PATTERN OF PULMONARY MANIFESTATIONS IN PATIENTS WITH SICKLE CELL DISEASE AND FEVER

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Objectives: The objective of this study was to determine the frequency and pattern of pulmonary manifestations in febrile patients with sickle-cell disease (SCD), a condition prevalent in the Eastern Province of Saudi Arabia.

Design: The main pulmonary complications in febrile adult SCD patients were studied between January 1986 and December 1990.

Material and Methods: The medical records, chest X-rays and microbiological data of all febrile (temperature >38°C) SCD patients >12 years of age admitted to KFHU during the study period were retrospectively reviewed.

Results: Of the 164 patient-episodes in 49 male and 19 female SCD patients, chest X-rays were abnormal in 33 (20.1%) episodes. Of these 33, there was consolidation in 17 (52%), pleural effusion in 6 (18%), pleural effusion and consolidation in 4 (12%), consolidation with collapse in 3 (9%), pleural thickening in 2 (6%) and bronchogenic carcinoma in one.

Conclusion: Pneumonia was the most common complication in Saudi SCD patients with abnormal chest X-rays. Chest X-rays are most useful in SCD patients with symptoms of chest infection, abnormal chest signs, or those with persistent fever during vaso-occlusive crisis.

Key Words: Chest X-ray, sickle cell disease, pulmonary manifestations.

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INTRODUCTION
Sickle-cell disease (SCD) is prevalent in the Eastern Province of Saudi Arabia, and many patients are admitted to hospitals with painful vaso-occlusive crises. Some patients present with fever as part of their symptomatology. However, whether this fever is part of the crisis itself or a manifestation of infection is sometimes difficult to judge. Pulmonary manifestations or complications of SCD have been reported. The most common single specific pulmonary complication of SCD at all ages is acute pulmonary involvement compatible with bacterial pneumonia evidenced clinically by cough, fever, leucocytosis, pleuritic pain and occasional dyspnea.\(^1\)\(^-\)\(^2\)

An acute pulmonary involvement (the chest syndrome), which may be precipitated by bacterial pneumonia is the most common single complication of SCD at any age. Multiple pulmonary micro-infarctions have been suspected as the cause of chest syndrome, although there is an increased risk of pneumococcal and hemophilus influenzae pneumonia in this group.\(^3\)\(^-\)\(^6\)

Pulmonary infarcts, which develop in patients with SCD, involve predominantly the lower lobes of the lungs and frequently cause pleural effusion.\(^3\)\(^,\)\(^5\)\(^,\)\(^7\) Cor pulmonale may also be a consequence and is due to an increased workload imposed on the right ventricle by anemia as well as by partial obliteration of the pulmonary capillary bed.\(^7\)

Lung parenchymal abnormalities have been detected in a significant number of patients. Infiltrate abnormalities due to either interstitial pulmonary edema or to so-called chronic sickle cell lung disease, were nearly as prevalent as cardiomegaly. In one series, pulmonary abnormalities were detected in the majority of patients\(^8\) and in another, chest X-ray abnormalities were detected in 40% of patients.\(^9\)

The well-known propensity of SCD patients to develop pneumonia was evident in the Stark’s series\(^8\) in which over 33% of patients presented with infectious intrathoracic complications. In some series, acute pulmonary disease was the single most common reason for hospitalization.\(^3\)\(^,\)\(^10\) The most frequent infection noted by several authors is a rapidly spreading but slowly resolving pneumonia.\(^11\) The most common organisms involved in patients with the acute chest syndrome are Chlamydia pneumonia and Mycoplasma pneumoniae.\(^4\)

To the best of our knowledge, there has been no report on the pulmonary manifestations or complications of SCD in Saudi Arabia. We report here an analysis of chest X-ray findings in SCD adult Saudi patients admitted to a teaching hospital.

MATERIAL AND METHODS
The medical records of all adult patients with SCD admitted to King Fahd Hospital of the University (KFHU) over a five-year period, between January 1986 and December 1990 were retrospectively reviewed. Those included in the study were Saudis, over 12 years of age, who had had a fever of 38°C on at least two occasions, a minimum of six hours apart. In addition to their clinical features, their radiological and microbiological data were reviewed.

