Clinical presentation of acute chest syndrome in sickle cell disease

C Taylor, F Carter, J Poulse, S Rolle, S Babu and S Crichlow

doi:10.1136/pgmj.2003.012781

Updated information and services can be found at:
http://pmj.bmj.com/cgi/content/full/80/944/346

These include:

References
This article cites 11 articles, 4 of which can be accessed free at:
http://pmj.bmj.com/cgi/content/full/80/944/346#BIBL

Rapid responses
You can respond to this article at:
http://pmj.bmj.com/cgi/eletter-submit/80/944/346

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Topic collections
Articles on similar topics can be found in the following collections

- Other respiratory medicine (1063 articles)
- Hematology Incl Blood Transfusion (550 articles)

Notes

To order reprints of this article go to:
http://www.bmjjournals.com/cgi/reprintform

To subscribe to Postgraduate Medical Journal go to:
http://www.bmjjournals.com/subscriptions/
Clinical presentation of acute chest syndrome in sickle cell disease

C Taylor, F Carter, J Poulose, S Rolle, S Babu, S Crichlow

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 χ² 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 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 elusive-ness 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.1 In this study we hope to add to the understanding of, and sensitise physicians to, the spectrum of the clinical presentation of this syndrome.

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 χ² 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
(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˚C, while that for teenagers was 36.8˚C and for adults 37.0˚C (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 caused 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,5–7 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 children8; this was, however, before the widespread 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

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

*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 Disease¹ found that the second most common examination finding was a normal examination, representing 35% of cases. In contrast, Agtmael et al documented abnormal examinations in at least 91%.¹⁰ In an analysis of 81 episodes in 53 Afro-Caribbean patients oxygen supplementation was not available and blood design limit this study. Arterial blood gas analysis was not performed which will include the patient who is apyrexial and has a normal examination at presentation, does not exclude the diagnosis.

Genotype analysis was not included in this study as it has been clearly and repeatedly shown that clinical presentation is independent of genotype., although HbSS and HbSβ thalassaemia patients may have more frequent episodes.¹¹¹² The small number of events evaluated and its retrospective nature should 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 afebrile 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 crises¹³ 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.

ACKNOWLEDGEMENTS
The authors would like to thank Dr P Gomez, Chief of Internal Medicine and Infectious Diseases, Princess Margaret Hospital, Bahamas; Dr SinQuee, Consultant in Paediatrics, Princess Margaret Hospital, Bahamas; Mr T Fountain, Health and Research Unit, Ministry of Health, Bahamas; and Dr M Hamon, Consultant in Haematology, Derriford Hospital, Plymouth, UK.

Authors’ affiliations
C Taylor, F Carter, J Poulose, S Rolle, S Babu, S Chichlow, Derriford Hospital, Plymouth, Devon, UK.

REFERENCE


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

<table>
<thead>
<tr>
<th>Investigation</th>
<th>&lt;13 years (n = 29)</th>
<th>13-18 years (n = 9)</th>
<th>≥19 years (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/l) (p = 0.107)</td>
<td>78.6 (14.0)</td>
<td>87.3 (12.6)</td>
<td>88.1 (19.3)</td>
</tr>
<tr>
<td>Packed cell volume (p = 0.063)</td>
<td>0.23 (0.04)</td>
<td>0.26 (0.04)</td>
<td>0.26 (0.06)</td>
</tr>
<tr>
<td>Platelets x10^12/l (p = 0.010)</td>
<td>296.25 (136.30)</td>
<td>440.17 (199.06)</td>
<td>426.10 (138.09)</td>
</tr>
<tr>
<td>White cell count x10^9/l (p = 0.062)</td>
<td>23.11 (14.62)</td>
<td>28.90 (23.32)</td>
<td>16.16 (5.41)</td>
</tr>
<tr>
<td>Urea (mmol/l) (p = 0.610)</td>
<td>10.6 (11.19)</td>
<td>8.75 (2.55)</td>
<td>8.32 (2.91)</td>
</tr>
<tr>
<td>Creatinine (μmol/l) (p = 0.187)</td>
<td>0.51 (0.33)</td>
<td>0.50 (0.18)</td>
<td>0.65 (0.18)</td>
</tr>
</tbody>
</table>

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

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)
Clinical Evidence—Call for contributors

Clinical Evidence is a regularly updated evidence based journal available worldwide both as a paper version and on the internet. Clinical Evidence needs to recruit a number of new contributors. Contributors are health care professionals or epidemiologists with experience in evidence based medicine and the ability to write in a concise and structured way.

Currently, we are interested in finding contributors with an interest in the following clinical areas:

- Altitude sickness
- Autism
- Basal cell carcinoma
- Breast feeding
- Carbon monoxide poisoning
- Cervical cancer
- Cystic fibrosis
- Cyclic pregnancy
- Grief/bereavement
- Halitosis
- Hodgkin's disease
- Infectious mononucleosis (glandular fever)
- Kidney stones
- Malignant melanoma (metastatic)
- Mesotheioma
- Myeloma
- Ovarian cyst
- Pancreatitis (acute)
- Pancreatitis (chronic)
- Polymyalgia rheumatica
- Post-partum haemorrhage
- Pulmonary embolism
- Recurrent miscarriage
- Repetitive strain injury
- Scoliosis
- Seasonal affective disorder
- Squint
- Systemic lupus erythematosus
- Testicular cancer
- Varicocele
- Viral meningitis
- Vitiligo

However, we are always looking for others, so do not let this list discourage you.

Being a contributor involves:

- Appraising the results of literature searches (performed by our Information Specialists) to identify high quality evidence for inclusion in the journal.
- Writing to a highly structured template (about 2000–3000 words), using evidence from selected studies, within 6–8 weeks of receiving the literature search results.
- Working with Clinical Evidence Editors to ensure that the text meets rigorous epidemiological and style standards.
- Updating the text every eight months to incorporate new evidence.
- Expanding the topic to include new questions once every 12–18 months.

If you would like to become a contributor for Clinical Evidence or require more information about what this involves please send your contact details and a copy of your CV, clearly stating the clinical area you are interested in, to Claire Folkes (cfolkes@bmjgroup.com).

Call for peer reviewers

Clinical Evidence also needs to recruit a number of new peer reviewers specifically with an interest in the clinical areas stated above, and also others related to general practice. Peer reviewers are health care professionals or epidemiologists with experience in evidence based medicine. As a peer reviewer you would be asked for your views on the clinical relevance, validity, and accessibility of specific topics within the journal, and their usefulness to the intended audience (international generalists and health care professionals, possibly with limited statistical knowledge). Topics are usually 2000–3000 words in length and we would ask you to review between 2–5 topics per year. The peer review process takes place throughout the year, and our turnaround time for each review is ideally 10–14 days.

If you are interested in becoming a peer reviewer for Clinical Evidence, please complete the peer review questionnaire at www.clinicalevidence.com or contact Claire Folkes (cfolkes@bmjgroup.com).