PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA WITH PREGNANCY

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Introduction

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare form of non-hereditary haemolytic anaemia of insidious onset with chronic outcome. It affects women slightly more frequently than men and its peak age of onset is during the reproductive years. However, there are a few case reports of pregnancy complicated by this disease. These patients tend to be less fertile. A case of PNH with pregnancy with a favourable outcome is reported and the literature reviewed to highlight the maternal and fetal risks involved in management of such a case.

Case Report

20-year-old primigravida had her first episode of intra vascular haemolysis in March three months after marriage, when she was diagnosed as a case of paroxysmal nocturnal haemoglobinuria on the basis of positive sucrose lysis and acidified serum (HAMs) test. She was then treated with four units of washed pack cell transfusion and placed on long term prednisolone therapy.

She conceived a year after marriage. Her last menstrual period was on 05 May and her expected date of confinement was 12 February. During present pregnancy, she had an acute episode of intravascular haemolysis in Nov at gestational age of 28 weeks lasting for twelve days. She complained of extreme weakness and passage of smoky urine. She was detected to be having marked pallor (Hb 6.0 g%), oedema, clinically detectable jaundice, hypertension (Max. BP 170/110 mm of Hg) and splenomegaly. Though hepatic enzyme studies and renal parameters were within normal limits, leucopenia (3400/cmm) was detected. Platelet count and other coagulation parameters were within normal limits. Peripheral blood picture was suggestive of haemolytic anaemia.

She was managed with six pints of washed compatible packed cells (B Rh D Positive) transfusion along with oral steroid therapy and Beta blockers as antihypertensive agents along with other supportive measures.

With further advancement of pregnancy, there was clinical and sonological evidence of intrauterine growth retardation along with pregnancy induced hypertension. There was no target organ involvement. A decision to terminate pregnancy was made and labour induced at thirty six weeks of gestational age on 11 Jan. Labour was shortened by means of outlet forceps and a live male baby was delivered at 12:40 pm the same day. Baby weighed 1.95 kg and had APGAR score of 6/10 at one minute after birth. The

transitory rise in blood pressure during labour was managed with sublingual nifedipine. During the first two days following delivery, patient had another bout of haemolysis which necessitated transfusion of two more units of washed packed cells. Haemoglobin at discharge from hospital was 11.5%. Patient was reviewed after six weeks when she was found to be normotensive. There was no further episode of intravascular crisis in the next six months when she was on regular follow-up before returning back to her village.

Discussion

PNH was first described by Marchiafava in 1928. It is an intracorpuscular defect acquired at the stem cell level and occurs primarily in young adults resulting in episodes of acute and chronic intravascular haemolysis with varying degree of anaemia. The structural or biochemical defect of the erythrocyte makes them susceptible to complement mediated intravascular haemolysis. There is no familial or racial tendency. The fertility rate of these patients is thought to be low. Only 23 patients had been pregnant and 38 pregnancies had been observed this far (4 in one case, 3 in two cases and 2 in eight cases). PNH was diagnosed in eight cases during pregnancy [1]. Mild granulocytopenia and thrombocytopenia are not uncommon. Gross haemoglobinuria is usually intermittent. Diagnosis is by demonstration of low leucocyte alkaline phosphatase and low RBC acetylcholine esterase. The red cells are usually normochromic normocytic unless deficiency has resulted from chronic loss in urine. Diagnosis is by positive acid haemolysis test or sucrose lysis test, both demonstrating enhanced sensitivity of PNH red cells to complement. Venous thrombosis is a common complication and may be cause of death as noted by Spencer [2].

In the present case reported, patient was diagnosed as a case of PNH prior to conception when she was treated with washed red cell transfusion and placed on long term steroid therapy. She continued to remain asymptomatic and reported for the first time during haemolytic crisis at 28 weeks of gestational age. She

was then noted to be having hypertension. Amongst the 19 cases of PNH with pregnancy only 6 (32%) had evidence of acute haemolysis antenatally and 5 (26%) during labour or immediate postpartum. The present case also had a bout of intravascular haemolysis within the first two days postpartum. Whether stress of labour is the precipitating factor remains unclear. Incidence of hypertension along with the PNH has not been noted by previous authors. Chronic anaemia associated with pregnancy induced hypertension had most likely resulted in IUGR in the present case. Hurd et al, while reviewing the literature noted 5 spontaneous abortions amongst 15 pregnancies, 4 of which were preceded by a serious haemolytic episode. Our patient was on oral steroids immediately after she was diagnosed to be suffering from PNH and continued to take the medicine which may have had a protective role in preventing haemolysis allowing the pregnancy to reach the state of viability.

The mainstay of treatment in the management of PNH in pregnancy is blood transfusion. It has been suggested that prophylactic early blood transfusion may suppress erythropoiesis and decrease the number of abnormal circulating cells. A haematocrit between 25 to 30% should be maintained to avoid antenatal thrombotic episodes and abortions [4]. Iron therapy precipitates an attack and is best avoided. Beneficial effect of corticosteroid therapy may be considered to reduce haemolysis.

Some authors have recommended use of anticoagulants of coumarin derivative postpartum to prevent thrombotic episodes. Hepatic venous thrombosis has been reported during low dose heparin administration in antenatal period and phenidione in puerperium.

Heparin shows a biphasic effect on PNH red cells in vitro such that low concentration stimulates haemolysis and higher concentration prevents haemolysis. In view of disputed role of anticoagulants, no anticoagulant treatment was exhibited to the present case in puerperium. It is felt that full anticoagulation therapy should be instituted only in presence of any thrombotic episodes till advantage of anticoagulant therapy is conclusively proved.

In a retrospective and prospective multicentre study carried out by Bramount et al, the authors observed that in about 1/3 of cases of PNH, pregnancy remains uncomplicated. Pregnancy can be managed even if hazardous by careful haematological and obstetric follow up. Though patients of PNH tend to be less fertile, a safe and effective contraception should be considered. Susceptibility to venous thrombosis rules out oral contraception and risk of thrombocytopenia and granulocytopenia makes an intrauterine device inadvisable. Barrier contraception, therefore, is the method of choice and was advised to this patient. Sterilisation operation can be carried out during quiescent stage of the disease to those willing to undertake a permanent method.

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