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Mixed Anaemic Crisis in Patients with Sickle-cell Anaemia

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Summary

Fatunde OJ, Ambe JB, Sodeinde O. Mixed Anaemic Crisis in Patients with Sickle-cell Anaemia. *Nigerian Journal of Paediatrics* **1999; 26: 30.** The three types of severe anaemic crises recognised in sickle-cell anaemia (SCA) are aplastic, acute splenic sequestration and hyperhaemolytic. However, among 104 consecutive SCA cases admitted to the Children Emergency Ward of the University College Hospital, Ibadan with severe anaemic crises recently, were ten (9.6 percent) children who had mixed features and did not fall neatly into any of the three recognised categories. The distributions of the sex and admission haematocrits in these ten children with 'mixed' anaemic crises were similar to those of the 94 others with easily classified ('pure') anaemic crises. However, using statistical test appropriate for the small numbers involved, Salmonella bacteraemia was significantly more common (5/10) among the patients with 'mixed' anaemic crises than in those (5/94) with 'pure' crises (P = 0.0006). The relative risk of Salmonella bacteraemia in 'mixed' crises was 9.4 times that among those with 'pure' crises (95% CI = 3.28-26.98). Although none of the 'mixed' cases died, compared with a mortality of 9.6 percent among the 'pure' cases, the difference was not significant (P=0.42). Bacteraemia appears to be associated with 'mixed' (indeterminate) anaemic crises in SCA. This finding suggests that such patients would benefit from appropriate antibiotic therapy.

Introduction

ANAEMIC crises are important causes of morbidity and mortality in patients with sickle-cell anaemia (SCA).[1,2] However, the features of these crises are not always clear-cut.[3] Minor episodes of acute splenic sequestration crises (ASSC) associated with less striking haematological and clinical changes occur.[4] Haematological findings in aplastic crises are variable, depending on the stage at which the patient presents. Thus, a mistaken diagnosis of hyperhaemolytic crisis may be made, because of the severe anaemia and marked reticulocytosis, if the patient presents during the recovery phase of an aplastic crisis. In spite of these possibilities, reports on anaemic crises in patients with SCA and features suggestive of more than one type of crises, are rare. Such patients will often pose problems in diagnosis and management that are different from those of patients with clear-cut diagnostic features. This communication presents our experience of the prevalence, presentation and outcome of patients with mixed features of anaemic crises.

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Patients and Methods

The study was undertaken at the Children's Emergency Ward (CHEW) of the University College Hospital (UCH), Ibadan, over a period of nine months. One hundred and four consecutive patients with confirmed SCA aged between six months and 15 years were admitted with severe anaemia defined as packed cell volume (PCV) ≤ 15 percent. Six other patients were excluded because of a history of blood

transfusion within the preceding three months. The criteria for classification of the patients into the different types of anaemic crises were as previously described.[1,2,4] Briefly, a patient was said to have hyperhaemolytic crisis if there was a recent recurrence or deepening of jaundice in association with reticulocytosis and a fall of the PCV from the steady state.[1,2] Patients with ASSC were those who had reticulocytosis with a rapid increase in splenic size,[4] and no jaundice or recent splenic enlargement.[1,2] Patients whose anaemia was associated with reticulocytopenia were classified as having aplastic crises.

Clinical parameters sought and recorded, in addition to routine features, included the presence or absence of jaundice, blood pressure in the supine position and splenic size, determined at admission and 24 hours after blood transfusion. Laboratory investigations undertaken included PCV, reticulocyte index (RI),[5] blood culture and blood films for malaria parasites. Reticulocyte Index (RI)[6] was calculated thus: RI = Reticulocyte count (percent) x Patient's PCV/Reference PCV. The reference PCV chosen for this study was 30 percent. Patients with a RI>1.0 were considered to have reticulocytosis and those with RI<1.0, reticulocytopenia.[5] Verbal informed consent was obtained from the parents/guardians. The study was approved by the Joint Ethical Committee of the University of Ibadan and UCH, Ibadan.

Presenting features were compared between patients with 'pure' anaemic crises and those with mixed crises, using chi-square (X^2) and Student's 't' tests for categorical and continuous variable, respectively. Yates correction of chi-square and Fisher's exact test were used where appropriate. P values <0.05 were considered significant.

