AVASCULAR NECROSIS OF THE FEMORAL HEAD IN SICKLE-CELL DISEASE

A SERIES FROM THE GUINEA SAVANNAH OF NIGERIA

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Of 899 patients with sickle-cell disease, aged between 6 and 28 years, who attended clinics in the Guinea Savannah of Nigeria in 1982 and 1983, 29 had symptoms of avascular necrosis of the femoral head. This group was studied in detail.

Twenty-eight patients had haemoglobin-SS electrophoretic patterns and one had haemoglobin-SC. The male to female ratio was 1 to 1.6, and most of the patients were aged between 6 and 15 years at the onset of hip symptoms. These symptoms correlated with the radiographic lesions, but were not related to the age or sex of the patient. The radiographic lesions varied widely and were related to the age at onset of hip symptoms. A new radiological classification is proposed.

Avascular necrosis of the femoral head is well recognised to occur in sickle-cell disease. It may affect both children and adults and needs to be distinguished from Perthes' disease in the child and from avascular necrosis in adults, either of the idiopathic type or that associated with alcoholism, prolonged steroid therapy, caisson disease or other rare conditions. This differentiation is made from the racial, social and occupational history of the patient and the electrophoretic pattern of the haemoglobin.

Various aspects of the condition have been described (Kraft and Bertel 1947; Legant and Ball 1948; Macht and Roman 1948; Carroll and Evans 1949; Hamburg 1950; Smith and Conley 1954; Tanaka, Clifford and Axelrod 1956; Cockshott 1958; Golding, MacIver and Went 1959; Middlemiss and Raper 1966; Chung and Ralston 1969). Early reports from Smith and Conley (1954) suggested that only patients with the Hb-SC electrophoretic pattern were affected by avascular necrosis. It has now been shown that it occurs in all types of sickle-cell disease with the same frequency, giving a distribution proportional to that of the types of haemoglobin electrophoretic pattern in any given population or geographical area (Tanaka *et al.* 1956; Golding *et al.* 1959; Chung and Ralston 1969; Nachamie and Dorfman 1974; Ebong 1977).

While Chung and Ralston (1969) proposed a useful, though limited, classification of the radiographic lesions, a more detailed classification would be useful in the

management of patients. In addition, no study has yet reported the relationship between the type and severity of the avascular necrosis and the haemoglobin electrophoretic pattern, the sex of the patient and the age at the onset of symptoms. Finally, although previous reports suggest that there is a regional variation in the frequency of the condition, the incidence in the northern part of Nigeria has not yet been determined.

With these considerations in mind, we reviewed the records of all patients over five years of age seen in the sickle-cell clinics at the Ahmadu Bello University teaching hospitals at Zaria and Kaduna during a two-year period.

MATERIAL AND METHODS

The records of 899 patients over five years of age with sickle-cell disease seen in the sickle-cell clinic at Zaria and Kaduna from January 1982 to December 1983 were reviewed, taking particular note of their sex and age, the electrophoretic pattern of their haemoglobin and the presence of hip symptoms. There were 429 men and boys, and 470 women and girls.

Table 1. Age at presentation and sex of patients with avascular necrosis of the femoral head in sickle-cell disease

Age (years)	Number of patients		
	Total	Male	Female
6-10	7	2	5
11-15	7	2	5
16-20	6	2	4
21-25	7	4	3
26-30	2	1	1
TOTAL	29	11	18

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Of these, there were 29 patients, 11 males and 18 females, aged from 6 to 28 years (mean 16.4 years) who had significant hip symptoms, such as pain and a limp (Table I). The age of the patient at the onset of these symptoms, the severity of symptoms, and the frequency of sickle-cell crises were the subject of further questions. A physical examination paid special attention to the hips. The electrophoretic pattern of the haemoglobin of each patient was confirmed and the radiographs of the hips were studied to determine the type of avascular necrosis.

The severity of pain in the hip and of limping was graded as "mild", "moderate" or "severe". Mild pain was present only on weight-bearing, moderate pain occurred at rest and severe pain restricted physical activities considerably or caused sleeplessness at night. The severity of the limp usually corresponded with that of pain.

