and indirect Donath Landsteiner (DL) antibody tests, direct and indirect antiglobulin tests and DL antibody titre and specificity of DL antibody was also done. Only three patients gave a history of passing dark coloured urine, although none of these presented to the hospital with evidence of acute haemolysis. Direct antiglobulin test (DAT) was positive with polyspecific anti-globulin reagent in four patients, who were also positive with monospecific anti-C3 antiglobulin reagent, but negative with anti-IgG. Elution studies showed a non-reactive eluate in these four cases. The indirect antiglobulin test was positive at 4°C and 22°C in seven of the 26 cases. Various tests were performed to detect the presence of DL antibody in these patients. Seven out of 26 patients (27%) showed evidence of DL antibody, including the three patients with a history of haemoglobinuria. Urine examination showed the presence of haemosiderin in two of the seven DL positive patients. (These seven all had secondary syphilis.) Anti-P specificity was also demonstrated in these cases. All the 25 controls were negative for DL antibody.

Reticulocyte count, used as an indicator of accelerated erythropoiesis, ranged from 2.5-7% to 7% (mean 4.92%) in the DL+ cases. A significant correlation was established between the presence of DL antibody and reticulocyte count (p < 0.01). Of the 26 patients, only 12 (46%) could be followed up after treatment, including all 7 DL+ cases. In three of these seven patients the DL antibody disappeared immediately after treatment. In the remaining four cases, one showed a decrease in DL antibody titre from 1:2 to 1:1 while in the rest it remained unchanged. DL antibody titres ranged from 1:1 to 1:4 and anti-P specificity was demonstrated in all seven DL positive cases. Direct antiglobulin test was found to be positive in four out of the seven DL positive cases showing complement component on the red cells, while none of the DL antibody negative patients had a positive DAT.

This study showed that the presence of DL antibody in syphilis patients can lead to paroxysmal cold haemoglobinuria, especially on exposure to cold, which may go unnoticed in the absence of a typical history. Detection of DL antibody may thus have therapeutic implications in syphilitic patients, especially in avoiding exposure to cold temperature; however, in severe haemolysis steroids may be helpful in some cases.

NEELAM DHINGRA KUMAR
SEEMA SETHI
R K PANDHI
University College of Medical Sciences, and Guru Tegh Bahadur Hospital, Shadara, Delhi-110095, India

Address for correspondence: Dr Neelam Dhingra Kumar, B-141, South Moti Bagh, New Delhi-110021

Paroxysmal cold haemoglobinuria in syphilis patients.

N D Kumar, S Sethi and R K Pandhi

*Genitourin Med* 1993 69: 76
doi: 10.1136/sti.69.1.76