Acquired hemolytic anemia are a group of disorders in which premature destruction of the red cells results from an extra corpuscular abnormality i.e. defect outside the red cell, unlike congenital hemolytic anemia in which the defect is intrinsic to the red cell. Normal compatible red cells transfused to a person with acquired hemolytic anemia are destroyed rapidly but the patients cells transfused to a normal recipient have normal survival. Some of the common acquired hemolytic anemia are discussed below.

IDIOPATHIC AUTO-IMMUNE HEMOLYTIC ANEMIA

This type of hemolytic anemia can occur at any age, although adults are more commonly affected than children. It affects females more often than males. The onset may be acute or insidious and hence the course of the disease may be rapid and fulminating or chronic. When the disease is acute, patient presents with severe anemia, weakness and jaundice. Complications of severe intravascular hemolysis like oliguria and cola colored urine may be present in some cases. Mild splenomegaly is usual. Circulatory collapse, renal failure and severe anemia can lead to death although it is rare. Majority of patients have insidious onset with symptoms and signs of anemia for which they have received hematinics without much relief. The spleen is nearly always palpable and mild to moderate jaundice is usually present but a small number of patients may not have jaundice either. As against the previously described acute type, hemoglobinuria and renal failure are rare in those with insidious or chronic disease. Presence of lymphadenopathy and massive splenomegaly should alert the physician to look for secondary causes of hemolytic anemia like chronic lymphocytic leukemia or non Hodgkin’s lymphoma.

Investigations: The blood picture shows anemia with reticulocytosis. The peripheral blood smear shows spherocytes and increased rouleaux formation. In acute hemolytic episodes the white cell count may be raised with shift to left showing myelocytes and metamyelocytes. The platelet count is usually normal.

Auto antibodies can be demonstrated in vitro in most cases of warm antibody hemolytic anemia, on the surface of red cells and in the serum. The direct Coomb’s test detects incomplete antibodies present on the red cell surface. The indirect Coomb’s test may be positive or negative depending upon the concentration of antibodies in the serum. Antibodies may be cold or warm depending upon the temperature at which they react. Warm antibodies react at 37° C whereas cold antibodies react at lower temperatures like 20° C. Patients with warm antibodies are usually associated with acute disease while those with cold antibodies are associated with chronic disease.

Once the diagnosis of autoimmune hemolytic anemia is established, search should be made to find out the cause. Patient should be investigated to exclude underlying lymphoma, leukemia or autoimmune disorder like systemic lupus erythematosus.

Treatment: Corticosteroids are the treatment of choice. They are known to induce a prompt reduction in the rate of hemolysis in about 80% of patients. The initial dose of prednisolone is 1-2mg/kg body weight daily. Parenteral steroids like methyl prednisolone may be required in acutely ill patients. Hemoglobin starts rising and reticulocyte count correspondingly falls with corticosteroid therapy. Steroids should be continued for 3 – 4 weeks before being considered as ineffective. After the hemoglobin stabilizes to near normal, steroids should be gradually tapered to maintain hemoglobin at least at 11gm/dl. In many patients this treatment induces remission which is maintained even after steroids are discontinued but in some patients prolonged treatment with low dose steroids (10 – 15mg/day ) may be necessary to maintain remission.

Red cell transfusions: If the onset of anemia is very acute, red cell transfusions can be life saving as steroids would take some time to produce the desired effect. Owing to the presence of auto antibodies, it may be difficult to get compatible cross match of donor blood. In such circumstances it is best to use donor blood of the same ABO and Rh group as the patient which is least incompatible, along with corticosteroids.

Patients with oliguria and renal failure may require dialysis hence urine output should be carefully monitored.

Splenectomy: Splenectomy is indicated if (i) there is lack of adequate response to steroids, (ii) patient requires high maintenance dose of steroids which produces undesirable side effects. It is not possible to predict from clinical or hematological picture whether a patient will respond to splenectomy. The result of splenectomy can be predicted to a certain extent by using Cr 51 labeled red cells and measuring splenic uptake of these red cells. If in vivo studies with Cr 51 labeled red cells shows excess uptake by the spleen, then splenectomy is likely to induce remission.

Immunosuppressive agents: Azathioprine, cyclophosphamide and other immunosuppressive agents have also been used in patients who fail to respond to splenectomy or in whom splenectomy is contraindicated.

