Cardiac Sarcoidosis Diagnosed by Incidental Lymph Node Biopsy

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SUMMARY

Cardiac involvement in systemic sarcoidosis sometimes provokes life-threatening ventricular tachyarrhythmia. Steroid administration is one of the fundamental anti-arrhythmia therapies. For an indication of steroid therapy, a definitive diagnosis of sarcoidosis is required. However, cases that are clearly suspected of cardiac sarcoidosis based on their clinical courses sometimes do not meet the current diagnostic criteria and result in the loss of an appropriate opportunity to perform steroid therapy.

Here we report a case that was diagnosed as sarcoidosis by incidental biopsy of an inguinal lymph node during cardiac resuscitation for cardiac tamponade. While the inguinal lymph node was not swollen on computed tomography, a specimen obtained from an incidental biopsy during the exposure of a femoral vessel for the establishment of extracorporeal cardio-pulmonary resuscitation showed a non-caseating granuloma.

This findings suggest a non-swelling lymph node biopsy might be an alternative strategy for the diagnosis for sarcoidosis if other standard strategies do not result in a diagnosis of sarcoidosis. (Int Heart J 2017; 58: 1-4)

Key words: Arrhythmia, Ventricular tachycardia

Sarcoidosis is a granulomatous disease of unknown etiology which involves multiple organs. Whereas cardiac involvement is a major prognostic factor of sarcoidosis, cardiac sarcoidosis still remains difficult to diagnose. Non-caseating granulomas on cardiac biopsy can clearly show the existence of cardiac sarcoidosis. However, the histologic diagnostic rate achieved with cardiac biopsy in cardiac sarcoidosis is reported to be low (only 19.2%). Thus, cardiac sarcoidosis is mainly diagnosed based on clinical diagnostic criteria including abnormalities on the electrocardiogram or echocardiography, cardiac radionuclide images, gadolinium-enhanced cardiac magnetic resonance images, or positron emission tomography with 2-deoxy-2-[fluorine-18]fluoro-D-glucose integrated with computed tomography. The most common and frequent problem in the process of diagnosis is a situation in which a patient in whom cardiac sarcoidosis was highly suspected by clinical diagnostic criteria cannot be diagnosed as having sarcoidosis because clinical features of sarcoidosis in other organs including the lungs, eyes, skin, nervous system or muscle were not observed. In general, a lymph node that is not swollen cannot be a target of biopsy to detect non-caseating granuloma. Here we present a case in which cardiac sarcoidosis was diagnosed by incidental biopsy of a femoral lymph node, which was not enlarged. Biopsy of a non-swollen lymph node may be a future alternative strategy for making a definitive diagnosis in patients suspected of having cardiac sarcoidosis.

CASE REPORT

A 58-year-old woman was transferred to our hospital for cardiac re-synchronization therapy with defibrillator (CRT-D) implantation. Cardiomegaly by chest X-rays was observed 15 months before the transfer during an annual medical check-up. She presented with dyspnea on effort equivalent to NYHA III, reduced ejection fraction (30-35%) without any asynergy of the left ventricle (LV), paroxysmal atrial fibrillation, complete left bundle branch block, and complete atrioventricular block. Her heart rate was not less than 50 beats per minute and she had never lost consciousness. Cardiac magnetic resonance (CMR), coronary angiography, and cardiac biopsy were performed before CRT-D implantation to determine the underlying cause. Although CMR showed a patchy late gadolinium enhancement (LGE) including epicardial enhancement (Figure 1), blood tests, gallium scintigraphy (Figure 2), and biopsy of myocardium did not show any evidence of sarcoidosis but was compatible with dilated cardiomyopathy (DCM). Respiratory physicians, dermatologists, and ophthalmologists did not find any signs of sarcoidosis by standard methods. We ultimately
diagnosed her with LV dysfunction compatible with DCM, but not cardiac sarcoidosis, at this point. CRT-D implantation was performed and she was prescribed an angiotensin converting enzyme inhibitor, beta-blocker, and warfarin, after which the LV dysfunction and symptoms improved.

