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REVIEW ARTICLE - VASCULAR

A review of spontaneous intracranial extradural hematoma in sickle-cell disease

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Abstract Sickle-cell disease is common among patients of Afro-Caribbean origin. Though it can precipitate neurological conditions, it only rarely causes neurosurgical problems, with very few reported cases. We describe the case of a 7-year-old girl with a background of sickle-cell disease (SCD) brought into an acute neurosurgical unit in extremis, signs of a raised ICP, and with no history of recent trauma. Following further investigations, an acute drop in the hemoglobin and hematocrit levels were noted, with the cause of her presentation being attributed to a sickling crisis causing skull convexity infarction and resulting in spontaneous bilateral extradural hematomas requiring emergency evacuation. We review the current literature and propose the pathophysiological mechanism behind this phenomenon.

Keywords Sickle-cell disease · Extradural hematoma · Skull convexity infarct · Spontaneous · Non-traumatic

Introduction

Non-traumatic intracranial extradural hematomas (EDHs) are rare, and reports have associated their etiology with infections [3, 9, 14, 20, 25, 29, 31, 33, 37], coagulation disorders [39, 43], hemodialysis, cardiac surgery [28, 38], neoplasms [6, 15, 18, 22, 41], and vascular malformations [35]. The first case report of a spontaneous EDH was described in 1951 [37].

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Sickle-cell disease, SCD, is a very common genetic disorder of red blood cells commonly affecting people of Afro-Caribbean descent (affects up to 7.3 % of the world's black population) [23]. It is characterized by sickle-shaped stiff cells and causes intermittent obstruction to intravascular blood flow. An acute episode of flow blockage in small blood vessels causing end tissue infarction is one of the manifestations of a 'crisis' [10, 38].

There is currently no known cure for the disease, but patients presenting acutely are managed symptomatically with supportive therapy such as analgesia, intravenous and oral fluids, intravenous antibiotics, if a source of infection is isolated (e.g., acute chest syndrome), and prophylactic low molecular weight heparin as patients tend to have vaso-occlusive crises; especially in the cerebro-vascular system, with hemorrhages being relatively rare (75 % are ischemic, 25 % are hemorrhagic) [30]. Here we describe a child with sickle-cell crisis who presented in coma due to spontaneous bilateral EDHs.

Case report

A 7-year-old Afro-Caribbean girl was found unresponsive in bed by her parents. On admission, she had a Glasgow Coma Score of 3, with a right fixed and dilated pupil, and with no history of recent trauma. After intubation and ventilation, a CT scan showed the presence of a large right parietal extradural hematoma, with significant midline shift, and a smaller left parietal EDH (Fig. 1). She was known to suffer from sickle-cell disease and suffered 3–4 crises a year. Her regular medication included penicillin V, folic acid, and zinc supplements. She had recently been discharged from the hospital with a recurrent episode of acute crisis (causing headaches) the day before she was found unresponsive. Blood tests

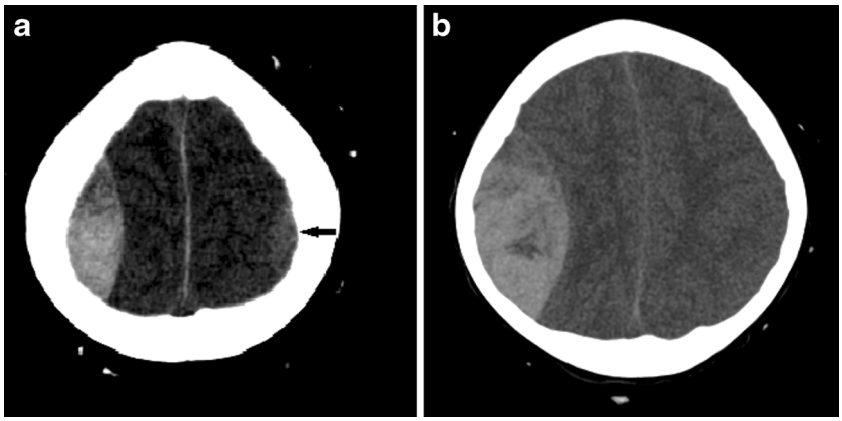

Fig. 1 Pre-operative: **a** Axial CT slices showing the bilateral EDH at the vertex of the skull and **b** the extent of the right-sided clot more inferiorly

on admission showed a hemoglobin level 8.4 g/dl, hematocrit 32 %, white blood cell (WBC) count 22,000/mm^3, platelets of 216,000/mm^3 with normal electrolytes and liver function.