RESULTS

The male to female ratio in sickle-cell patients in this series of 899 patients was 1 to 1.1. Avascular necrosis of the femoral head was confirmed in 11 males and 18 females, giving a frequency of 3.2% and a male to female ratio of 1 to 1.6 (Table II). There was bilateral necrosis in five patients, giving 34 affected hips, of which 15 were right and 19 were left. The relevant electrophoretic patterns of the whole population with sickle-cell disease and of the group with avascular necrosis are shown in Table III.

No patients were in crisis when reviewed. Most looked fit, having only hip symptoms, while a few had evidence of sickle-cell anaemia such as pale conjunctivae and general weakness, as well as their hip problem. Their haemoglobin levels ranged from 5.1 to 12.9 g/dl.

In 28 of the 29 patients the Hb-SS electrophoretic pattern was present, but there was a wide range of radiographic lesions, some of which could not be classified according to the criteria of Chung and Ralston (1969). A new classification was developed (Table IV),

Table II. Incidence and sex incidence of avascular necrosis of the femoral head in 899 cases of sickle-cell disease

	Number of patients			
	Total	Male	Female	Ratio M:F
Sickle-cell disease	899	429	470	1:1.1
Avascular necrosis	29	11	18	1:1.6
<i>Per cent incidence</i>	3.2	2.6	3.8	—

Table III. Incidence of avascular necrosis of the femoral head in patients with sickle-cell disease, and different Hb electrophoretic patterns

	Number of patients	Hb electrophoretic pattern			
		SS	SS + F	SS and SS + F	SC
Sickle-cell disease	899	570	283	853	46
Avascular necrosis	29	20	8	28	1
<i>Per cent incidence</i>	3.2	—	—	3.3	2.2

and it was found that these lesions were related to the age of the patient at the onset of hip symptoms, but not to the sex of the patient.

The radiographs showed subchondral sclerosis (Fig. 1) in four hips, Perthes' like lesions (Figs 2 and 3) in 15 hips, total destruction of the femoral head with partial reformation and failed remodelling (Fig. 4) in six, central necrosis (Fig. 5) in four and diffuse necrosis of the femoral head (Fig. 6) in five hips, including that of the only patient with the Hb-SC electrophoretic pattern. There was associated acetabular involvement in three hips. Avascular necrosis of the head of the right humerus and of the condyles of the right femur was also found in one 16-year-old woman.

The clinical symptoms and the signs found in the affected hips generally corresponded with the severity of the radiographic change, but seemed to be unrelated to the age or sex of the patients. Where only subchondral sclerosis was present the patients had mild occasional

Table IV. Radiographic lesions in avascular necrosis (AVN) related to age, sex, Hb electrophoretic pattern and severity of symptoms

Radiographic change	Number of hips	Number of patients		Electrophoretic pattern			Age at onset of symptoms in each hip					Severity of symptoms
		Male	Female	SS	SS + F	SC	6-10	11-15	16-20	21-25	26-30	
Subchondral sclerosis	4	0	4	3	1	0	3	1	0	0	0	Mild and occasional
Perthes'-like lesions	15	5	7	7	5	0	4	9	2	0	0	Mild to moderate
Total destruction	6	3	2	3	2	0	1	4	1	0	0	Moderate to severe
Central necrosis	4	2	2	3	0	1	0	1	0	2	1	Moderate to severe
Diffuse sclerosis	5	1	3	4	0	0	0	1	2	2	0	Moderate to severe
TOTAL	34	11	18	20	8	1	8	16	5	4	1

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 5

Fig. 6

Radiographs to show radiographic lesions in avascular necrosis. Figure 1—Subchondral sclerosis in the right femoral head of a 10-year-old girl. This could progress to a Perthes'-like Type 1 lesion (Fig. 2) or to central necrosis (Fig. 5). Figure 2—Perthes'-like Type 1 lesion, with segmental necrosis of the epiphysis of the right femoral head in a 12-year-old girl. Figure 3—Perthes'-like Type 2 lesion, showing involvement of the whole epiphysis in an 8-year-old boy. Figure 4—Total destruction of the left femoral head with subluxation in a 20-year-old man whose hip symptoms had started 5 years earlier. There is some evidence of remodelling of the head and the acetabulum is involved. Figure 5—Central necrosis of the right femoral head with diffuse necrosis of the left in a 22-year-old man with a one-year history of bilateral hip pain. Figure 6—Diffuse necrosis of the right femoral head in a 16-year-old woman with a one-year history of hip pain.

pain with little or no limp. Those with Perthes'-like lesions had mild to moderate pain and a definite limp, while those with total destruction, central necrosis or diffuse necrosis of the femoral head had moderate to severe pain and a gross limp.

