SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2023; 40 (3): e2023042 DOI: 10.36141/svdld.v40i3.14519

Life threating onset of cardiac sarcoidosis with mediastinal involvement

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Abstract. We have described a clinical case with atypical onset of sarcoidosis. A young patient presented to the emergency room with acute heart failure and severe cardiac dysfunction simulating dilated cardiomyopathy or severe myocarditis. Hypoxic respiratory failure refractory to oxygen therapy was treated with steroids. The diagnosis was made by a multidisciplinary team who decided to perform EndoBronchial UltraSound-guided TransBronchial Needle Aspiration (EBUS TBNA) in addition to a cardiac MRI. The result was to obtain, in this case, a prompt therapeutic response in order to preserve the patient cardiac function.

Key words: EBUS TBNA, Acute respiratory failure, Cardiac arrhythmias, Cardiac failure

Sarcoidosis is a systemic granulomatous disease characterized by a frequently mild or asymptomatic clinical manifestation but with possible aggressiveness, progressive fibrosis of the involved organs and poor prognosis or death. The development of new diagnostic imaging techniques such as PET and MRI, has led to the recognition of cardiac involvement in up to 25% of all forms (1,2). We have described a clinical case with atypical onset of sarcoidosis in a young female arrived in the emergency room (ER) in pulmonary edema. She presented with severe cardiac dysfunction simulating dilated cardiomyopathy or severe myocarditis with severe hypoxic respiratory failure refractory to oxygen therapy successfully treated with steroids.

A 37-year-old non-smoking woman without pathological history in breastfeeding came to our observation in ER with progressive dyspnea and evidence of acute cardiac failure, hypotension, nonsustained ventricular tachycardia, reduced ejection fraction. She was admitted to the cardiological intensive care unit. She has never had fever, cough, or skin.

The clinical presentation was associated with severe hypoxemic respiratory failure refractory to oxygen therapy. At the admission arterial blood gas analysis showed PaO2 49 mmHg, PaCO2 27mmHg, pH 7.56, HCO3 standard 26 mmol/l, oxygen saturation SpO2 86%. After administration of oxygen through ventury mask at 50% FiO2, the PaO2/FiO2 ratio was 110. Blood analysis highlighted high levels of troponin, brain natriuretic peptide and D-dimero values. We started O2 therapy with Continuous Positive Pression (CPAP) set up with 7.5 cm H2O and inhaled oxygen fraction of 60%. At the 12 leads ECG no sign of myocardial ischemia was presented but several premature ventricular complexes with long runs of non-sustained ventricular tachycardia were recorded. The basal echocardiogram documented atrium and left ventricle severe dilatation, reduction in ejection fraction to 28%, mild pericardial effusion, moderate mitral regurgitation, normal right sections and normal Pulmonary Pression. At admission, the Thoracic Computed Tomography

