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

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هدف الدراسة: هدف هذه االدراسة هو معرفة نمط مضاعفات الجهاز التنفسي ومدى حدوثها في مرضى فقر الدم المنجلي عند ارتفاع درجة الحرارة لديهم حيث إن هذا المرض شائع الانتشار في المنطقة الشرقية في المملكة العربية السعودية.
طريقة الدراسة: لقد تم دراسة مضاعفات الجهاز التنفسي عند مرضى الأنيميا المنجلية المصاحبة بارتفاع درجة الحرارة من يناير 1986م حتى ديسمبر 1990م.
مكان الدراسة: مستشفى الملك فهد بالخبر.
مادة الدراسة: ملفات المرضى المنومين بالمستشفى, أشعة الصدر والفحوص المخبرية الميكروبيولوجية للمرضى,. مع ارتفاع درجة الحرارة أكثر من 38 درجة مئوية ممن تزيد أعمارهم عن 12 سنة , تمت دراستها ومراجعتها للخروج بنتائج الدراسة.
نتائج الدراسة: لقد تمت دراسة 164 حالة مرضية استدعت الدخول للمستشفى في 49 من الذكور و 19 من الإناث المصابين بالأنيميا المنجلية. اتضح من الدراسة أن 33 حالة (20,1%) أشعة الصدر كانت غير طبيعية.
من هذه 33 حالة : 17 حالة مصابة بالتهاب رئوي (52%) و 6 حالات (18%) تجمع سائل في التجويف البلوري و 4 حالات (12%) التهاب رئوي مع سائل في التجويف البلوري و 3 حالات (9%) التهاب رئوي مع انكماش في جزء من الرئة , 2 حالة (6%) زيادة في سمك الغشاء البلوري , حالة واحدة مصابة بسرطان الرئة.
خاتمة: لقد وجد أن الالتهاب الرئوي أكثر مضاعفات الجهاز التنفسي شيوعيا عند مرض الأنيميا المنجلية مع ارتفاع درجة حرارتهم خصوصاً عندما تكون أشعة الصدر غير طبيعية. كما اتضح أن أشعة الصدر أكثر الفحوصات فائدة للتشخيص عند مرضى الأنيميا المنجلية الذين يشكون من أعراض التهابات الصدر خصوصاً عند ارتفاع درجة حرارتهم المصاحبة لنوبة الآلام الشديدة لديهم.

الكلمات المرجعية: أشعة الصدر, مرض الأنيميا المنجلية, مضاعفات الجهاز التنفسي.

***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, leucocyctosis, 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.[5,10] 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^{o}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.

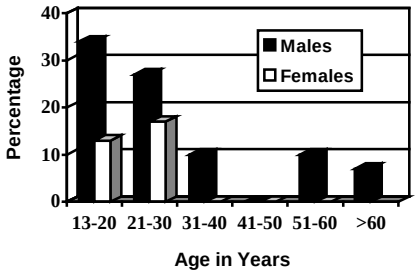

Figure 1: *Age and sex distribution of sickle cell disease patients*

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/mm^3), moderate leucocytosis (WBC 11,500 – 19,500/mm^3) in 12 episodes and severe leucocytosis (WBC 20,000 – 42,000/mm^3) 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).

Table 3*: Assciated disease*

Disease	**Abnormal Chest X-ray**	**Normal Chest X-ray**
G6PD	3	7
β-Thalassemia	1	8
G6PD & β-Thalassemia	1	1
IDDM	-	3

One patient had an associated platelet dysfunction

Table 4*: Correlation between chest X-ray and physical examination*

Findings	**Normal X-ray (%)**	**Abnormal X-ray (%)**
Abnormal chest findings	2 (1.5)	14 (42.4)
No chest findings	129 (98.5)	19 (57.5)
Total	**131**	**33**

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

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^{o}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.

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