Operation

An emergency craniotomy was performed to evacuate the right-sided hematoma. The left-sided EDH was not evacuated as it was small enough to be managed conservatively. Intra-operatively, no skull fracture was seen, nor was any other bony abnormality evident. Numerous bleeding points were seen arising from the dura, and intra-operatively the patient was found to be coagulopathic, with a platelet count of 46,000/mm^3 and an international normalized ratio (INR) of 1.9, thought to be related to disseminated intravascular coagulopathy (DIC).

Multiple transfusions of blood products including fresh frozen plasma (FFP), platelets, red blood cells, and prothrombin concentrate (Octaplex) were given intra-operatively to help control the bleeding. The bone flap was replaced, and she was kept intubated and ventilated for 24 h after the operation with intracranial pressure (ICP) monitoring. The dilated pupil became reactive a few hours post-operation and she was then slowly weaned off sedation and extubated.

Post-operative course

Initially the patient was alert, orientated, and obeying commands with a left hemiparesis and diplopia secondary to a right third-nerve palsy. After several weeks of neuro-rehabilitation, her deficits improved such that she was able to mobilize independently. Her HbS% was 22 %, not requiring exchange transfusion. She was kept on intravenous antibiotics and high flow oxygen to avoid any further sickle crises.

Multiple investigations were undertaken to identify the etiology of her spontaneous intracranial hematomas, including coagulation screen, blood films, cultures, and vascular imaging. Post-operative CT scans of the brain revealed some right parietal contusions around the site of the previously large EDH, while the left-sided hematoma remained small with no mass effect. MRI scans ruled out an underlying vascular malformation, but did show bilateral convexity skull infarcts over the site of the EDHs, which were felt likely to be secondary to a sickle related bony crisis (Fig. 2).

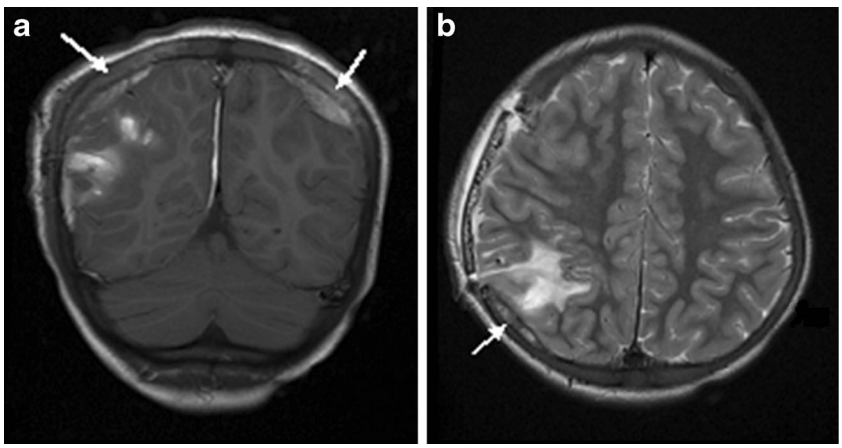

Fig. 2 Post-operative: **a** T1-weighted coronal MR images and **b** T2-weighted axial MR images. There are focal areas of T1 and T2 high signal within the skull vault (see *arrows*) and represent edema from bone infarction secondary to sickle-cell disease. There is a further shallow extradural hematoma overlying the left parietal convexity immediately adjacent to the vault abnormality

Literature review

Sickle-cell anemia or drepanocytosis is an autosomal recessive genetic blood disorder common among the black races, where red blood cells exhibit an abnormal elongated shape described as a "sickle" in low-oxygen tension. Sickling causes numerous medical complications, and shortening life expectancy. Homozygous patients suffer from a chronic hemolytic anemia, with susceptibility to infections, vaso-occlusive crises and neurologically can exhibit cerebrovascular disorders, in particular cerebral ischemia [42].

