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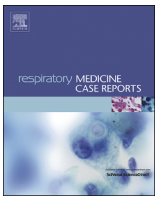

Case Report

Case of stage 0 pulmonary sarcoidosis pathologically diagnosed via transbronchial lung cryobiopsy

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ABSTRACT

A 45-year-old male was diagnosed with arrhythmia during a routine health examination. Findings from different modalities, such as echocardiography and radiography, were consistent with cardiac involvement in sarcoidosis. There was no ocular involvement or superficial lymph node enlargement. A chest computed tomography scan did not reveal any pulmonary lesions or bilateral hilar lymphadenopathy. To pathologically diagnose systemic sarcoidosis, transbronchial lung cryobiopsy was performed. Results showed pathological evidence of noncaseating epithelioid granulomas. Herein, we present a case in which sarcoidosis diagnosis was confirmed via transbronchial lung cryobiopsy despite the absence of respiratory lesions on computed tomography scan.

1. Introduction

Sarcoidosis is a systemic disease characterized by pulmonary, cardiac, and ophthalmic lesions [1]. Pulmonary involvement, including pulmonary infiltration and lymphadenopathy, is most frequently observed and classified into stages 0–4 based on these findings [2]. The diagnosis of stage 0 pulmonary sarcoidosis is confirmed if none of these pulmonary abnormalities are observed on computed tomography (CT) scan [1]. Among patients with stage 0 pulmonary sarcoidosis, confirming the presence of noncaseating epithelioid granulomas, crucial for the pathological diagnosis of sarcoidosis, can be challenging, particularly in the absence of skin or superficial lymph node involvement. Herein, we report the case of a patient considered to have stage 0 pulmonary sarcoidosis who presented with noncaseating epithelioid granuloma pathologically confirmed via transbronchial lung cryobiopsy (TBLC).

2. Case presentation

The patient, a 45-year-old Japanese man without any past medical history, was referred to the department of cardiology due to multifocal ventricular premature contractions, abnormal Q-waves, and inverted T-waves observed on electrocardiogram during a routine health check-up. Transthoracic echocardiography revealed thinning of the interventricular septum and decreased wall motion of the anterior wall to the septum. Additionally, delayed myocardial enhancement on gadolinium-enhanced cardiac magnetic resonance imaging (MRI) and ^{18}F-fluoro-2-deoxyglucose (^{18}FDG) accumulation in the basal anteroseptal myocardium on positron emission tomography (PET) (Fig. 1A and B) were consistent with cardiac involvement in sarcoidosis.

Abbreviations: CT, computed tomography; TBLC, transbronchial lung cryobiopsy; MRI, magnetic resonance imaging; ^{18}FDG, ^{18}F-fluoro-2-deoxyglucose; PET, positron emission tomography; BAL, bronchoalveolar lavage; TBLB, transbronchial lung biopsy; CS, cardiac sarcoidosis.

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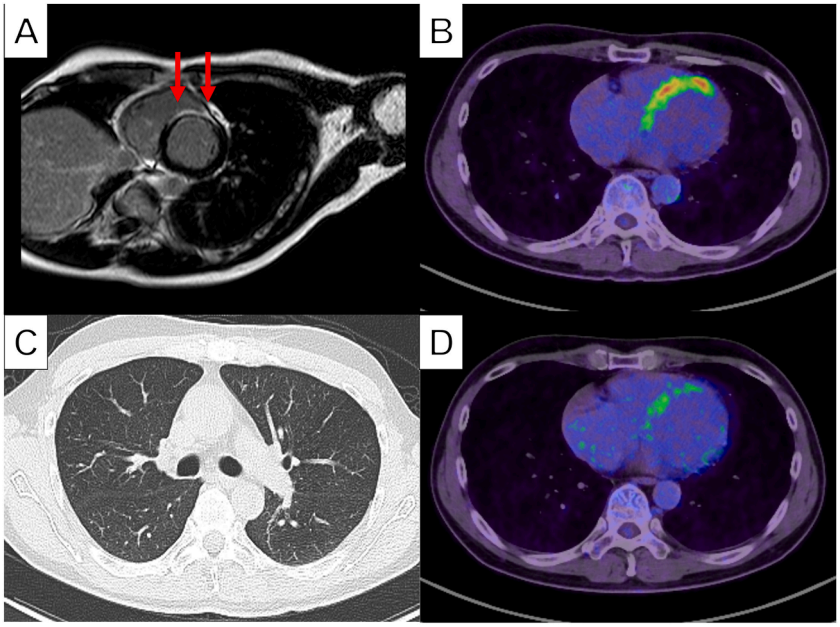