DISCUSSION

Sex incidence. The patients with sickle-cell anaemia showed an almost equal sex incidence (429 males, 470 females), so the male to female ratio of 1 to 1.6 for hip disease may be significant. This suggests that, in the region under study, females are more prone to avascular necrosis than males. This is at variance with the findings of Hawker *et al.* (1982) who reported 50 patients with Hb-SS and hip disease, 29 of whom were males and 21 were females. Ebong (1977) reported an almost equal sex incidence in his series of 22 patients (14 Hb-SC, 4 Hb-SS and 4 Hb-AS electrophoretic patterns).

Age of onset. The most common age group at the onset of hip symptoms, as distinct from the age at presentation,

was 11 to 15 years (Table IV). The disease rarely developed after the age of 25 years; no cases older than 28 years were seen in this review.

Electrophoretic pattern of the haemoglobin. Twenty-eight of the 29 patients with hip disease (96.6%) had the Hb-SS pattern. Since 853 of 899 sickle-cell patients had this pattern, the incidence of hip disease among them is 3.3%. One patient had hip disease among the 46 with the Hb-SC pattern, giving an incidence of 2.2% for that electrophoretic pattern.

It is not surprising that most of the patients with hip disease in this series have the Hb-SS pattern, since this is in proportion to the distribution of this electrophoretic pattern in the total population with sickle-cell disease (Fleming *et al.* 1979). Some authors (Smith and Conley 1954; Cockshott 1958; Golding *et al.* 1959) hold that hip disease is more common with Hb-SC than with Hb-SS disease but our findings and those of Hawker *et al.* (1982) suggest that the comparison should apply only in relation to populations in which the two electrophoretic

patterns are both significantly represented. The Yoruba area of Nigeria, in which the SS:SC ratio is about 2:1, represents such a population. Ebong (1977) reported ratios in hip disease of SS:SC:AS=2:7:2, which are significant.

Clinical and radiographic characteristics. The severity of hip pain and limp generally corresponded with that of the radiological lesions (Table IV) which have been classified as follows:

- A. *Subchondral sclerosis.* An area of increased radiographic density in the epiphyseal region of the femoral head, which has previously been described by Middlemiss (1958) and probably represents early infarction (Fig. 1).
- B. *Perthes'-like lesion, Type 1.* There is necrosis of a segment of the epiphysis or of the head (Fig. 2). This has also previously been described but not distinguished from the Type 2 lesion which apparently has a worse prognosis. Type 1 responds to bone-grafting more readily and remarkably than Type 2.
Perthes'-like lesion, Type 2. Necrosis here involves the whole epiphysis and the appearance is more like that of a classical Perthes' lesion (Fig. 3).
- C. *Total destruction.* This type is probably that described as "severe hip deformity" by Chung and Ralston (1969). The whole femoral head has been destroyed at an earlier stage and reformation and remodelling have been only partially successful (Fig. 4).
- D. *Central necrosis.* There is a cavity in the central area of the femoral head (Fig. 5). This may be of variable size and could possibly arise either from a subchondral sclerotic lesion or primarily.
- E. *Diffuse necrosis.* The whole head is necrotic and there are a number of punctate translucencies (Fig. 6). This probably represents progression of the central necrosis described above.

In the present series there was a relationship between the type of radiographic lesion and the age of the patient at the onset of hip symptoms. The younger patients tended to have the milder forms of the disease (subchondral sclerosis and Perthes'-like lesions), whereas disease of later onset tended to be of the type with central or diffuse necrosis. Furthermore, a serial study of the radiographs suggests that subchondral sclerosis, Perthes'-like lesions and total destruction of the femoral head with partial remodelling are stages of the same lesion, and that central and diffuse necrosis may represent different stages of another type of lesion. There was no lesion resembling osteochondritis dissecans in this series.