We performed a non-language restricted literature search using the MEDLINE, EMBASE, SCOPUS, OVID SP, and INFORMA databases to identify citations relevant to spontaneous intracranial hemorrhage in sickle-cell disease. We searched the following keywords: Sickle-cell disease + extradural hematoma + skull convexity infarct + spontaneous + non-traumatic, and also carried out a reference check of the articles retrieved from the above search to include other references missed from the original search.

Inclusion criteria

- All articles pertaining to intracranial hemorrhage in SCD
- Articles of all languages
- No publication date limit

Using the inclusion criteria above, we were able to identify 39 cases related to our study. These were extracted for further data analysis.

Discussion

Analysis of the extracted data resulted in a total of 22 cases (Table 1), including our index case, where spontaneous intracranial EDH has occurred [2, 4, 8, 10, 34]. In all cases, the patients presented within the first four decades of life (mean age is 15).

Fifty percent (11) of the patients had surgical evacuations of their EDH [4, 8, 10]. In the other reported cases, the EDH was small enough to be managed conservatively [11, 17, 19, 21, 27, 40]. There are very few cases in the literature where

Table 1 The clinical data of 22 cases of spontaneous extradural hematomas (EDHs) in sickle-cell patients. *M* male; *F* female; *Hb* hemoglobin; *HbSS* sickle-cell anemia; *HbS-thalassemia* hemoglobin s-beta-thalassemia; *HbSc* sickle-cell-hemoglobin SC disease; *Y* yes; *N* no; *EDH* extradural hematoma; *RIP* dead

	Type of Hb defect	Skull infarct present Y/N?	Lateralization of EDH	Location of EDH	Treatment	Outcome	Authors and year
13, M	HbSS	Y	Bilateral	Frontal	Bilateral craniotomies	Unknown	Mallouh et al. [24]
19, M	HbSS	Y	Left	Frontal	Conservative management (dexamethasone)	Unknown	Karacostas et al. [19]
35, M	HbS - thalassemia	Y	Left	Frontal	Conservative	Discharged home	Tony et al. [40]
14, F	HbSS	Y	Bilateral	Frontal	Bilateral craniotomies	Unknown	Cabon et al. [8]
14, M	HbSS	Y	Bilateral	Frontal (+ left parietal)	Conservative	Discharged home	Resar et al. [34]
16, M	HbSS	Y	Right	Frontal	Conservative	Discharged home	Naran and Fontana [27]
11, M	HbSS	Y	Bilateral	Frontal	Conservative	Discharged home	Ganesh et al. [11]
2, M	HbSS	Unknown	Right	Fronto-temporal	Craniotomy	RIP	Kalala Okito et al. [17]
12, M	HbSS	Y	Left	Parietal	Conservative	Discharged home	Kalala Okito et al. [17]
10, M	Unknown	Y	Left	Frontal	Conservative	Discharged home	Kotb et al. [21]
18, M	HbSS	Y	Bilateral	Parietal (+ right frontal)	Bilateral craniotomies	Discharged home	Dahdaleh et al. [10]
19, M	HbSc	Y	Right	Parietal	Conservative	Discharged home	Arends et al. [2]
15, M	Unknown	N	Bilateral	Frontal	Bilateral craniotomies	RIP	Sangle et al. [36]
18, M	HbSS	N	Right	Frontal	Craniotomy	Discharged home	Babatola et al. [5]
19, M	Unknown	Y	Left	Frontal	Craniotomy	RIP	Bölke and Scherer [7]
13, M	Unknown	Unknown	Bilateral	Parietal	Craniotomy	Discharged home	Patra et al. [32]
12, M	Unknown	Y	Unknown	Unknown	Conservative	RIP	Page et al. [30]
20, M	HbSS	Y	Left	Frontal	Conservative	Discharged home	Page et al. [30]
19, F	Unknown	N	Left	Parietal	Craniotomy	Discharged home	Serarslan et al. [38]
15, M	Unknown	Y	Right	Frontal	Conservative	Discharged home	Ilhan et al. [16]
18, M	Unknown	N	Right	Parietal	Craniotomy	Discharged home	Mishra et al. [26]
7, F	HbSS	Y	Bilateral	Right frontal + Left	Craniotomy	Discharged home	Hettige et al. current review