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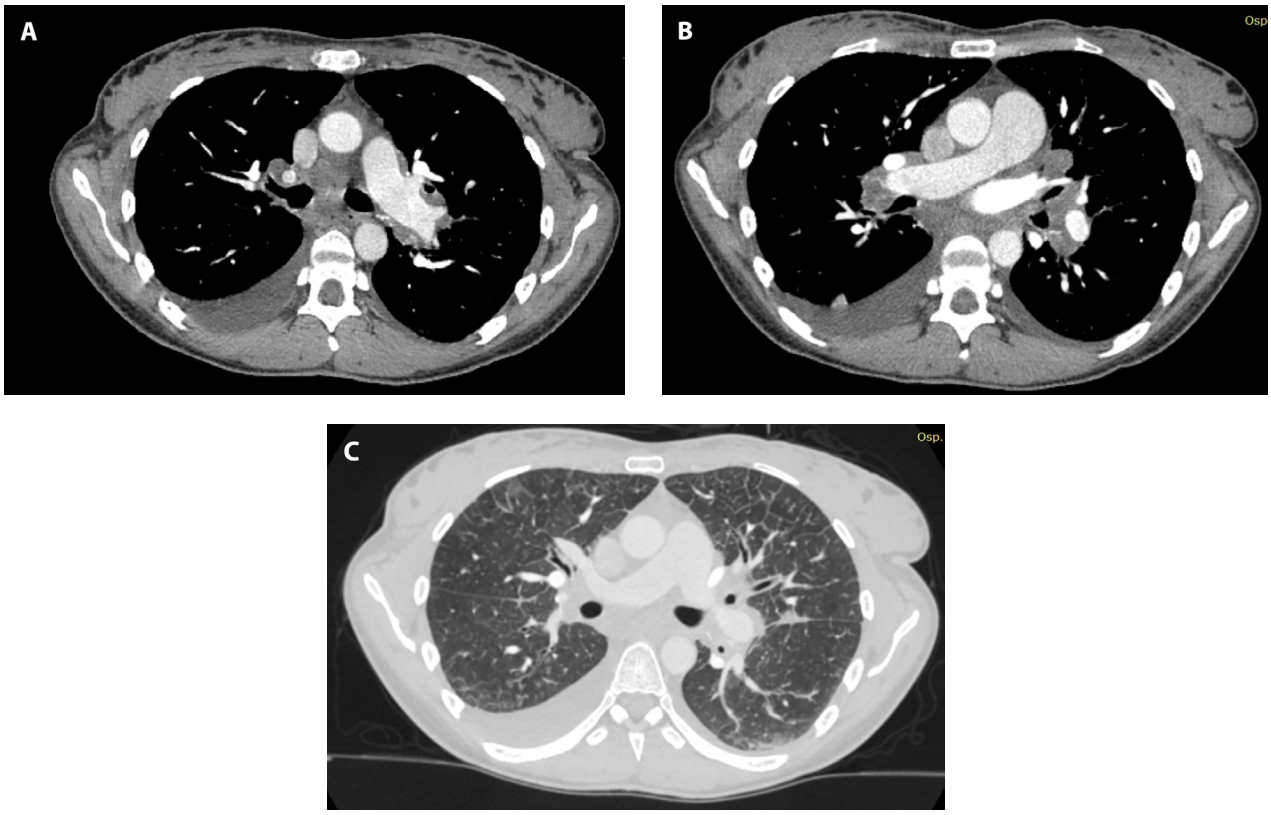

Figure 1. (**A**, **B**) CT Scan (chest windows) lymphadenopathies in mediastinal right paratracheal (station 4R), subcarinal (station 7) and bilateral hilar stations (station 10,11). (**C**) (CT scan parenchymal window)Bilateral pleural effusion, interstitial oedema with intralobular septa thickening, ground glass opacities, radiological pattern compatible with cardiogenic pulmonary oedema.

(CT) Scan (Figure 1 A, B, C) excluded pulmonary embolism and documented bilateral pleural effusion, interstitial edema with intralobular septa thickening, ground glass opacities, radiological pattern compatible with cardiogenic pulmonary edema. CT scan also showed lymphadenopathies in the mediastinal right paratracheal (station 4R), subcarinal (station 7), and bilateral hilar stations (station 10,11).

The provisional diagnosis was myocarditis with severe ventricular dysfunction and hemodynamic instability. Serological microbiological tests were negative. A pharmacological treatment with diuretics, antibiotics and inotropic agents was started. Therapy with prolactin inhibitors was started to interrupt breastfeeding. CPAP therapy was maintained for 72 hours with FiO2 deescalation and replacement with High Flow Oxygen Therapy set up 50 liters/minute FiO2 60%. After 72 hours we were able to withdraw inotropes, the hemodynamic was stable and oxygen saturation was acceptable, so we planned a radiological investigation to confirm myocarditis. We performed Cardiac Magnetic Resonance (CMR) (Figure 2 A, B) which confirmed severe biventricular systolic dysfunction (left ventricle ejection fraction was 22% and right ventricle ejection fraction was 28%), with diffuse myocardial wall motion abnormalities and thinning. T2-weighted imaging was characterized by areas of myocardial edema with thickened walls. After contrast agent administration, Late Gadolinium Enhanced (LGE) imaging demonstrated large areas of myocardial infiltration and scar zones, both midwall, patchy and subendocardial, the latter similar to those seen in myocardial infarction but with a non-coronary distribution compatible with several diseases included vasculitis or granulomatosis (3).

