AUDIT

Clinical presentation of acute chest syndrome in sickle cell disease

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In this study the records of 45 patients with sickle cell disease involved in 63 presentations of acute chest syndrome at the Princess Margaret Hospital in Nassau, the Bahamas, between 1997 and 2001 were examined. Patients were divided into three groups on the basis of age (<13 years, 13–18 years, ⩾19 years) with a view to assessing clinical presentation. The incidence of symptoms, physical signs, and laboratory findings were enumerated and significant differences between age groups determined. The data were analysed using analysis of variance, *t* test, and χ^2 test and compared with existing knowledge on the subject.

This study proposed to evaluate the clinical presentation of acute chest syndrome with emphasis on historical and physical findings, and to encourage the physician to maintain a high index of suspicion for the condition in susceptible patients. It was found that presentation varied significantly with age groups, children presenting most classically with fever and cough and adults, with chest pain. The 13–18 age group emerged as the group which presented most frequently with the typical symptoms of chest infection, thus potentially making diagnosis easier. Of note, the most frequent finding was a normal examination, while the second commonest physical finding was crepitations on auscultation of the chest.

The diagnosis of acute chest syndrome (ACS) in sickle cell disease represents an important challenge to the physician. It may present insidiously and non-specifically, often complicating other conditions. It is, however, imperative that we correctly identify and aggressively treat this condition as it is the major cause of mortality in sickle cell disease, accounting for 25% of deaths and occurring across all age ranges.[1 2] This syndrome has been well documented to be multifactorial in nature with underlying factors including fat embolism, infection with a wide range of organisms, and infarction. The greatest concern is the elusiveness of the significant number of patients that may have a normal or slightly abnormal examination on presentation but are at no less risk of significant disease.[3] In this study we hope to add to the understanding of, and sensitise physicians to, the spectrum of the clinical presentation of this syndrome.

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METHODS

A retrospective cohort study during a five year period beginning January 1997 and ending December 2001 was done. The records of all patients with sickle cell disease who were admitted to the Princess Margaret Hospital, Nassau, in the Bahamas, during the period specified by the study were carefully perused. Those admitted to the study fulfilled two criteria: (i) lower respiratory tract symptoms and (ii) new pulmonary infiltrates on the chest radiograph.

This is in keeping with the most widely accepted definition of ACS. Historical, clinical, and laboratory data were obtained and analysed with a view to determining common modes of presentation and assessing whether these differed between age groups. Sixty three cases of ACS involving 45 patients were found. Analysis of variance and *t* test were used to assess means and the χ^2 test was used to assess statistical differences between groups. The groups compared were <13 years, 13–18 years, and ⩾19 years.

RESULTS

Profile of patients

All of the patients were Afro-Caribbean. The patients' ages ranged from 1–37 years with 46% of cases under 13 years (mean 15.6, median 15 years). Altogether 62% of the cases were female and 38% were male. The number of admissions for each patient ranged from one to four.

Reason for admission

The admitting diagnosis in 79% of the cases was ACS, while the remaining 21% were admitted for vaso-occlusive crises (most common) and surgical procedures but subsequently developed ACS during their hospital stay.

Presenting symptoms

The most common presenting symptoms were cough, fever, and chest pain respectively. The frequency of presenting symptoms was dependent on the age of the patient (fig 1). In children younger than 13 years fever and cough were the two commonest symptoms while in those older than 13 years, cough and chest pain were more frequent. Those aged 13–18 years were more likely to present with sputum production than those in the other age groups. Statistically significant differences were observed for the presenting symptoms fever ($p = 0.020$), shortness of breath ($p = 0.045$), and sputum production

Abbreviations: ACS, acute chest syndrome; LOS, length of stay

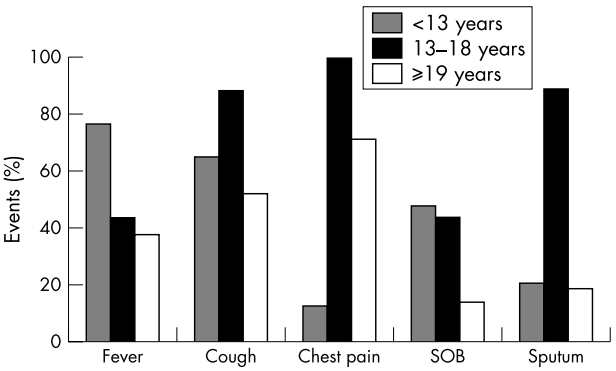

Figure 1 Percent of events with selected symptoms by age group (n = 63) (SOB, shortness of breath).

