HEREDITARY SPHEROCYTOSIS : A STUDY OF 16 PATIENTS FROM UNIVERSITY HOSPITAL, KUALA LUMPUR

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ABSTRACT

Hereditary spherocytosis is a rather uncommon disease in Malaysia as only 16 patients were seen in our hospital over a 13 year period. Pallor, jaundice and splenomegaly were common physical signs. Clinical severity of the disease was variable and more than half of them needed splenectomy. Complications including haemolytic crisis and cholelithiasis were encountered but not aplastic crisis. All 10 patients who underwent splenectomy had uniformly good results and none of them had post-operative complications.

Keywords : Hereditary spherocytosis, complications, splenectomy, Malaysian

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INTRODUCTION

Hereditary spherocytosis(HS) is an inherited red cell membrane disorder characterised clinically by anaemia, jaundice and splenomegaly. The disease may manifest itself in the neonatal or early infancy period or may not become apparent until late childhood or adolescence. To date, no large series report on local patients is available. We report 16 patients seen in our institution which is a referral centre for haematological disorders in Malaysia.

PATIENTS AND METHODS

Between 1974 and 1986, a total of 16 patients were diagnosed to have HS on the basis of presence of spherocytes on peripheral blood films, negative Coombs tests and osmotic fragility tests which showed presence of osmotically fragile red cells both on direct study and overnight incubation. The osmotic tests were carried out with the method as outlined in Dacie and Lewis[1]. The case notes of these patients were analysed.

RESULTS

Biodata : There were 8 male and female patients respectively (Table I) and their age at presentation ranged from one month to 38 years (mean : 8.65 years). There were 10 Chinese and 6 Malay patients. One of the 16 patients was an adopted child and therefore was excluded from the analysis. Of the remaining 15 patients, 8 had a clear-cut family history of HS at presentation or on study of the family members. Two of those 8 patients had a family member who had undergone splenectomy in the past for symptomatic anaemia. The mean age at presentation for patients with family history was 3.8 years (range : 1 month to 18 years) while it was 12.3 years (range 1 to 38 years) for those without family history.

Presenting problems : Nine (56%) of the patients presented with either acute or recurrent anaemia. Jaundice consequent to haemolysis was the presenting problem in 2 adults and in an infant (Table II). It is interesting to note that 3 patients had a history of prolonged neonatal jaundice (beyond two weeks after birth). Right hypochondral (RHC) pain was the presenting complaint in one patient and as an associated symptom in 3 other patients. Of the 4 patients with RHC pain, only one patient had gallstone; the cause of RHC pain in the remaining 3 patients was not apparent. On the other hand, 4 patients who did not have RHC pain at any time were found to have multiple gallstones either on ultrasound or at the time of the operation. None of our patients were noted to have "aplastic crisis". Two patients presented with acute haemolysis, probably precipitated by an upper respiratory tract infection in one of them.

Time interval between the initial presentation and diagnosis: Although the diagnosis of HS did not normally pose much of a problem, patients may not seek medical treatment especially if they were asymptomatic. Occasionally, the diagnosis was missed by doctors for many years as exemplified by Case 2 who had symptomatic anaemia for 10 years before the diagnosis was made.

The longest time-interval of 22 years between initial manifestations of the disease and the diagnosis was seen in the oldest patient, aged 60 years. He had persistent mild jaundice since the age of 38 years, not accompanied by any other symptoms although he had multiple gallstones on ultrasound.

Physical findings : Pallor was present in 12 (75%) of the patients and so was hepatomegaly. A palpable spleen was the commonest finding and was present in all but one patient who was the one month old infant who presented with prolonged neonatal jaundice. Jaundice of varying degree was seen in about 11 (70%) of the cases (Table III). The size of the spleen ranged from 3 to 10 cm below the costal margin. The spleen size did not appear to be linked with the degree of anaemia at presentation.

Haematological data : All but 2 patients had a haemoglobin concentration of >11g/dl. Nine (56%) patients had a Hb between 8 to 10.9g/dl. The reticulocyte count ranged from less than 2% to more than 20% at presentation. In 9 of them the reticulocyte counts were between 5 to 15%. None of the patients had thrombocytopenia and/or leucopenia to suggest development of hypersplenism.

