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Research Article

Incidence of Tuberculosis and Sarcoidosis in Patients with Histopathologic Granulomatous Inflammation

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Abstract

Background: Granulomatous inflammation is a distinct form of chronic inflammation in response to a variety of infectious, autoimmune, toxic, allergic and neoplastic conditions. Our aim in this study was to determine the incidence of tuberculosis and sarcoidosis in patients with granulomatous inflammation.

Materials and methods: Eight hundred and sixty five patients, who were histopathologically diagnosed with granulomatous inflammation between October 2010 and January 2021, were included in the study. Diagnoses of tuberculosis and sarcoidosis were confirmed by reviewing patient reports and hospital records.

Results: Of 865 patients, 181 had caseating granulomatous inflammation, 224 had non-necrotizing granulomatous inflammation and 460 had other granulomatous inflammation. Sarcoidosis was diagnosed in 52 patients with non-caseating granulomatous inflammation and 12 patients with other granulomatous inflammation. Tuberculosis was diagnosed in 255 patients (181 caseating granulomatous inflammation, 45 non-caseating granulomatous inflammation, and 29 other granulomatous inflammation).

The mean age of the 64 patients (46 women, 18 men) with sarcoidosis was 44.8 years. Of the 255 tuberculosis patients (152 women, 103 men), the mean age was 32.3 years. In sarcoidosis patients, the most common biopsy sites were hilar/mediastinal lymph nodes (46.8%) and lung (26.5%), whereas, in tuberculosis patients, the most common biopsy sites were the extra thoracic lymph nodes (36.4%), pleura (15.2%) and lung (13.7%).

Conclusion: In this study, tuberculosis and sarcoidosis were detected in 36.9% of reports of granulomatous inflammation. A higher incidence of tuberculosis was observed in granulomas from extra thoracic sites that showed caseating necrosis on pathology, whereas a higher incidence of Sarcoidosis was observed in intrathoracic biopsies that showed non-necrotizing granulomatous inflammation.

Keywords: Tuberculosis; Sarcoidosis; Caseating necrosis; Non-Necrotizing granulomatous inflammation

Introduction

Granulomatous inflammation is characterized by histiocytes and lymphocytes responding to various chemical mediators of cell damage. The granulomatous reaction may develop in various organs due to some infectious causes, mainly tuberculosis, as well as foreign bodies and non-infectious diseases such as sarcoidosis [1].

The disease of tuberculosis has a very broad spectrum and can affect every organ and tissue in the body [2]. Histopathologically, it is characterized by epithelioid histiocytes (macrophages) resembling round epithelial cells forming clusters, Langhans-type giant cells, and central caseous necrosis [1,2].

Sarcoidosis is a chronic, multisystemic inflammatory disease of unknown etiology characterized by the presence of non-caseating granulomas. Although sarcoidosis mostly affects the lungs, it may also involve different organs such as the skin, eyes, lymph nodes, salivary glands, spleen, liver, and nervous system [3]. The definitive diagnosis of sarcoidosis is based on the clinical manifestations, radiologic findings, and histopathological evidence of granulomas without any evidence of caseating necrosis.

In this study, we aimed to investigate the incidence of tuberculosis and sarcoidosis in patients with granulomatous inflammation.

Materials and Methods

The study included cases diagnosed as granulomatous reactions in the Department of Pathology between October 2010 and January 2021.

Tissue samples were from various organs including intrathoracic and extra thoracic lymph nodes, lung parenchyma, pleura, breast, prostate, bladder, and skin (Table 1). Granulomas were classified as caseating granulomatous inflammation, non-necrotizing granulomatous inflammation, and other granulomatous inflammation.

Ziehl Neelsen staining for Acid-Fast Bacilli (AFB) and CSM (Chromic Acid Silver Methenamine) staining for fungi were performed in almost all tissue samples.

Diagnosis for tuberculosis

The histopathological diagnosis was made by detecting caseating granulomatous inflammation or granulomatous inflammation in the biopsy material, in which no caseification was observed and other diagnoses were clinically excluded; the microbiological diagnosis

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Table 1: Distribution of sites of tissue sampling in tuberculosis and sarcoidosis.