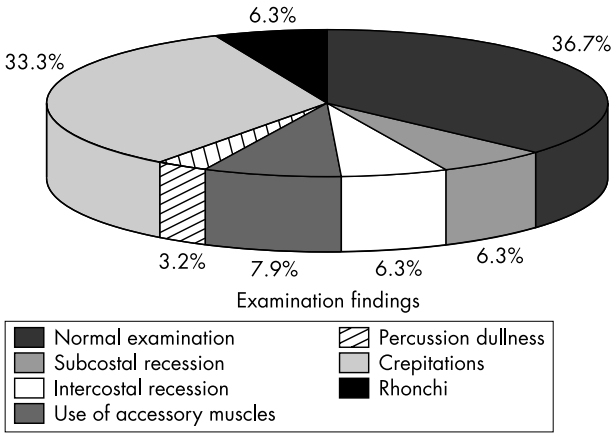

Figure 2 Findings on physical examination as a percentage of total study group (n = 63).

(p<0.005) when the age groups were compared. None of the patients reported haemoptysis or wheeze.

Physical findings

Vital signs on presentation were shown to be age dependent with children presenting with higher temperature, respiratory rate (p = 0.004), and pulse rate (p<0.005) than adults. The average temperature in children under 13 years of age was 37.3℃, while that for teenagers was 36.8℃ and for adults 37.0℃ (see other examination variables in table 1). The most common physical finding was a normal examination (36.7%), crepitations on lung auscultation being the second most common finding (fig 2).

Laboratory findings

The level of platelets on admission was lower in the <13 age group (p = 0.01) but there were no other statistically significant differences between age groups (table 2).

The mean (SD) haemoglobin concentration (in g/l) was 78.6 (1.4), 87.3 (12.6), and 88.1 (19.3) in the <13, 13–18, and ≥19 age groups respectively; white cell count was higher in the <13 and 13–18 age groups.

Hospital course

The average length of stay (LOS) was 10 days (range 3–35 days) with 60% of patients staying more than eight days. Male patients on average were hospitalised longer than their female counterparts (mean LOS male 11.4 days and female LOS 9.7 days). Five patients died giving an in-hospital mortality rate of 7.9%.

DISCUSSION

ACS can be defined as the occurrence of lower respiratory tract symptoms in combination with new pulmonary infiltrates on chest radiography, in a patient with sickle cell disease.

It has long been known that this syndrome is a multifactorial process with the likely final common pathway being in situ microvascular thrombosis. Great light was shed on the relative weighting of the possible aetiological factors by Vichinsky *et al*.[4] In the largest series of its kind 671 episodes of ACS in 538 patients were evaluated extensively to identify possible aetiological factors. In this series Vichinsky reported no identifiable cause in 45.7% of cases, infection was documented in 29.4% of cases (with only 15% of infection being cased by typical bacteria), infarction occurred in 16.1%, and fat embolisation in 8.8%. The clinical presentation of ACS is linked to the dominant aetiological factor so it is not at all surprising that a wide spectrum is seen.

The paediatric presentation in this series was consistent with previous trends,[3 6 7] with fever, cough, and shortness of breath being the predominant symptoms. Additionally, our finding of increased temperature, pulse rate, and respiratory rate in children was consistent with the cooperative study.[3] Early studies showed a high percentage of proven bacterial infection in children[8 9]; this was, however, before the wide spread use of pneumococcal vaccine and penicillin prophylaxis. Interestingly more recent studies show the same clinical pattern but with most cases being culture negative; this may represent an increased relative role of atypical bacterial and viral infections in children. Sputum production was significantly higher in the 13–18 year age group (p<0.001). In the Cooperative Study of Sickle Cell Disease,[3] which was the largest series on clinical presentation of ACS, sputum production was shown to progressively increase with age from the <2 to the >20 year age groups, in contrast to what was seen in our study.