Results

Of the 104 patients with anaemic crises, 10 (9.6 percent) had mixed anaemic crises (MAC) and 94 (90.4 percent) had 'pure' crises. The latter included 51 cases of hyperhaemolytic, 29 cases of ASSC, and 14 cases of aplastic crises. The patients classified as having MAC had clinical and laboratory features which did not fit into any of the three categories of 'pure' anaemic crises. The age, sex, clinical and laboratory features in the 10 patients with MAC are shown in the Table. Six of the ten patients had peripheral circulatory failure and acute splenic enlargement but also had reticulocytopenia and were not jaundiced. The tenth patient had only an acute

Table

Age, Sex, Clinical and Laboratory Features in Ten Patients with Mixed Anaemic Crises

Age (yr)	*Sex*	*Spleen Size (cm)*	*BP (mm Hg)*	*Steady State PCV (percent)*	*Admission PCV (percent)*	*MP*	*RI*
1.0	F	0	90/60	20	12	+ve	1.02
1.25	M	0	95/65	27	15	+ve	1.94
3.0	F	4	100/60	21	15	-ve	1.28
6.0	F	6	105/65	24	14	+ve	1.84
7.0	M	0	105/65	23	6	+ve	1.02
8.0	M	0	100/65	21	10	+ve	1.14
1.25	M	6	40/25	28	15	+ve	0.10
3.0	M	6	45/20	18	6	-ve	0.34
8.0	F	7	NR	25	9	+ve	0.02
5.0	F	10	NR	18	11	-ve	0.03

BP = Blood pressure
MP = Malaria parasite (+ve present; -ve absent)
RI = Reticulocyte Index
NR = Not recorded

increase in spleen size in association with reticulocytopenia, but no circulatory failure or jaundice. The splenic enlargement of the four patients with reticulocytopenia regressed within 24 hours of receiving blood transfusion.

Three of the 10 patients with MAC compared with 16 of the 94 with 'pure' anaemic crises were attending the emergency ward for the first time (Fisher's exact test P = 0.38); in all these 19 first time attenders, the diagnosis of SCA had not been previously made. Seven of the 10 patients with MAC had been receiving pyrimethamine prophylaxis following earlier diagnosis, and in five of these seven, blood cultures yielded Salmonella spp. The other five blood culture isolates were Salmonella species two, *Staphylococcus aureus* two, and Klebsiella spp. one. Thus, salmonella bacteraemia was more common in MAC (5/10) than in 'pure' (easily classified) anaemic crises (5/94) (Yate's corrected X^2 = 15.94; Fisher's exact test P = 0.0006; relative risk of bacteraemia in MAC = 9.4; 95% Confidence Interval = 3.28 - 26.98). There were no differences between the mean PCV of patients with MAC (11.33 ± 3.3) and those of patients with 'pure' anaemic crises (hyperhaemolytic 11.5 ± 2.66, ASS 11.8 ± 2.3, and aplastic 11.3 ± 3.6) (ANOVA F = 0.40, p = 0.753). All the ten patients with MAC received blood transfusion and survived. One eight-year old girl who initially presented with reticulocytopenia and peripheral circulatory failure but no jaundice, was however, readmitted three months later with ASSC and a fatal cerebrovascular accident.

Discussion

The results of this study indicate that MAC is not rare in children with sickle-cell anaemia presenting with anaemic crises. As far as we are aware, there are no published reports on anaemic crises of more than one form occurring in SCA patients in Nigeria. Six of our patients might have been in the recovery phase of aplastic crises during which there was outpouring of reticulocytes by the bone marrow.[1,7,8] Also, but for the absence of reticulocytosis, the remaining four patients had the characteristics of ASSC. These patients are illustrative of the possible diagnostic dilemma which patients with MAC can pose. Although it is not clear why the bone marrow in some cases of ASSC would not respond with the usual erythroid hyperplasia and reticulocytosis, the factor(s) which resulted in the ASSC could conceivably also cause erythroid aplasia. Similarly, malaria parasitaemia, which was a common finding in these patients, can cause anaemia of a mixed pattern and is associated with reticulocytopenia.[9,10] Thus, the role of malaria parasitaemia as a causal agent for the various anaemic crises needs further study. However, the seven patients with malaria parasitaemia included four of the bacteraemic (Salmonella spp.) patients in whom toxic depression of the marrow would be an alternative explanation for reticulocytopenia.

One reason for the need for an awareness of the problem of MAC is that minor cases of ASSC can be missed, especially if they occur in association with aplastic crises. Bearing in mind that ASSC has a propensity for recurrence, there is the possibility of missing its initial episode that may have features of MAC, which could later recur with a possible fatal outcome, as occurred in one of our patients. Although sensitive discriminatory criteria are needed for the correct diagnosis of the various forms of SCA anaemic crises, it is more important for each paediatric emergency unit to maintain efficient facilities for urgent blood transfusion in emergency situations.

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