Fig. 1. Radiological findings.
Sagittal plane of gadolinium-enhanced cardiac magnetic resonance imaging revealed delayed myocardial enhancement (red arrow) (A). PET indicated ^{18}FDG accumulation in the basal anteroseptal myocardium (B). Chest computed tomography scan showed no lymphadenopathy or pulmonary involvement (C). After steroid administration, the ^{18}FDG uptake in the myocardium decreased on PET (D).
PET, positron emission tomography; ^{18}FDG, ^{18}F-fluoro-2-deoxyglucose.

After 5 months, the patient was referred to the department of respiratory medicine for a comprehensive evaluation of systemic sarcoidosis. Upon admission, there were no abnormalities in vital signs, eyes, or skin involvement. Blood test results showed normal corrected calcium levels of 8.8 mg/dL, an angiotensin-converting enzyme level of 13.4 U/L, and a soluble interleukin-2 receptor level of 461 U/mL. Inflammation markers were not observed (white blood cell count, 4580/μL; C-reactive protein level, 0.03 mg/dL). Chest radiography and CT scan did not show bilateral hilar lymphadenopathy or pulmonary involvement (Fig. 1C). Therefore, bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) as well as TBLC were performed to obtain pathological specimens on the 2nd day of hospitalization. BAL performed on the right middle lobar bronchus revealed the following differential cell counts: total cell count, 1.4×10^5/mL; macrophages, 80.3 %; lymphocytes, 19.4 %; and eosinophils, 0.3 %. Fluid analysis during cytology yielded negative results, and the CD4/CD8 ratio (0.6) did not increase. Furthermore, four specimens (maximum diameter: 1–2 mm) for TBLB and two specimens (maximum diameter: 5–8 mm) for TBLC were collected from the left lower lobe (B^9a bronchus). Minimal bleeding associated with TBLC was observed, which was managed using an endobronchial balloon for bronchial blockage to maintain hemostasis [3], without any other complications, including pneumothorax. Pathological examinations revealed no typical sarcoidosis findings, such as granulomas, in the samples obtained from TBLB (Fig. 2A). However, samples obtained from TBLC contained tiny noncaseating epithelioid granulomas with Langerhans cells (Fig. 2B), leading to the pathological diagnosis of systemic sarcoidosis.

After bronchoscopy, the patient was discharged from the hospital, and treatment with prednisolone at a dose of 30 mg/day was initiated. No changes were observed on electrocardiogram, transthoracic echocardiography, or gadolinium-enhanced MRI. However,

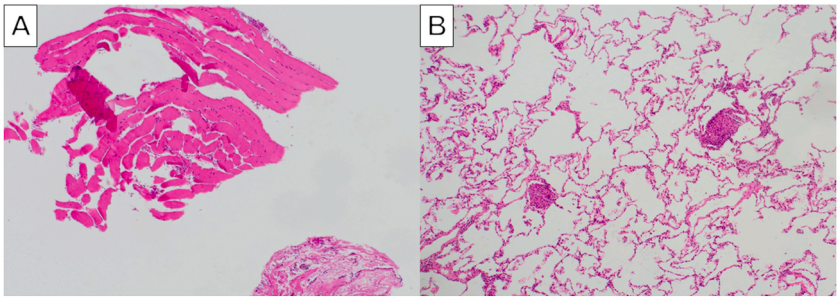

Fig. 2. Pathological findings.
Pathological analysis of samples from transbronchial lung biopsy showed no granulomas (A: medium-power view, hematoxylin and eosin staining). In contrast, transbronchial lung cryobiopsy identified tiny noncaseating epithelioid granulomas with Langerhans cells (B: low-power view, hematoxylin and eosin staining).