sickle-cell disease has caused other neurosurgical complications [1, 23].

The commonest SCD genotype in the review was the HbSS genotype (54.5 %), with the others being HbS Thalassemia or HbSc. Most patients (72.7 %) had skull infarcts, confirmed radiologically ± intra-operatively, while there was no evidence of skull infarction in 18.1 % of cases.

There was an even spread in the lateralization of the EDHs; 36.3 % were bilateral, 31.8 % left sided, and 27.3 % right sided. The majority of the EDH were located exclusively in the frontal lobe (54.5 %), the parietal lobe (22.7 %), the fronto-parietal lobes (13.6 %), and the fronto-temporal lobe (4.5 %).

There was a 68.2 % EDH survival rate (15 patients made good progress and were eventually discharged home), with four mortalities (18.2 %), and the outcome data for three patients not known. Of the patients who died, two had unilateral craniotomies, one had a bilateral craniotomy, and one was treated conservatively.

There are several cases where skull infarction related to sickle-cell disease has been described [2, 10, 12, 13, 24, 34], although bony infarction in sickle-cell disease usually affects the long bones. The skull infarction in each case correlates anatomically with the spontaneous EDHs, but a direct causation is difficult to explain. One group suggested skull bone infarction could be responsible for a diploic venous thrombosis with subsequent spontaneous EDH [8], but this does not explain in some cases how such a large extradural collection occurred: the size of this girl's hematoma suggested arterial bleeding rather than venous. Another group proposed that skull infarction led to periosteal elevation with bleeding and effusion filling the space [10, 30, 36].

Only one case described subgaleal collections opposite to the extradural collection adjacent to the infarcted bone [10]. The same authors suggested an alternative explanation for the etiology of these spontaneous SCDs; the chronic skull bone medullary hematopoiesis results in the distortion of the normal skull anatomy, which in the presence of anemia (as in a sickle crisis) can cause a rapid growth and expansion of bone marrow (hematopoietic) tissue. This results in the disruption of integrity of the skull cortex, triggering the infiltration of blood ± hematopoietic tissue into the subgaleal and extradural spaces.

We believe that in our patient's case, local coagulopathy, perhaps related to DIC, caused bleeding from edematous, inflamed, and friable vessels within the infarcted bone after periosteal stripping had occurred.

Conclusions

Clinicians must be aware of this rare potentially fatal phenomenon of spontaneous EDH in sickle-cell crises, especially when patients complain of headaches without neurological deficit, as the classically described lucid interval prior to sudden deterioration with EDH may not occur.

In cases where there are no associated neurological symptoms or headache, other key warning signs to look out for include an acute drop in the hematocrit and the presence of subgaleal swellings/hematoma. These should lower the threshold for brain imaging.

In terms of the patient outcomes early recognition and diagnosis are the most important factors for good clinical outcomes.

Conflict of interest None.

Informed patient consent statement The patient's next of kin has consented to the submission of the case report for submission to the journal.

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Comment

Hettige et al. have drawn attention to a rare but important complication of sickle-cell anemia, namely the spontaneous extradural hematoma. They have provided a plausible hypothesis for the pathogenesis. Because of the increasing transnational migration and mobility of various peoples, neurosurgeons in the Western countries should become more familiar with sickle-cell anemia and its potential neurological sequelae.

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