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DIAGNOSTIC IMAGING IN THE EVALUATION OF PATIENTS WITH SICKLE CELL ANEMIA IN ACUTE THORACIC SYNDROME

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Abstract: Sickle cell anemia is a genetic disease first described in 1910 and is an anomaly caused by a mutation on chromosome 11 that results in the substitution of a glutamic acid for valine at position 6 of the N-terminal end of the globin chain, which gives rise to hemoglobin S, resulting in sickle-shaped red blood cells that do not circulate as they should in the microcirculation, resulting in obstruction of capillary blood flow. The pathophysiological mechanism of sickle cell disease leads to serious clinical manifestations, including Acute Thoracic Syndrome, which is responsible for 25% of deaths. This literature review aims to assess how imaging methods can help in the diagnosis of Acute Thoracic Syndrome in patients with Sickle Cell Anemia, and which would be the best imaging test for the etiological identification of Acute Thoracic Syndrome.
Keywords: Sickle Cell Anemia, Imaging Diagnosis, Acute Thoracic Syndrome.

INTRODUCTION

Sickle cell anemia (SCA) is a genetic disease that is common, but not exclusive, in individuals of African descent or origin. It was first described in 1910 and is an anomaly caused by a mutation on chromosome 11 that results in the substitution of a glutamic acid for valine at position 6 of the N-terminal end of the globin chain, which gives rise to hemoglobin S. The content of the erythrocytes, predominantly hemoglobin S, takes on the shape of a sickle under hypoxic conditions, thus giving rise to the name sickle cell. [1]

The sickle-shaped red blood cells do not circulate as they should in the body microcirculation, which results in the obstruction of capillary blood flow and, consequently, in the early destruction of the blood capillary itself. [1]

The pathophysiological mechanism of sickle cell disease leads to serious clinical manifestations, including Acute Thoracic Syndrome (ATS). As an important cause of mortality and morbidity in sickle cell patients, it is essential that ATS is diagnosed as soon as possible in order to improve the patient's prognosis. Imaging exams are therefore an important tool in the diagnosis of acute sickle cell disease.

METHODOLOGY

This study refers to a literature review, which is a form of research based on the literature on a given topic. In this sense, this review incorporated the construction of an analysis on Sickle Cell Anemia and the relationship with diagnostic imaging in the evaluation of Acute Thoracic Syndrome. This study contributes to the structuring of the theme presented, based on the theoretical foundation and analysis of pre-existing scientific production, enabling the identification of knowledge gaps for the development of new studies.

Thus, in order to answer the guiding question - "How can imaging tests diagnose and assess acute chest syndrome in sickle cell patients?" - the terms to be used in the search were defined, using descriptors with the most appropriate concepts for the research question, through structured health vocabularies, presented as subject descriptors - Medical Subject Headings (MESH), coordinated by the US National Library of Medicine (US NLM).

The searches were carried out in January 2023 by the three authors of this review in a PubMed database. The following search terms were used: ((Sickle Cell Anaemia[MeSH Major Topic]) AND (Acute Chest Syndrome[MeSH Major Topic])) AND (Diagnostic Imaging[MeSH Major Topic]) were used as descriptors to survey data from the last twenty years (2003 - 2023).

The selection of the articles analyzed in this study met the following inclusion criteria: prospective or retrospective cohort studies, literature reviews, systematic reviews, free access, in Portuguese or English, in pediatric and adult populations, whose object is of interest to this review. The exclusion criteria were: duplicate articles and/or articles that did not address the objects of this study, failing to mention any of the terms.

RESULTS

The PubMed search identified 14 articles, 8 of which were excluded because they did not meet the inclusion criteria. Therefore, the search resulted in 6 studies which were used in this review.

DISCUSSION

Acute Thoracic Syndrome (ATS) is the main cause of mortality in adult patients with Sickle Cell Disease (SCD), accounting for around 25% of deaths[2 5 6 8]. It is estimated that 17% of children with FD and fever will have STA and up to a third of patients with FD will have STA at least once in their lives [3]. STA can be caused by infectious or non-infectious causes, such as emboli or infarction[3]. As an important cause of mortality and morbidity in sickle cell patients, it is essential that STA is diagnosed and etiologically defined as soon as possible in order to avoid a worse outcome [3]. In this way, imaging exams are an important tool in the diagnosis of STA and can improve prognosis[5]. Ultrasound (US), radiography (X-ray), computed tomography (CT) and positron emission tomography (PET) can be used, with different sensitivities, specificities and indications for diagnosing STA, as will be discussed below.

Study Name	Author	Year of Publication	Type of Study
Positron Emission Tomography With 18F-Fluorodeoxygluco se in Patients With	de Prost N, et al. [2]	2015	Prospective Cohort Study
Sickle Cell Acute Chest Syndrome Accuracy of Point-of-care Lung Ultrasonography for Diagnosis of Acute Chest Syndrome in Pediatric Patients with Sickle Cell Disease and Fever	Daswani DD, et al. [3]	2016	Prospective Cohort Study
Which Febrile Children With Sickle Cell Disease Need a Chest X-Ray?	Eisenbrown K, et al[4]	2016	Retrospective Literature Review
Bedside ultrasound as a predictive tool for acute chest syndrome in sickle cell patients	Colla JS, et al. [5]	2018	Prospective Cohort Study
Utility of Point-of-Care Lung Ultrasonography for Evaluating Acute Chest Syndrome in Young Patients With Sickle Cell Disease.	Cohen SG, et al. [6]	2020	Prospective Cohort Study
What is the role of chest X-ray imaging in the acute management of children with sickle cell disease?	Griffin R, et al. [7]	2021	Retrospective Cohort Study

Chart 1 - Articles included in the retrospective literature review. Own authorship, Campinas, SP, Brazil, 2023.