We decided to repeat the thoracic CT scan with intravenous contrast to study mediastinal and hilar lymphadenopathy because a lymphoproliferative disease, infections, inflammatory granulomatous or neoplastic pathologies were suspected. Thoracic CT scan documented the reduction of mediastinal

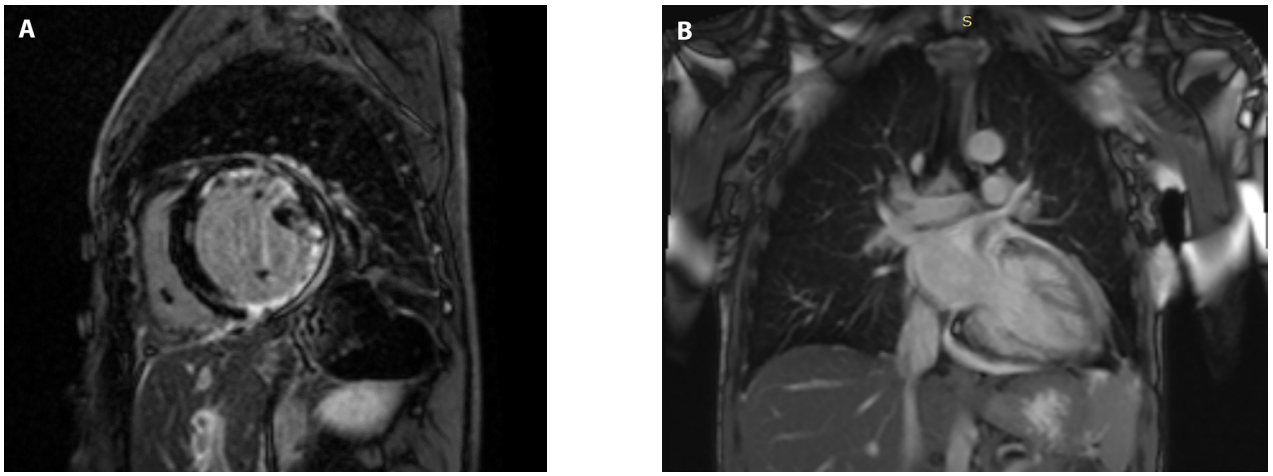

Figure 2. (**A**) Cardiac Magnetic Resonance PSIR 2ch SA Image: presence of multiple/diffuse LGE areas with varied location and distribution (mid-wall; spotty; subendocardial; sub epicardial), pericardial effusion; (**B**) Cardiac magnetic resonance, coronal view.

