Blood Reviews (2008) **22**, 17—31

ELSEVIER

www.elsevierhealth.com/journals/blre

REVIEW

Hemolytic anemia due to warm autoantibodies

Charles H. Packman *

University of North Carolina School of Medicine, Chapel Hill, North Carolina
Hematology-Oncology Section, Department of Internal Medicine and Blumenthal Cancer Center, Carolinas Medical Center, 1000 Blythe Boulevard, MMP-6, Charlotte, NC 28203, United States

KEYWORDS
Autoantibodies;
Hemolytic anemia;
Spherocytes;
Reticulocytes;
Direct antiglobulin test;
Coombs test;
Immunoglobulin;
Complement

Summary The diagnosis of autoimmune hemolytic anemia (AHA) requires evidence of shortened red blood cell (RBC) survival mediated by autoantibodies directed against autologous RBCs. About 80 percent of patients with AHA have warm-reactive antibodies of the IgG isotype; the remainder exhibit cold-reactive autoantibodies. Typical patients exhibit anemia, reticulocytosis, spherocytes and polychromasia on the blood film and a positive direct antiglobulin test (DAT). Increased indirect serum bilirubin, urinary urobilinogen and serum lactate dehydrogenase (LDH), and decreased serum haptoglobin are not required for the diagnosis, but are frequently present.

Patients with AHA and no underlying associated disease are said to have primary or idiopathic AHA. AHA in patients with associated autoimmune disease and certain malignant or infectious diseases is classified as secondary. The etiology of AHA is unknown.

Patients with symptomatic anemia require transfusion of RBCs. Prednisone and splenectomy may provide long term remission. Rituximab, intravenous immunoglobulin, immunosuppressive drugs and danazol have been effective in refractory cases and for patients who are poor candidates for surgery.
© 2007 Elsevier Ltd. All rights reserved.

Introduction

Hemolytic icterus was familiar to clinicians by the start of the 20th century. Two forms, congenital (or familial) and acquired, were recognized but they could not be precisely distinguished and some authorities doubted the existence of acquired hemolytic icterus.[1] Many patients with hemolytic icterus exhibited jaundice, splenomegaly, anemia, spherocytosis, reticulocytosis and increased osmotic fragility of red blood cells (RBCs). Sera from some patients with hemolytic icterus directly agglutinated normal or autologous RBCs in vitro. Sera from other patients caused hemolysis. The responsible serum factors were respectively termed direct (saline) agglutinins or hemolysins. Much later it was determined that most agglutinins were IgM antibodies and that hemolysins were

* Tel.: +1 704 355 2884; fax: +1 704 446 5143.
E-mail address: cpackman@carolinas.org

0268-960X/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.blre.2007.08.001

also antibodies that required the presence of fresh serum complement to mediate lysis. However, most patients with hemolytic icterus exhibited neither direct agglutinins nor hemolysins and their infrequent association with hemolytic icterus offered no distinguishing diagnostic information.

That was the general state of affairs for over 50 years,[1] until the seminal paper of Coombs, Mourant, and Race[2] in 1945 reported that RBCs coated *in vitro* with nonagglutinating Rh antibodies (later shown to be IgG isotype) could be agglutinated by rabbit antiserum to human γ-globulin; this is now termed the indirect antiglobulin test (IAT). Initially unknown to Coombs and colleagues, the antiglobulin principle, i.e., that antiglobulin serum could cross-link antibody—coated particles to produce visible agglutination, had been previously described 37 years earlier in an obscure German-language journal by Moreschi.[3] Credit was given to Dr. Moreschi in a subsequent paper[4] and later by Dr. Coombs in other articles and lectures. Shortly thereafter, Boorman, et al.,[5] and Loutit, et al., [6] reported that rabbit antiglobulin serum agglutinated RBCs taken directly from patients with suspected acquired hemolytic anemia, including those lacking saline agglutinins or hemolysins. This procedure is now termed the direct antiglobulin (Coombs') test (DAT). RBCs from patients with presumed congenital hemolytic anemia, which we now recognize as hereditary spherocytosis, did not agglutinate. The positive direct antiglobulin reaction in AHA is attributable to *in vivo* coating of the RBCs with immunoglobulins (mainly IgG) and/or complement proteins and it is the main distinction between hereditary spherocytosis (congenital hemolytic icterus) and AHA (acquired hemolytic icterus).

Demographics and classification of AHA

Warm antibody AHA is uncommon, with an annual incidence of about 1 per 75,000—80,000 population.[7] It has been diagnosed in people of all ages, but most patients are over age 40, and the peak incidence occurs around the seventh decade. This age distribution may be related to the increased frequency of lymphoproliferative malignancies in the elderly, resulting in an age-related increase in secondary AHA due to lymphoma. Most cases of primary AHA arise sporadically; familial cases are rare.[8—10]

Table 1 CLASSIFICATION OF HEMOLYTIC ANEMIA MEDIATED BY ANTIBODIES.

I.	Warm-autoantibody type
A.	Primary or idiopathic warm antibody AHA
B.	Secondary warm antibody AHA associated with:
1.	Lymphoproliferative disorders, e.g., Hodgkin disease, lymphoma
2.	Rheumatic/ autoimmune disorders, e.g., SLE, ulcerative colitis
3.	Certain nonlymphoid neoplasms, e.g., ovarian tumors
4.	Ingestion of certain drugs, e.g., α-methyldopa
II.	Cold-autoantibody type
A.	Mediated by cold agglutinins
1.	Idiopathic (primary) chronic cold-agglutinin disease (most of these exhibit evidence of monoclonal B-lymphoproliferation)
2.	Secondary cold-agglutinin hemolytic anemia associated with:
a.	Infections (e.g., *Mycoplasma pneumoniae* or infectious mononucleosis)
b.	Clinically-evident malignant B-cell lymphoproliferative disorder
B.	Mediated by cold hemolysins
1.	Idiopathic (primary) paroxysmal cold hemoglobinuria
2.	Secondary
a.	Donath-Landsteiner hemolytic anemia, usually associated with an acute viral syndrome in children
b.	Associated with congenital or tertiary syphilis in adults
III.	Mixed cold and warm autoantibodies
A.	Primary or idiopathic mixed AHA
B.	Secondary mixed AHA
1.	Associated with the rheumatic disorders, especially SLE
IV.	Drug-immune hemolytic anemia
A.	Hapten or drug-adsorption mechanism
B.	Ternary (immune) complex mechanism
C.	True autoantibody mechanism

Download English Version:

https://daneshyari.com/en/article/2106332

Download Persian Version:

https://daneshyari.com/article/2106332

Daneshyari.com