CHEST X-RAY

The diagnosis of STA requires a new pulmonary infiltrate detected by chest radiography (X-ray) and one or more of the following: fever, chest pain, hypoxemia or respiratory symptoms, including tachypnea, wheezing, cough or increased exertion respiratory.

Chest X-rays, according to the study by Griffin R, et al [7], showed that out of a total of 915 X-rays performed on children with sickle cell disease, only 28.2% had clinically significant findings that altered management or the final diagnosis. On the other hand, the study by Eisenbrown K, et al [4], showed that sickle cell children who arrived at the emergency room with fever, shortness of breath, tachypnea, rales or chest pain (criteria for indication of radiography by the National Heart, Lung, and Blood Institute - NHLBI), had an 85% rate of identification of acute chest syndrome using chest radiography, concluding that in these cases, the examination guided by the clinical symptoms described, should be indicated.

Pediatric patients with FD may receive repeated radiographs over the years, with an average of 27 radiographic examinations by the age of 18, which could result in high cumulative doses of ionizing radiation and an associated increased risk of cancer.[3]

LUNG ULTRASOUND

Ultrasound (US) is widely accepted as a diagnostic tool for use in the emergency department (ED) and is particularly useful in pediatrics, as it does not use ionizing radiation[3]. In addition, children have a thinner chest wall, less wide chest wall and smaller lung mass than adults, which makes lung ultrasound imaging easier [3]. Lung ultrasound has the potential to detect consolidations compatible with STA in febrile patients with FD. In a study of adult patients with FD and STA, it was shown that US outperformed X-ray for the diagnosis of consolidation when compared to chest computed tomography (CT) [3].

The study carried out by Daswani DD, et al[3], showed that lung ultrasound performed by pediatric emergency physicians is sensitive and specific for diagnosing STA in pediatric patients with sickle cell anemia and fever, and can also reduce the need for routine radiography and exposure of patients to ionizing radiation. This prospective study of 91 patients up to the age of 21 with sickle cell disease and fever showed a sensitivity of 87% (95% confidence interval [CI] = 62% to 96%) and specificity of 94% (95% CI = 88% to 97%). Another study, carried out by Colla JS,

et al [5], with 20 sickle cell patients, median age 31 years, showed that lung abnormalities on bedside lung ultrasound appear earlier than on chest X-ray (median 3.6 vs. 31.8 h), with bedside lung ultrasound being a promising predictive tool for STA. The prospective observational study carried out by Cohen et al [6], with 191 patients with sickle cell disease aged between 0 and 21 years, concluded that point-of-care lung ultrasound detected acute chest syndrome in 92% of cases, with a sensitivity of 88% and specificity of 93% compared to chest X-ray, making it a viable alternative to chest X-ray, since ultrasound does not expose the patient to radiation.

COMPUTED TOMOGRAPHY (CT) AND POSITRON EMISSION TOMOGRAPHY (PET) OF THE CHEST

Using positron emission tomography (PET) with F-fluorodeoxyglucose [18F-fluorodeoxyglucose (F-FDG)] and Computed Tomography, de Prost N, et al [2] explored the relationship between regional lung density and pulmonary metabolism as a reflection of pulmonary neutrophilic infiltration during acute chest syndrome in 17 patients (16 with SS disease and 1 with S-β+ thalassemia disease) with a mean age of 28.3 ± 6.4 years, in a single-center prospective study. The study concluded that patients with STA have higher 18F-FDG uptake, with foci of hypermetabolism located in consolidated lung bases and lung apices had normal aeration and lower 18F-FDG uptake than the lung bases, but higher 18F-FDG uptake than the lungs of controls without STA, suggesting early inflammation in these regions and a greater involvement of the lung during STA than indicated by conventional imaging.

CONCLUSION

Imaging exams have proved to be an important means of diagnosing Acute Thoracic Syndrome (ATS) in patients with Sickle Cell Disease (SCD). Among the articles included in this study, it can be seen that bedside lung ultrasound (US) showed greater benefits than chest radiography (X-ray), due to its greater specificity, sensitivity and non-exposure of the patient to ionizing radiation. Positron emission tomography (PET) with F-fluorodeoxyglucose [18F-fluordesoxyglucose (F-FDG)], according to the study, can indicate greater lung involvement during STA than conventional imaging.

This study encountered some limitations during its development. No extensive literature was found on the subject and the studies taken into consideration for the review had a small sample of patients in their cohort studies, and most of them were carried out in the same institution, with no sample variability. More studies will be needed to conclude which would be the best imaging method in STA, with a larger sample size and in different institutions in order to make a comparison.

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