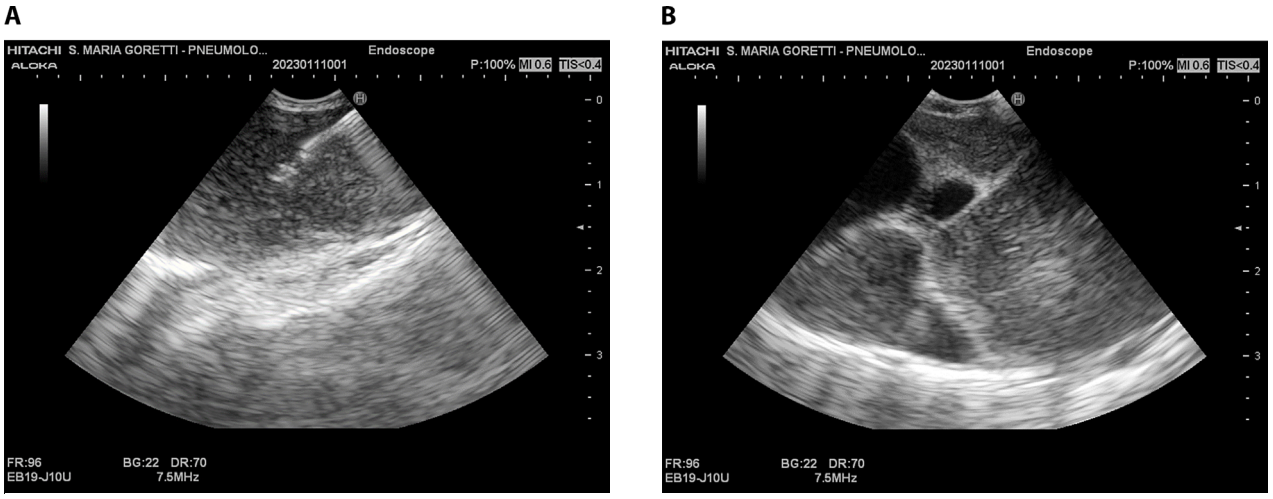

Figure 3. (**A**) EBUS TBNA station 7 Subcarinal lymph node. (**B**) Linear EBUS: right hilar lymph node (station 11 R).

lymphadenopathy persisting in the regions above mentioned, the disappearance of the pleural effusion and the improvement of the cardiogenic alveolar congestion.

In order to define the diagnosis, histological analysis was needed. Since myocardial biopsy is a high-risk rate procedure, it was decided to perform *EndoBronchial UltraSound-guided TransBronchial Needle Aspiration* (EBUS TBNA) under general anesthesia (4). The subcarinal stations 7 and the right inferior hilar 11R were sampled with a 22G needle (Figure 3 A, B). Both stations showed well-demarcated hypoechoic areas representing conglobated lymph nodes.

The histological examination showed lymphocytes of medium and small size and aggregates of epithelioid cells (CD68/KP-1+, pan-cytokeratin AE1/3-) consistent with granulomas, in the absence of necrosis (P.A.S. and Ziehl-Neelsen stains did not reveal the presence of microorganisms) (Figure 4 A, B). The microbiological tests performed with bronchial lavage documented the absence of pathogens as well as the PCR for mycobacteria was negative. In order to reduce the amount of fluid instilled by bronchoscopy we didn't perform the bronchoalveolar lavage to obtain alveolar cytogram and the lymphocyte subpopulation (CD4/CD8 ratio), the reduced cardiac function was a risk factor for worsening symptoms.