Two years after the implantation, she visited our emergency department with the complaints of dizziness followed by chest dull pain. Intracardiac electrocardiogram images logged by a CRT-D device showed episodes of ventricular tachycardia that were successfully terminated by shock deliver. She was diagnosed with symptomatic sustained ventricular tachycardia (VT). Her LV function did not deteriorate so we decided to perform an electrophysiological study and radiofrequency catheter ablation for the VT. Substrate mapping using CARTO 3 showed a low voltage area and fragmentation potentials in the right interventricular septum. After voltage mapping, programmed electrical stimulation was able to induce...
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Clinical VT. After several radiofrequency applications at this site, VT became non-inducible.

We suspected once again that she had cardiac sarcoidosis because her symptomatic VT had been evoked without progression of the LV dysfunction or decompensation of heart failure. Ocular sarcoidosis and skin sarcoidosis were again not observed by various experts. Whole-body computed tomography showed subtle consolidation in the bilateral lung field, which was not seen 2 years earlier, and a 9 mm lymph node in the left inguinal area (Figure 4). This left inguinal lymph node enlargement was considered to be of no clinical significance as interpreted by radiologists and an additional invasive diagnostic strategy was not performed. The patient was subsequently discharged.

However, she came to our emergency department again with chest dull pain. Recurrence of symptomatic sustained VT was observed and an intracardiac electrogram recorded with a CRT-D device showed episodes of ventricular tachycardia and sequential antitachycardia pacing attempts were followed by a delivery of an electrical shock. We decided to conduct another electrophysiological study and catheter ablation. However, a sheath perforated the right ventricle during the intervention, and emergency drainage was performed with venoarterial bypass with extracorporeal membrane oxygenation (VA ECMO). After successful epicardial fluid drainage, her vital signs stabilized. During weaning from VA ECMO, the left inguinal area was exposed to remove the VA ECMO catheter. There was a solid lymph node which had been observed on a CT scan. We resected and analyzed this lymph node because a cardiac surgeon had suggested that it was unusually solid. Pathologists concluded that the lymph node had a non-caseating granuloma, leading us to make a diagnosis of sarcoidosis. After this definitive diagnosis, we thought that re-evaluation of the cardiac inflammation and steroid therapy should be undertaken. However, these tests and steroid therapy were not performed because consent could not be obtained. On the other hand, the sustained ventricular tachycardia disappeared after catheter ablation without any additional medical treatment.

Discussion

Yoshida, et al reported in 1997 that approximately 11.2% of Japanese patients with high-degree atrioventricular block were diagnosed with cardiac sarcoidosis. In this population, they also mentioned that 32% of the women aged 40 to 69 years had had cardiac sarcoidosis. On the other hand, a diagnosis of cardiac sarcoidosis is difficult, especially in patients without lung involvement. Japanese diagnostic standards and guidelines for sarcoidosis revised in 2006 and 2015 enable us to make a diagnosis of sarcoidosis without any biopsy. The Heart Rhythm Society and World Association of Sarcoidosis and Other Granulomatous Disorders also support this idea. However, this guideline still requires 2 of 5 prerequisites: bilateral hilar lymphadenopathy, high plasma level angiotensin converting enzyme or lysozyme, a high plasma level of soluble interleukin 2 receptor, abnormal accumulation by 67 gallium scintigram or fluorine-18 fluorodeoxyglucose positron emission tomography (PET), and a CD4/CD8 ratio > 3.5 in bronchoalveolar lavage. Based on these strict criteria, we should make a thorough evaluation of the involvement of organs such as the heart, lung, eye, and skin.

George, et al reported a case who had significant swelling of an inguinal lymph node (measuring 6 cm) and presented with isolated unilateral peripheral edema without any other abnormality. Ultrasound-guided core needle biopsy showed non-caseating granulomatous inflammation. In this case, signifi-
cant lymph node swelling should have been sufficient to perform lymph node biopsy. However, in our case, inguinal lymph node was not swollen enough to perform lymph node biopsy in daily practice. We did not find any other report in which cardiac sarcoidosis was diagnosed with invasive lymph node biopsy in a patient who did not exhibit any other features of sarcoidosis.

It might be prudent to consider lymph node biopsy more assertively in patients who are suspected of having cardiac sarcoidosis clinically, even when we cannot identify any other signs of sarcoidosis and the lymph nodes are not overly enlarged. This aggressive lymph node biopsy might improve the sensitivity of the diagnosis and prognosis of cardiac sarcoidosis.

**References**