Classifications of various abnormalities shown on chest X-rays included parenchymal infiltration consistent with pneumonic infection and was considered consolidation. Loss of costophrenic angle with positive decubitus film for free fluid was considered pleural effusion. Thickening of the pleura with negative decubitus film was considered pleural thickening.

RESULTS
Between January 1986 and December 1990, 164 patient episodes of SCD were admitted to KFHU with fever. Out of 68 patients, 49 (72%) were males. Figure 1 shows the age and sex distribution. In 131 episodes (79.9%), chest X-rays were normal and in 33 (20.1%) there were abnormalities. The pattern of pulmonary manifestations (complications) in those who had abnormal chest X-rays is shown in Table 1. Seventeen (52%) showed consolidation, 6 (18%) had pleural effusion, 4
(12%) consolidation with pleural effusion, 3 (9%) had consolidation with collapse, 2 (6%) pleural thickening and one X-ray showed bronchogenic carcinoma with total lung collapse diagnosed by sputum cytology.

**Table 1: Abnormalities in chest x-ray in 33 episodes**

| Abnormalities                              | No. of patients (%) |
|--------------------------------------------|---------------------|
| Consolidation                              | 17 (52)             |
| Pleural effusion                           | 6 (18)              |
| Pleural thickening                         | 2 (6)               |
| Consolidation with pleural effusion        | 4 (12)              |
| Consolidation and collapse                 | 3 (9)               |
| Collapse                                   | 1 (3)               |

**Table 2: Microbiological results**

| Culture                        | No. of patients (Episodes) |
|--------------------------------|----------------------------|
| **Episodes with normal chest X-ray** |                           |
| Blood:                         | 5                          |
| *Salmonella Typhi*            | 3                          |
| *Brucella Melitensis*         | 1                          |
| *Staphylococcus Aureus*       | 1                          |
| Throat:                       | 9                          |
| *Strep. Group B*              | 4                          |
| *Strep. Fecalis*              | 1                          |
| *Staph. Aureus*               | 4                          |
| **Episodes with abnormal chest X-ray** |                     |
| Gram negative bacteria        | 1                          |
| Sputum:                       |                            |
| *Staph. Aureus*               | 1                          |
| *Staph. + Klebsiella*         | 2                          |

The microbiological results showed that of the patients with normal chest X-ray, blood culture was positive in five episodes with *salmonella typhi* as the most common organism isolated. Throat culture was positive in nine episodes, the most common organism isolated being *streptococcus* Group B (Table 2).

Table 2 also shows the microbiological results among episodes with abnormal chest X-ray. While three sputum samples grew organisms, in only one blood culture was an organism isolated.

The pattern of white blood cell count (WBC) in episodes with abnormal chest X-ray showed a normal count in seven episodes (<10,000/mm³), moderate leucocytosis (WBC 11,500 – 19,500/mm³) in 12 episodes and severe leucocytosis (WBC 20,000 – 42,000/mm³) in 14 episodes. SCD patients evaluated in the study were found to have other associated diseases, namely, G6PD deficiency and β-Thalassemia as shown in Table 3.

The correlation between the findings in chest X-ray and physical examination are shown in Table 4. Only 2 (1.5%) of our 131 patients with normal chest X-rays had abnormal physical findings. The difference was statistically significant (p<0.0001).

**DISCUSSION**

Sickle-cell disease is prevalent in the Eastern Province of Saudi Arabia. The major disabilities suffered by patients with sickle-cell anemia are related to painful vaso-occlusive crises. There is frequently no identifiable precipitating event although infection may be associated with the onset of the episode. In
In general, the onset of the fever occurs one or two days after the onset of the pain and parallels the degree of tissue necrosis resulting from the ischemic infarction.12