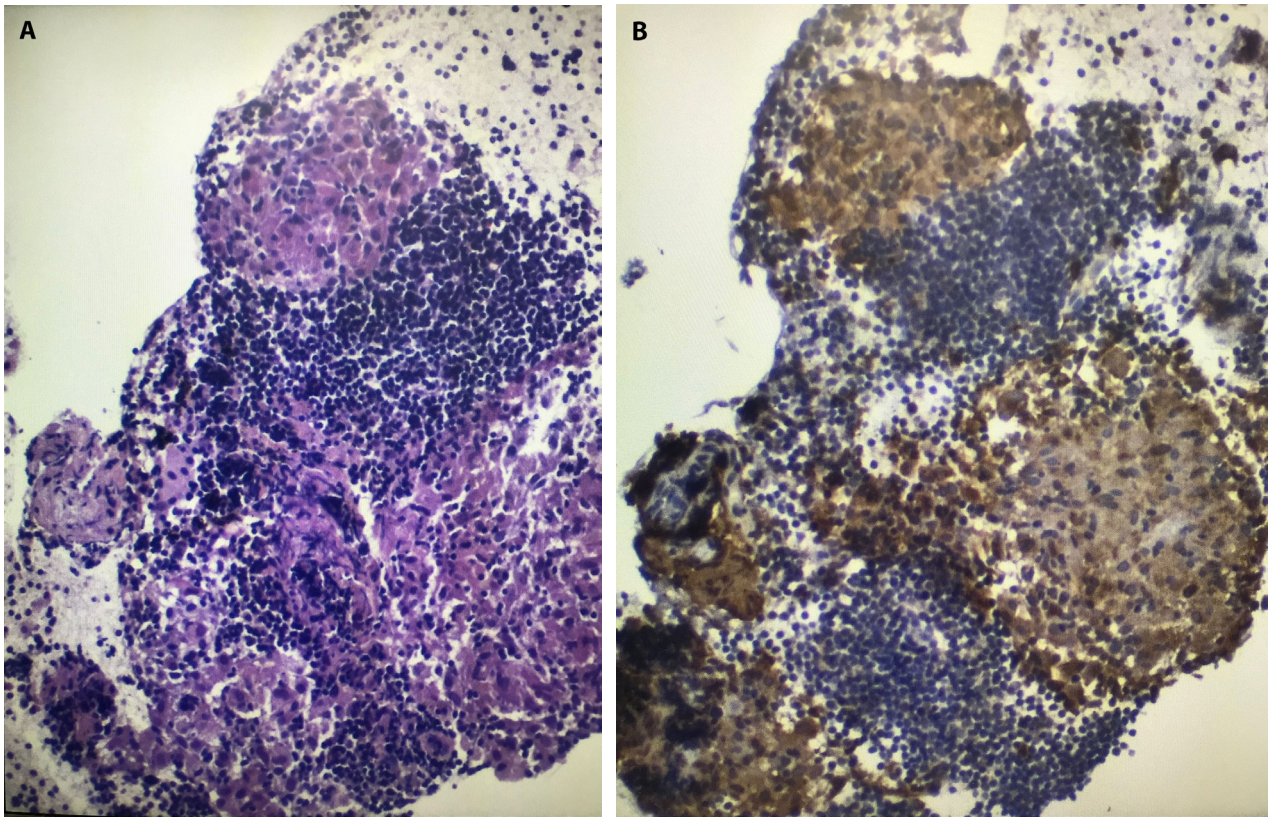

Figure 4. (**A**) Hematoxylin and Eosin stained histological examination, 10X (EBUS TBNA); (**B**) CD68/KP-1, Immunohistochemistry (IHC).

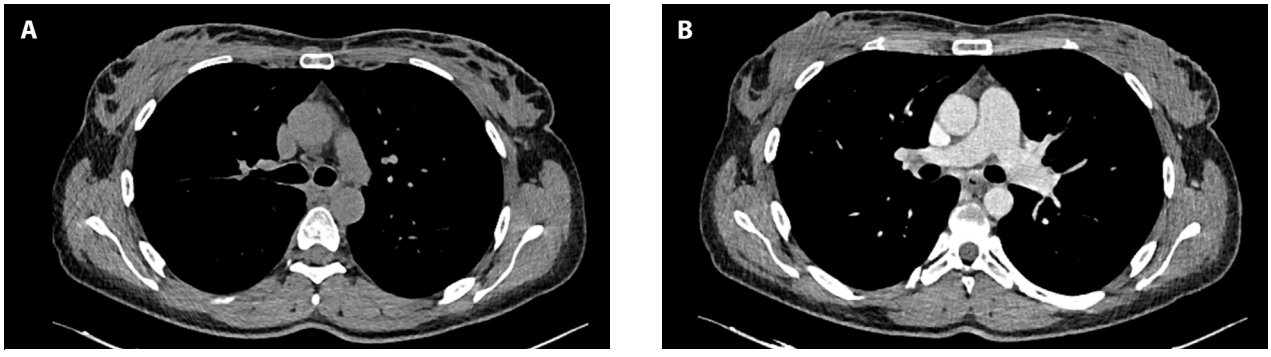

Figure 5. (**A**, **B**) Thoracic CT Scan: significant improvement of the lymphadenopathies after steroids therapy.