Of considerable interest, we found that the age group 13–18 years presented with the greatest number of symptoms consistently, potentially making them the easiest to diagnose on clinical grounds (see fig 1) with cough, chest pain, and

Table1 Physical findings by age group (n = 63); values are mean (SD)

Examination	<13 years (n = 29)	13–18 years (n = 9)	≥19 years (n = 25)
Pulse rate/min* (p<0.00005)	119.54 (20.17)	95.78 (22.55)	87.32 (13.88)
Respiratory rate/min* (p = 0.004)	32.07 (10.59)	26.67 (11.87)	22.44 (3.11)
Systolic pressure (mm Hg)* (p = 0.024)	94.33 (35.22)	109.78 (9.38)	124.21 (22.78)
Diastolic pressure (mm Hg)* (p = 0.084)	54.17 (22.96)	61.89 (6.77)	69.11 (13.71)

*Statistically significant differences exist for these variables (analysis of variance p<0.05).

Table 2 Investigation by age group (n = 63); values are mean (SD)

Investigation	<13 years (n = 29)	13-18 years (n = 9)	⩾19 years (n = 25)
Haemoglobin (g/l) (p = 0.107)	78.6 (14.0)	87.3 (12.6)	88.1 (19.3)
Packed cell volume (p = 0.063)	0.23 (0.04)	0.26 (0.04)	0.26 (0.06)
Platelets $\times 10^9$/l* (p = 0.010)	296.25 (136.30)	440.17 (199.06)	426.10 (138.09)
White cell count $\times 10^9$/l (p = 0.062)	23.11 (14.62)	28.90 (23.32)	16.16 (5.41)
Urea (mmol/l) (p = 0.610)	10.6 (11.19)	8.75 (2.55)	8.32 (2.91)
Creatinine (μmol/l) (p = 0.187)	0.51 (0.33)	0.50 (0.18)	0.65 (0.18)

*Statistically significant differences exist for these variables (analysis of variance $p<0.05$).

sputum production being nearly always present. The other two age groups had far less consistent clinical findings.

Clinical examination is potentially the most misleading aspect of assessment of this syndrome. The Cooperative Study of Sickle Cell Disease[3] found that the second most common examination finding was a normal examination, representing 35% of cases. In contrast, Agtmael *et al* in an analysis of 81 episodes in 53 Afro-Caribbean patients documented abnormal examinations in at least 91%.[10] In our series 36.7% had a normal examination, the commonest finding. This is a feature we wish to highlight as it can lead the unwary doctor to assume that less aggressive management is warranted when in fact, clinically there are no good predictors of which patients may succumb.[3]

Genotype analysis was not included in this study as it has been clearly and repeatedly shown that clinical presentation is independent of genotype,[3 9] although HbSS and HbSβ thalassaemia patients may have more frequent episodes.[11 12] The small number of events evaluated and its retrospective design limit this study. Arterial blood gas analysis was not included, as consistent information on its relationship to oxygen supplementation was not available and blood cultures were not uniformly taken, making it impossible to draw conclusions on the range of causative organisms. For this reason as well, it was not possible to ascertain which mechanism (pathologically) was responsible for the cases of ACS encountered. We also acknowledge that there may be some interobserver variation with respect to the presence or absence of critical clinical signs but we believe this to be an inherent part of any study of this nature and must always be borne in mind.

In summary, one of the most important aspects of management of ACS is early diagnosis. However symptoms can vary widely and examination is frequently non-contributory. Teenagers may represent the age group in which there is the greatest number of symptoms but even in the absence of classical signs a high index of suspicion should be maintained. The most sensitive definition of this syndrome is lower respiratory tract symptoms in the presence of new pulmonary infiltrates in a patient with sickle cell disease, which will include the patient who is apyrexial and has a normal examination. It must be appreciated that this syndrome frequently complicates unrelated hospital admissions (for example, in half of patients, ACS is preceded by vaso-occlusive crises[13] and in our study it was 21%), and should be actively sought out with each inpatient review so that early management can be instituted and morbidity and mortality limited.

Absence of pyrexia or, indeed, a normal examination at presentation, does not exclude the diagnosis.

Known and proposed causes of ACS

- Infection:
  - Bacterial infection.
  - Atypical bacterial pneumonia.
  - Viral pneumonia.
  - Parvovirus B19.
- Pulmonary vascular occlusion:
  - In situ pulmonary thrombosis.
  - Fat embolism.
  - Peripheral thromboembolism.
- Hypoventilation/atelectasis:
  - Thoracic bony infarction.
  - Abdominal pain.
  - Opioids.
- Pulmonary oedema:
  - Intravenous fluids.
  - Opioids.
  - Pulmonary vascular injury.
- Other:
  - Bronchospasm.

(Adapted from Quinn and Buchanan[5])

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