Massive pericardial effusion causing cardiac tamponade accompanied by elevated CA-125 and thoracic lymphadenopathy in sarcoidosis: a case report

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1. Introduction

Sarcoidosis is a systemic granulomatous disease of unknown etiology, characterized by the formation of epithelioid granulomas in lungs, peripheral lymph nodes, skin, eyes and liver [1]. Cardiac sarcoidosis is a rare entity, and occurs in 2–7% of patients, while latent course is much more frequent [2]. It occasionally occurs in the absence of pulmonary or systemic involvement [2,3].

Cardiac sarcoidosis can involve the myocardium, endocardium and pericardium, with a variety of clinical manifestations, with the most frequent being arrhythmia and conduction disturbances, and heart failure [4–7].

Pericardial effusion is detected on echocardiography in 10–21% of patients with pulmonary or systemic sarcoidosis, even in the absence of symptoms [3]. Isolated pericardial involvement is infrequent and may be manifested as pericardial effusion, constrictive pericarditis and very rarely tamponade [3,4,8–11]. Confirming the diagnosis of cardiac sarcoidosis is a difficult task [6]. The clinical manifestations of cardiac sarcoidosis with pericardial lesions are similar to those of pericardial diseases of other etiologies [3,4]. Cardiac sarcoidosis is accompanied by high mortality and is one the main causes of death in sarcoidosis [12].

We describe a first case of cardiac sarcoidosis manifested by symptomatic severe pericardial effusion, with signs of cardiac tamponade, and accompanied by increased carbohydrate antigen-125 (CA-125) levels and mediastinal and pericardial lymph node
enlargement, verified by histological examination of pericardial lymph node specimen and successfully treated by pericardial drainage and excision of lymph node at Scientific Research Institute of Heart Surgery and Organs Transplantation.

The work has been reported in line with the SCARE criteria [13].

1.1. Presentation of case

A 51-year-old female patient was admitted with complaints of sickness, severe shortness of breath on minimal exertion, moderate swelling in lower extremities, and heaviness in right upper abdomen. The patient felt sick during one month before admission when shortness of breath and swelling of legs had appeared. Before admission, the patient received therapy with non-steroidal antinflammatory drugs, antibiotic and diuretic. However, due to lack of positive response to treatment after two weeks, the patient was referred to our cardiac surgery clinic with diagnosis of pericardial effusion of unknown etiology and bilateral pleural effusion. Patient had no history of gynecologic diseases. Informed consent was obtained from patient for all diagnostic and treatment procedures.

General physical examination was unremarkable except for peripheral edema. There was hepatomegaly on palpation and diminished lung sounds and weakened heart sounds on auscultation. The patient had NYHA functional class III.

Laboratory results (Table 1) demonstrated mild lymphocytosis (lymphocyte count of 42%), negative antistreptolysin O, C-reactive protein and rheumatoid factor tests, negative tests for markers of viral hepatitis, human immunodeficiency virus, cytomegalovirus and herpes virus. However, the high values of tumor marker CA-125 (201 IU/L) were detected, while other tumor markers (Table 1) were negative.

ECG showed sinus tachycardia (90 beats/min) and low voltage QRS. Chest X-ray displayed a water-bottle configuration of the heart with an increased cardiothoracic ratio and a small amount of fluid in both pleural spaces.

Echocardiography (Table 2, Fig. 1) demonstrated large pericardial effusion, with maximum width of fluid up to 38 mm, 24 mm, 35 mm and 22 mm behind LVPW, LV apex, RV and RA, respectively, and collapses of the RA and RV. Additional echocardiographic findings were minimal mitral, tricuspid and pulmonary regurgitations, LV diastolic dysfunction and preserved LV ejection fraction (68%) with no hypokinesia zones.

Computed tomography (CT) revealed large pericardial effusion, (Fig. 2) with localized mass in pericardial fat (possibly lymph node), small pleural effusion and enlarged lymph nodes in anterior mediastinal compartment (Fig. 3).

Due to clinical and imaging signs of symptomatic large pericardial effusion, with signs of tamponade and presence of pericardial mass (possible lymph node), the patient underwent drainage of pericardial cavity and excision of pericardial lymph node through subxiphoid approach under endotracheal anesthesia using standard technique. During the procedure, pericardium was found to be thickened and a total of 850 mL of serous-sanguineous fluid was evacuated. Part of pericardium was excised for bacteriological and histological examination.

There was an enlarged lymph node in pericardium, which was dissected and sent for histological examination. Central venous pressure reduced from 120 mm to 30 mm after procedure.

Cytological examination showed no atypical cells in the pericardial fluid. Histological examination of lymph node revealed non-caseating granulomas with accumulation of epithelioid cells (giant multi-core cells) (Fig. 4A) in the center (Fig. 4B) and along the periphery (Fig. 4C); pericardial specimen demonstrated focal pericardial lymphocytic infiltration (Fig. 4D), the findings associated with sarcoidosis.