PET-CT scan showed a clear reduction in ^{18}FDG uptake in the myocardium (Fig. 1D). The prednisolone dose was reduced to 5 mg/day, and the patient's condition did not deteriorate.

3. Discussion

TBLC was performed on a patient without pulmonary involvement detected on CT scan, resulting in a pathological diagnosis of sarcoidosis. The novelty of our case lies in the ability to confirm the presence of granulomas via TBLC, whereas TBLB did not yield similar results in patients with stage 0 pulmonary sarcoidosis on CT scan.

TBLB is a commonly used approach for lung biopsies in patients with sarcoidosis. Previous Japanese studies have shown that 88 of 163 patients with stage 0 pulmonary sarcoidosis on CT scan were pathologically diagnosed with sarcoidosis via TBLB (diagnostic probability of 54 %) [4]. However, other studies have revealed that TBLC is more useful than TBLB in diagnosing diffuse parenchymal lung disease because of the specimen volume and presence of fewer compression artifacts [5–7]. Further, some studies reported that TBLC was complementary to TBLB even for the diagnosis of radiologically suspected sarcoidosis [6,7]. However, there is no evidence that TBLC is useful for diagnosing sarcoidosis without any pulmonary involvement. To the best of our knowledge, this is the first report on the feasibility of TBLC in the pathological diagnosis of stage 0 pulmonary sarcoidosis on CT scan. The sample size of TBLC was larger than that of TBLB, and this could have contributed to the diagnosis of sarcoidosis. To validate our results, further accumulation of cases is a future prospect.

Initially, our patient was suspected to have isolated cardiac sarcoidosis (CS). The clinical diagnosis of isolated CS is confirmed if four or more of the following five major criteria are met: 1) high-grade atrioventricular block or fatal ventricular arrhythmia, 2) basal thinning of the ventricular septum or abnormal ventricular wall anatomy, 3) left ventricular contractile dysfunction, 4) abnormally high tracer accumulation in the heart on ^{67}gallium citrate scintigraphy or ^{18}FDG-PET, and 5) delayed contrast enhancement in the myocardium on gadolinium-enhanced MRI [8]. In our case, because the criteria from 2) to 5) were met and no clinical characteristics associated with sarcoidosis were observed in any organs other than the heart, this patient was likely to have isolated CS. However, isolated CS is important to differentiate from cardiac involvement in systemic sarcoidosis because the prognosis is different, which includes the prevalence of ventricular arrhythmia [9]. If it is difficult to diagnose sarcoidosis pathologically and there are no abnormal findings on chest CT scan, tissue collection via TBLC could be useful for obtaining an accurate diagnosis.

Myocardial biopsy is another alternative for the pathological diagnosis of cardiac involvement in sarcoidosis. However, it occasionally shows granulomas, with a rate of as low as 19 %, and it has a risk of complications such as bleeding and infection [10]. Considering these issues, myocardial biopsies were not performed in this case. However, compared with TBLB, TBLC also has a higher risk of complications such as pneumothorax and bronchial bleeding. A previous meta-analysis reported that the incidence rates of bleeding and pneumothorax were 30 % and 8 %, respectively [11]. According to a Japanese study, 67 % and 16 % of patients presented with mild or moderate bronchial bleeding, respectively, and 3.6 % of patients developed pneumothorax after TBLC [3]. This relatively low complication rate was attributed to the established balloon occlusion method and the use of real-time fluoroscopy [3]. We were also able to perform TBLC using these methods, resulting in no critical complications. It is crucial that TBLC should be conducted with a focus on preventing unexpected complications.

4. Conclusion

TBLC can be a valuable tool for obtaining sufficient specimen samples that are useful for the pathological diagnosis of patients presumed to have stage 0 pulmonary sarcoidosis and for assessing systematic lesions in sarcoidosis.

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CRediT authorship contribution statement

Hikari Ishii: Writing – original draft, Investigation, Formal analysis, Data curation. **Nobuyasu Awano:** Writing – review & editing, Validation, Supervision, Project administration, Investigation, Formal analysis, Data curation. **Minoru Inomata:** Investigation. **Yuan Bae:** Investigation. **Takehiro Izumo:** Writing – review & editing, Validation, Supervision, Project administration.

Declaration of competing interest

None.

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