Although there was predominance of the Hb-SS electrophoretic pattern, there were five different types of radiographic lesion of varying severity. This agrees with the findings of Chung and Ralston (1969), and suggests that factors other than the electrophoretic pattern are at play. The only patient with hip symptoms and a Hb-SC

pattern had central necrosis; her symptoms were similar to those of the three patients with the Hb-SS pattern who had central necrosis.

The age at onset of hip disease is probably important. It would be helpful to know the types of radiographic change and the age at the onset of hip symptoms in the 50 patients with Hb-SS disease reported by Hawker *et al.* (1982). With the exception of subchondral sclerosis, which is perhaps best considered as a transitional lesion, each lesion was almost equally represented in male and female patients (Table IV), suggesting that there is no significant sex difference in the type and severity of the radiographic and clinical lesions.

Conclusions. In the Guinea Savannah of Nigeria, the majority of patients with sickle-cell disease have the Hb-SS electrophoretic pattern, as have the majority of those with avascular necrosis. The incidence of symptoms of avascular necrosis of the femoral head among the population with sickle-cell disease in this region is about 3%. Females are more prone to the condition than males in the ratio of 1.6 to 1.

The most susceptible age group for hip disease is from 6 to 15 years. The severity of hip symptoms varies with the type of radiographic lesion but not with the age or the sex of the patient. The type and severity of the radiographic lesions vary widely and appear to be related to the age of the patient at the onset of hip symptoms.

REFERENCES

- Carroll DS, Evans JW. Roentgen findings in sickle-cell anemia. *Radiology* 1949;53:834-44.
- Chung SMK, Ralston EL. Necrosis of the femoral head associated with sickle-cell anemia and its genetic variants: a review of the literature and study of thirteen cases. *J Bone Joint Surg [Am]* 1969;51-A:33-58.
- Cockshott WP. Haemoglobin SC disease. *J Fac Radiol* 1958;9:211-6.
- Ebong WW. Avascular necrosis of the femoral head associated with haemoglobinopathy. *Trop Geogr Med* 1977;29(1):19-23.
- Fleming AF, Storey J, Molineaux L, Iroko EA, Attai ED. Abnormal haemoglobins in the Sudan savanna of Nigeria. I: prevalence of haemoglobins and relationships between sickle cell trait, malaria and survival. *Ann Trop Med Parasitol* 1979;73(2):161-72.
- Golding JSR, MacIver JE, Went LN. The bone changes in sickle cell anaemia and its genetic variants. *J Bone Joint Surg [Br]* 1959;41-B:711-8.
- Hawker H, Neilson H, Hayes RJ, Serjeant GR. Haematological factors associated with avascular necrosis of the femoral head in homozygous sickle cell disease. *Brit J Haematol* 1982;50:29-34.
- Hamburg AE. Skeletal changes in sickle-cell anaemia: report of an unusual case. *J Bone Joint Surg [Am]* 1950;32-A:893-900.
- Kraft E, Bertel G. Sickle cell anemia: case report with unusual roentgen findings. *AJR* 1947;57:224-31.
- Legant O, Ball RP. Sickle-cell anemia in adults: roentgenographic findings. *Radiology* 1948;51:665-75.
- Macht SH, Roman PW. Radiologic changes in sickle-cell anemia. *Radiology* 1948;51:697-707.
- Middlemiss JH. Sickle-cell anaemia. *J Fac Radiol* 1958;9(1):16-24.
- Middlemiss JH, Raper AB. Skeletal changes in the haemoglobinopathies. *J Bone Joint Surg [Br]* 1966;48-B:693-702.
- Nachamie BA, Dorfman HD. Ischaemic necrosis of bone in sickle cell trait. *Mt Sinai J Med NY* 1974;41:527-36.
- Smith EW, Conley CL. Clinical features of genetic variants of sickle cell disease. *Bull Johns Hopkins Hosp* 1954;94:289-318.
- Tanaka KR, Clifford GO, Axelrod AR. Sickle cell anemia (homozygous S) with aseptic necrosis of the femoral head. *Blood* 1956;11:998-1008.