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

This is a chronic hemolytic disease with intermittent hemoglobinuria. The fundamental abnormality is an acquired defect of the red cell membrane which makes it prone to complement mediated lysis. This disorder affects mainly adults, usually in the middle age. Both sexes are equally affected. The patient complains of passing red or dark
brown colored urine in the morning on waking, intermittently. Characteristically, only the urine passed in the night or in the morning on waking is red. But in severe cases all urine samples are colored. At times hemoglobinuria occurs even during the day time especially when there are some precipitating factors like infection, trauma, surgery, pregnancy etc. Mild hepatosplenomegaly are usually present as also is mild jaundice.

The disease is associated with aplastic anemia. In many cases it begins as aplastic anemia and features of paroxysmal nocturnal hemoglobinuria(PNH) appear later in the course of the disease. Venous thrombosis is a frequent complication of the disease. Intravascular hemolysis releases thromboplastic material into the circulation which is probably responsible for increased thrombotic tendency. It commonly involves intracranial vessels and hepatic and portal vessels.

Diagnosis: Anemia and reticulocytosis, associated with varying degrees of leuopenia and thrombocytopenia along with characteristic intermittent hemoglobinuria and demonstration of hemosiderin in urine suggest the diagnosis of PNH. The diagnosis is confirmed by sucrose lysis test and acid Ham test. Sucrose lysis test is very sensitive and hence a good screening test for PNH. PNH red cells, but not normal red cells, undergo lysis when suspended in isotonic solutions of low ionic strength. The diagnosis is confirmed by acid Ham test. PNH red cells undergo lysis in compatible acidifed serum at 37º C.

Although the Ham test has been the gold standard for the diagnosis of PNH, it is cumbersome and time consuming and hence now a days flow cytometric demonstration of deficiency in CD55 and CD59 is rapidly replacing the older techniques for the diagnosis of PNH.

Treatment: Treatment is mainly supportive. Packed red cells and especially saline washed red cell transfusions are often necessary to treat anemia. Infections should be treated promptly with broad spectrum antibiotics.

Iron deficiency occurs in patients with PNH due to urinary loss of iron and should be treated with iron supplements although sometimes iron therapy may lead to increased hemolysis due to increased production of PNH cells by the marrow.

Steroids and especially androgens have been used in the treatment of PNH with success in some cases.

Due to increased incidence of thrombosis in these patients, use of prophylactic anticoagulants has been advocated but there is no clear cut evidence of benefit. Anti coagulants should be administered in patients with evidence of thrombosis.

As in other stem cell disorders, stem cell transplantation is an effective treatment for PNH.

HEMOLYTIC DISEASE OF THE NEWBORN

With pregnancy, delivery, abortions and other obstetric maneuvers there is increased chance of feto maternal hemorrhage. If fetal and maternal red cells are of the same blood group, then it is of no consequence but if they are not compatible especially the Rh group, complications can arise.

If the mother is Rh(D) negative and the fetus is Rh(D) positive, the first pregnancy and delivery may be without any complications, but sensitizes maternal immune system for antibody production in case of subsequent exposure to the same antigen. Thus the first Rh(D) positive child is not affected. The first child may also be affected if the mother has received Rh(D) positive transfusions in the past. Each subsequent Rh(D) positive child will be more severely affected because of rise in antibody titres with repeated exposure to the antigen. Thus Rh(D) antibodies produced by the mother will enter the fetal circulation and cause lysis of Rh(D) positive fetal cells. The disease can be of varying severity ranging from anemia and jaundice at birth to intrauterine death (hydrops fetales) of the fetus due to severe anemia.

The mother’s blood group should be checked in the antenatal period and if she is Rh(D) negative her husband’s blood group should also be checked to anticipate the risk to the baby if the father is Rh(D) positive. The newborn baby’s cord blood should be examined for hemoglobin, serum bilirubin and Rh(D) blood group. If the child is Rh(D) positive his hemoglobin and bilirubin should be checked periodically to assess the severity of hemolysis.

Treatment: It is important to assess the viability of the fetus to decide the mode of therapy. If the fetus is viable, caesarean section should be done to deliver the baby as soon as possible.

Intrauterine transfusions may be required in order to save the fetus so that it can be delivered by caesarean section subsequently.

The newborn should be given exchange transfusion soon after birth if the cord blood shows evidence of hemolysis.

Prevention: All Rh(D) negative women should receive an injection of Rh antibodies within 48-72 hours of delivery of a Rh(D) positive child or even an abortion, to prevent maternal sensitization with Rh(D) antigen and hence prevent hemolytic disease of newborn in subsequent delivery.

Asha Shah
Consultant Hematologist, BSES MG Hospital and Holy Family Hospital, 6/32, Hari-Kripa, S. V. Road, Santacruz (W), Mumbai - 400 054, India.
E-mail: asshah@eth.net