Relatively frequently, (in 20% of crises) patients present with acute chest syndrome.5 This typically starts with bone pain in the thoracic cage, often accompanied by pleurisy, tachycardia and tachypnea. Inspiratory crackles and signs of consolidation usually occur later. Radiological shadowing usually appears first at the bases, and in severe cases spreads throughout the lungs. The episode is accompanied by fever, a fall in hemoglobin and, in severe cases, a fall in platelet count as well.3,4 Apart from the acute chest syndrome, patients with sickle-cell disease may be at increased risk of infection, including pneumonia, though this diagnosis may often be made in error when pulmonary infarction occurs. Furthermore, there may also be a greater risk of pulmonary embolism in pregnancy.13

There is also some evidence that patients with sickle cell disease develop a restrictive pattern of lung function and pulmonary hypertension as a consequence of repeated episodes of sickling in the pulmonary vasculature.10

In our present study, we found that out of 164 patients' episodes admitted to KFHU over a 5-year period, 131 episodes (77.6%) had normal chest X-ray, and 33 episodes (22.4%) had various abnormalities on chest X-ray. The most common abnormality was pulmonary consolidation. These findings are similar to previous reports that the most common pulmonary complication of SCD is pneumonia.7 Oppenheimer reported in his series that the most common single specific complication of SCD at all ages is acute pulmonary involvement, compatible with bacterial pneumonia evidenced clinically by cough, fever, leucocytosis, pleuritic pain and occasional dyspnea.1 These data are important as fever is a very common symptom in SCD patients admitted to hospitals, but whether this fever is part of the vaso-occlusive crises of SCD or a manifestation of infection is sometimes difficult to determine.

The data, however, demonstrate that chest infection is common in SCD patients admitted to hospitals with fever. The chest X-ray is particularly important in identifying those fevers that are due to chest infection. The data also demonstrate the pattern of pulmonary manifestations and complications of SCD in Saudi patients admitted to hospitals with fever. To the best of our knowledge, this has not been reported in the literature. The association of G6PD deficiency and beta-thalassemia may have had an impact on the pulmonary complications

The important question to be addressed is when a chest X-ray should be requested in such SCD patients presenting to hospitals, especially when an abnormality is likely to be found in only 20% of cases.

We conclude that a chest X-ray would be more useful and should be requested for any SCD patient presenting to hospital with fever (>38°C), cough, and pleuritic pain or dyspnea and/or leucocytosis. In other cases, it should be requested when the symptoms of vaso-occlusive crisis subside but the fever persists.

REFERENCES
1. Oppenheimer EH, Esterly JR. Pulmonary changes in sickle cell disease. Am Rev Resp Dis 1971; 103:858-9
2. Petch MC, Sergenat GR. Clinical features of pulmonary lesions in sickle cell anemia. BMJ 1970;3:31.
3. Vinchinsky EP, Styles LA, Colangelo LH. Acute chest syndrome in sickle cell disease: Clinical presentations and course. Blood 1997; 89 (5):1787-1792
4. Vinchisky EP, Neumayr LD, Earles AN. Causes and outcome of the acute chest syndrome in sickle cell disease. N Engl J Med 2000;342:1855-1865
5. Barret-Connor E. Acute pulmonary disease in sickle cell anemia. Am Rev Resp Dis 1971;104:159-65.
6. Vinchisky E, Williams R, Das M. Pulmonary fat embolism: a distinct cause of severe acute chest syndrome in sickle cell anemia. Blood 1994;83:3107-12
7. Collins FS, Orringer EP. Pulmonary hypertension and core pulmonary in the sickle hemoglobinopathies. Am J Med 1982;73:814.
8. Stark P, Pfeiffer WE. Intrathoracic manifestations of sickle cell disease. Radiologie 1985;25:33-5.
9. Reynaldo J. The roentgenological features of sickle cell disease and related hemoglobinopathies. Springfield III Chus C. Thomson 1985; p130-2.

10. Bromberg PA. Pulmonary aspects of sickle cell disease. Arch Intern Med 1974;133:652-7.

11. Barret-Connor E. Anemia and infection. Am J Med 1972;52:242-53.

12. Cecil Textbook of Medicine. Wyngaarten and Smith, 18th ed. IE Saunders; p939-40.

13. Crofton and Douglas’s Respiratory Diseases. 4th ed. Oxford: Blackwell Scientific Publications. p1020-1.