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Table I
Clinical Data of Patients

Case No.	Age at		Sex	FH	Spleen size (cm)	Blood indices on admission				Gall stones	Splenectomy
	Presentation	Diagnosis				Hb g/dl	Reticulocyte %	TWC x 10^9/l	Platelet x10^9/l		
1	38 yr	60 yr	M	No	1	12.6	10.2	8.8	112	Yes	No
2	22 yr	34 yr	F	A	10	8.9	10.0	7.1	207	No	Refused
3	1 mth	1 mth	M	Yes	NP	10.7	4.8	14.6	208	No	No
4	5 yr	8 yr	F	No	8	5.9	26.0	5.9	198	No	Yes
5	1 yr	9 yr	F	No	8	8.3	33.0	7.5	235	No	Default
6	1 yr	1.5 yr	F	Yes	4	7.8	11.0	13.5	Adeq	No	Yes
7	18 yr	22 yr	F	Yes	4	9.2	8.0	8.9	420	No	Yes
8	2 mth	3 yr	M	Yes	5	9.8	5.0	6.4	242	No	Yes
9	14 yr	20 yr	M	No	8	8.5	20.0	6.8	NA	Yes	Yes
10	7 yr	8 yr	M	No	7	10.0	18.0	6.9	299	No	Yes
11	7 yr	13 yr	M	Yes	6	1.7	0.1	7.4	72	Yes	Yes
12	3 yr	6 yr	M	No	4	8.9	NA	NA	NA	No	Yes
13	3 mth	3 mth	M	Yes	5	7.1	20.1	12.8	324	No	Planned
14	2 yr	2 yr	F	Yes	4	8.1	12.0	13.9	317	No	No
15	2 yr	14 yr	F	Yes	6	5.3	15.6	7.1	92	Yes	Yes
16	18 yr	31 yr	F	No	3	11.7	8.9	9.8	386	Yes	Yes

FH = family history
NP = non-palpable
NA = not available
A = adopted child
Adeq = adequate

Table II
Presenting Problems in Hereditary Spherocytosis

	No. of Patients
Recurrent anaemia	9
Acute haemolysis	2
Congestive heart failure	1
Jaundice	3
Right hypochondrial pain	1
TOTAL	16

Table III
Physical Signs in Hereditary Spherocytosis

	No. of Patients
Pallor	12
Splenomegaly	15
Hepatomegaly	12
Jaundice	11

Surgical outcome : Ten (62.5%) of the 16 patients underwent splenectomy for symptomatic anaemia and in 8 patients repeated blood transfusions were needed during haemolytic crisis. The age of the patients at which splenectomy was carried out ranged from 6 years to 31 years. Eight of these patients were less than 15 years when splenectomy was done. The mean interval between diagnosis and splenectomy was 3 years. There were no post-operative complications. Multiple gallstones were removed in 3 patients.

Uniform good responses were seen in the patients who underwent splenectomy. The mean haemoglobin concentration before and after splenectomy was 8.5g/dl and 14.2g/dl respectively. The reticulocyte count fell from a mean of 15% to 1.2%. Only paediatric patients were put on long-term oral penicillin treatment after splenectomy as the risk of overwhelming post-splenectomy infection (OPSI) was greatest in this group of patients. The mean follow-up period was 4.5 years and none of our patients developed overwhelming post-splenectomy infection or problems related to gallstone.

DISCUSSION

Hereditary spherocytosis (HS) is best known as a disorder affecting people of European origin and the incidence has been estimated to be 200-300 per million[2]. HS appears to be an uncommon disorder locally as only 16 patients were seen over a 13 year period. A positive family history was present in about half of our cases. KC Haven et al[3] reported that 75% of their 100 patients with HS had a family history. The absence of family history could be due to spontaneous mutation or more likely, the result of incomplete penetrance of the abnormal gene[4].

The clinical presentations were variable : some patients were symptomatic even in infancy while others were diagnosed in adult life. The variable clinical severity of HS suggested that the molecular defects would be heterogeneous. To date, two distinct molecular defects had been described; namely partial spectrin deficiency[5] and defective binding of spectrin to protein 4.1[6]. The frequent clinical findings of pallor and hepatosplenomegaly were similar to other large series[3]. The mean age presentation in

patients who had positive family history was younger than those without family history and this was probably due to earlier detection of such patients during family screening and greater awareness of the disease rather than due to milder nature of the disease.

. The treatment of HS is splenectomy with the possible exception of fully compensated, very mild cases lacking jaundice, anaemia or a history of crises[4]. The benefits of splenectomy include elimination of anaemia, prevention of further aplatic crises and also reduction in the incidence of complicating cholelithiasis and cholecystitis. Ten (62.5%) of our patients required splenectomy for symptomatic anaemia which yielded good results with normalisation of haemogoblin concentration and reticulocyte count and resolution of clinical signs. In view of the risk of overwhelming post-splenectomy infection, prophylaxis in the form of pneumococcal vaccine and long term oral penicillin are probably recommended in the paediatric patients who have the greatest risk[7]. Aplastic crisis which could be precipitated by parvovirus[8] was not seen in our patients; this could be due to the transient nature of attacks and also possibly, this complication was not actively looked for in our patients.

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