	Tuberculosis	Sarcoidosis
	n (%)	n (%)
Extrathoracic LN	36.4 (93)	10.7 (7)
Intrathoracic LN	0.03 (8)	46.8 (30)
Lung	13.7 (35)	26.5 (17)
Pleura	15.2 (39)	15.2 (39)
Other	31.4 (80)	14 (9)

LN: Lymph Node; Chi-square=111.157; p=0.001

was made by direct observation of Acid-Fast Bacillus (AFB) and/or production of bacillus in the mycobacterial culture of material obtained from lung or extrapulmonary localization (lymph gland puncture material, pleural fluid, urine, etc.); The diagnosis with other diagnostic methods was made clinically radiologically, additional laboratory findings and exclusion of other possible diagnoses.

The diagnosis of sarcoidosis was based on clinical and radiologic findings, histologic presence of non-necrotizing granulomas, and complete exclusion of other causes.

Demographic data, admission symptoms, sputum AFB and culture results, blood and urine calcium levels, Purified Protein Derivative (PPD) values, and radiological findings (lung radiography, lung tomography) of the patients were examined. Diagnoses of tuberculosis and sarcoidosis were confirmed by reviewing patient reports and hospital records.

The study protocol was approved by Clinical Research ethics committee of the hospital in accordance with the Declaration of Helsinki (29/07/2022, protocol number 2022/07-03).

Statistical Analysis

Descriptive statistics for continuous variables were expressed as Mean ± Standard Deviation, while descriptive statistics for categorical variables were expressed as numbers and percentages. The chi-square test was used to determine the relationship between categorical variables. The statistical significance level was considered to be 0.05 and SPSS (Ver: 21) statistical package program was used for the calculations.

Results

Of 865 patients, who were histopathologically diagnosed with granulomatous inflammation between October 2010 and January 2021, were included in the study. Caseating granulomatous inflammation was detected in 181 reports (Figure 1), non-necrotizing granulomatous inflammation in 224 reports (Figure 2), and other granulomatous inflammations in 460 reports. Sarcoidosis was diagnosed in 52 patients with non-caseating granulomatous inflammation and 12 patients with other granulomatous inflammation. Tuberculosis was identified in 255 patients (181 caseating granulomatous inflammation, 45 non-caseating granulomatous inflammation, and 29 other granulomatous inflammation) (Figure 3).

The mean age of the 64 patients (46 women, 18 men) with sarcoidosis was 44.8 years. Of the 255 tuberculosis patients (152 women, 103 men), the mean age was 32.3 years. PPD was negative in 93.7% of the patients. PPD was positive in 67% of patients with tuberculosis.

In sarcoidosis patients, the most common biopsy sites were hilar/mediastinal lymph nodes (46.8%) and lung (26.5%), whereas, in tuberculosis patients, the most common biopsy sites were the extra thoracic lymph nodes (36.4%), pleura (15.2%) and lung (13.7%).

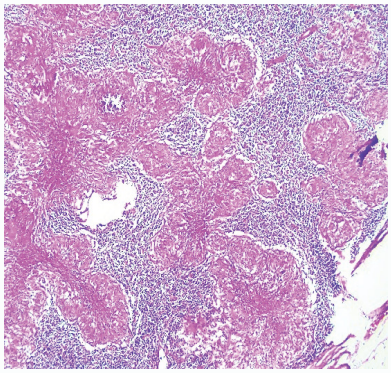

Figure 1: The section shows central caseification necrosis and epithelioid histiocytes lined around it (Hematoxylin-eosin x100).

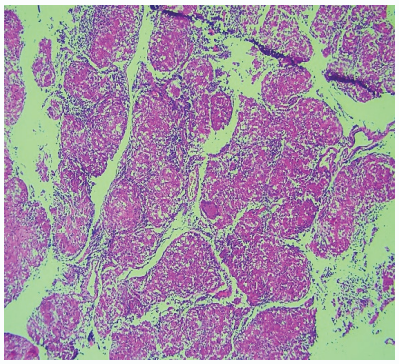

Figure 2: The section shows noncaseating granulomas of similar size and shape consisting of epithelioid histiocytes with large cytoplasm (Hematoxylin-eosin x100).