The presence of lymphadenopathy associated with the evidence of LGE on the MRI and the finding of a non-necrotizing granuloma made the diagnosis of sarcoidosis plausible. We started steroid therapy at a dosage of 50 mg/day of methylprednisolone. After 30 days, a control chest CT was performed which documented significant improvement of the lymphadenopathies (Figure 5 A, B).

Indeed lymphadenopathies reduced in the second CT scan, maybe due to bolus steroids administered, in the occasion of dyspnea attacks. The echocardiogram showed an increase in the ejection fraction which reached 42% with an improvement in the cardiac diameters. Currently, three months after hospitalization, she is asymptomatic due to dyspnea, she is taking 12.5 mg of steroids and she is undergoing cardiological and pulmonary follow-up. Pulmonary function test is normal CVF 3.48 L (95% predicted), FEV1 2.82 (88% predicted) FEV1/FVC 81% with mild reduction of

DLCO value 70% predict. The ejection faction is now 50%.

The second CMR after 60 days scan showed an important improvement in the biventricular systolic function and in reduction of the areas of edema although the areas of hyperenhancement were similar. Unfortunately, the extent of LGE is a negative prognostic factor for arrhythmia and death in these patients (5).

In the differential diagnosis, we have taken into consideration giant cell myocarditis, the presence of evident granulomas in the histological examination, significant mediastinal involvement, and the initial good response to treatment, which lead us to consider sarcoidosis as a likely diagnosis (6). However, it should be noted that cardiac sarcoidosis and giant cell myocarditis share many histopathologic and clinical features (7). Let us consider the clinical case presented as atypical because, to our knowledge, the onset of sarcoidosis rarely occurs with severe cardiopulmonary impairment. It is a presentation that can be misunderstood in a specialized cardiological department as the presentation mimicked other more frequent conditions in that setting: the diagnosis was made by a multidisciplinary team that decided to perform EBUS TBNA in addition to cardiac MR. The result was to obtain, in this case, a prompt therapeutic response so as to preserve the cardiac function of a young patient. Although this case may still have recurrences, prompt recognition and treatment has avoided more aggressive treatments or death.

Conflict of Interest: we declare that we have no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Birnie DH, Nery PB, et al. Cardiac Sarcoidosis. J Am Coll Cardiol 2016; 68 (4): 411-21.
2. Gilotra NA, Griffin JM, Pavlovic N, et al. Sarcoidosis-Related Cardiomyopathy: Current Knowledge, Challenges, and Future Perspectives State-of-the-Art Review. J Card Fail. 2022 Jan;28(1):113-132. doi: 10.1016/j.cardfail.2021.06.016.
3. Muser D, Santangeli P, et al Characterization of the electroanatomic substrate in cardiac sarcoidosis: correlation with imaging findings of scar and inflammation. JACC Clin Electrophysiol 2018; (4): 291–303.
4. Trisolini R, Baughman R, et al. Endobronchial Ultrasound guided transbronchial needle aspiration in sarcoidosis: beyond the diagnostic yield. Respirology 2019; (24): 531–542.
5. Stevenson A, Bray JJH, Tregidgo L, et al. Prognostic Value of Late Gadolinium Enhancement Detected on Cardiac Magnetic Resonance in Cardiac Sarcoidosis. JACC Cardiovasc Imaging. 2023 Mar;16(3):345-357. doi: 10.1016/j.jcmg.2022.10.018.
6. Blauwet LA, Cooper LT, et al. Idiopathic giant cell myocarditis and cardiac sarcoidosis. Heart Fail Rev. 2013 Nov;18(6):733-46.
7. Nordenswan HK, Lehtonen J, Ekström K, et al. Manifestations and Outcome of Cardiac Sarcoidosis and Idiopathic Giant Cell Myocarditis by 25-Year Nationwide Cohorts. J Am Heart Assoc. 2021 Mar 16;10(6):e019415. doi: 10.1161/JAHA.120.019415.