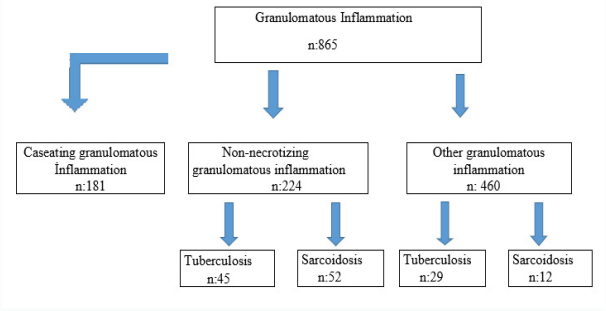

Figure 3: Incidence of tuberculosis and sarcoidosis in granulomatous inflammations.

Discussion

In our study, it was found that of 865 patients with granulomatous inflammation in the pathology reports, 29.4% were diagnosed with tuberculosis, and 0.07% with sarcoidosis. For the diagnosis of sarcoidosis, the most frequent biopsy site was the hilar/mediastinal lymph nodes (46.7%) and lung (26.5%), and for tuberculosis, the extra thoracic lymph nodes (36.4%), lung (13.7%) and pleura (15.2%).

Although the definitive diagnosis of tuberculosis is the presence of AFB and isolation in culture, there are sometimes problems in diagnosis, especially in extrapulmonary tuberculosis. In addition to definitive diagnostic methods, histopathological examination still maintains its importance in tuberculosis cases. Caseating granulomatous inflammation is a dominant finding supporting tuberculosis [4-6]. In this study, TB was diagnosed in almost all

patients with caseating granulomatous inflammation. In the absence of caseification necrosis, the diagnosis of tuberculosis is based on granulomatous inflammation. In our study, it was determined that only 6% of the patients with granulomatous inflammation and 20% of the patients with non-necrotizing granulomatous inflammation were diagnosed with TB.

Non-necrotizing granulomatous inflammation is more likely to be seen in non-infectious conditions such as sarcoidosis [7,8]. The diagnosis of sarcoidosis requires histological evidence of non-necrotizing granulomas in addition to the typical clinical and radiological findings and the complete exclusion of other causes [9]. For the diagnosis of sarcoidosis, tissue should be studied histologically; appropriate staining and cultures should be performed to exclude potential granulomatous pathogens such as mycobacteria and fungi, and serologic testing when appropriate. In this study, sarcoidosis was detected in 52 (23.2%) patients with non-necrotizing granulomatous inflammation.

The identification of necrosis in granulomatous inflammations is a useful predictor of diagnostic etiology. Diagnosis is difficult in granulomatous inflammations where caseous necrosis and non-necrotizing are not defined. In these cases, alternative causes should be excluded and a history of potential exposure to infectious agents and environmental agents that may cause granulomatous inflammation should be elicited. In our study, 6.3% of patients with only granulomatous inflammation in the report were diagnosed with tuberculosis, and 2.6% with sarcoidosis.

Although tuberculosis typically involves the lungs, it is a disease that can affect every organ in the body [10]. While tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis in many studies, pleural tuberculosis is the most common form of involvement in some studies [11-14]. In our study, tuberculosis was identified in the extra thoracic lymph nodes in 36.4% of patients and the pleura in 15.2%.

The most commonly involved structures in sarcoidosis are intrathoracic lymph nodes and lungs, but any organ can be involved [15]. For pathologic sampling, easily accessible areas such as lymph nodes, skin lesions, and parotid glands should be preferred. In this study, the most common biopsy sites for sarcoidosis were hilar/mediastinal lymph nodes (46.8%) and lungs (26.5%).

Conclusion

Tuberculosis and sarcoidosis play a substantial role in the differential diagnosis of granulomatous diseases, where histological patterns (necrotizing, non-necrotizing, suppurative, and foreign body granulomas) guide the diagnosis.

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