After pericardial drainage, patient’s condition had improved, there was only minimal fluid posteriorly (0.8 mm) on echocardiogram (Table 2), and minimal pleural effusion on chest X-ray. She was discharged on 8th day, and her follow-up at 6 months after treatment was uneventful without complaints.

2. Discussion

We presented as a rare case of cardiac sarcoidosis in a female patient manifested as massive pericardial effusion, with signs of cardiac tamponade and elevated CA-125 tumor marker, mediastinal and pericardial lymphadenopathy, diagnosed using histological analysis of pericardial lymph node specimen and successfully treated by pericardial drainage and excision of enlarged pericardial lymph node.

Cardiac sarcoidosis without extracardiac manifestations is seen in young and middle-aged women, and is manifested by arrhythmias and conduction disturbances and heart failure [6,7,14]. Isolated large pericardial effusion, and cardiac tamponade are rare in sarcoidosis [3,4,8,10,11]. Our case was remarkable due to signs of large pericardial effusion, on ECG (low voltage QRS), chest X-ray (water-bottle configuration), CT, echocardiogram and signs of tamponade on echocardiography (RA and RV collapse).

The search for specific etiology of pericardial effusion, in our patient was negative according to laboratory results. The presence of high level of CA-125, known as a tumor marker in ovarian carcinoma [15], posed a diagnostic dilemma. However, our patient had no associated gynecologic pathology. CA-125 is a glycopro-
tein with embryonic epithelial source including not only fallopian tubes, endometrium, endocervix, but also pleura, pericardium, and peritoneum [15].

Elevated level of CA-125 in sarcoidosis was associated with pleural effusion [16] and peritoneal involvement [15].

Presence of pleural effusion in our patient corroborates with previously reported case [15]. However, there are no reports on association of pericardial effusion, with CA-125 level in sarcoidosis, as we established in our patient. Thus CA-125, as glycoprotein responsible for origin of pericardium from embryonic source can be increased in cases of sarcoidosis with pericardial effusion.

Our case is notable by absence of clinical signs of cardiac sarcoidosis with incidental finding of enlarged lymph node of pericardium, mimicking pericardial mass and mediastinal lymphadenopathy on CT, further confirmed by histological examination of pericardial lymph node specimen.

Table 1
Laboratory blood tests data of a patient before and after treatment.

| Parameters                                      | Before treatment        | After treatment        |
|------------------------------------------------|-------------------------|------------------------|
| Hemoglobin                                     | 137 g/dL                | 150 g/dL               |
| Red blood cell count                           | 4.5 × 10¹²/L            | 5 × 10¹¹/L             |
| Hematocrit                                      | 41%                     | 45%                    |
| Platelets                                      | 216 × 10⁹/L             | 240 × 10⁹/L            |
| White blood cell count                         | 6.6 × 10⁹/L             | 7.9 × 10⁹/L            |
| Stab                                           | 5%                      | 4%                     |
| Neutrophils                                    | 44%                     | 65%                    |
| Eosinophils                                    | 3%                      | 4%                     |
| Basophils                                      | 0%                      | 0%                     |
| Monocytes                                      | 6%                      | 7%                     |
| Lymphocytes                                    | 42% (normal value 19–37%)| 20%                   |
| Sedimentation rate                             | 11 mm/h                 | 18 mm/h                |
| Human immunodeficiency virus test              | negative                | –                      |
| Virus hepatitis test                            | negative                | –                      |
| Wasserman reaction                             | negative                | –                      |
| Antistreptolysin O                             | 200 IU/ml (normal value 0–200 IU/ml) | –                     |
| Rheumatoid factor                              | Negative                | –                      |
| C- reactive protein                            | Negative                | –                      |
| Carbohydrate antigen - 125                    | 201 IU/L (normal value < 35 IU/L) | –                     |
| Cytokeratin 19 fragment - CYFRA 21 – 1         | 1.5 ng/ml (normal value 0–3.3 ng/ml) | –                     |
| Human chorionic gonadotropin                   | 1.37 IU/L (normal value <2 IU/L). | –                     |
| Carbohydrate antigen 15 – 3                   | 5.5 IU/L (normal value <30 IU/L) | –                     |
| Carcinoembryonic antigen                       | 0.97 ng/ml (normal value <5 ng/mL) | –                     |
| Antibody titer to cytomegalovirus              | 230 U/mL                | –                      |
| Antibody titer to herpes virus                 | 33.7 U/mL               | –                      |

Table 2
Echocardiography data before and after treatment.

| Parameters                                      | On admission            | After pericardial drainage |
|------------------------------------------------|-------------------------|---------------------------|
| Aorta                                          | Unremarkable, ascending part diameter 24 mm | –                         |
| Descending aorta                               | Unremarkable            | –                         |
| Aortic valve                                   | Tricuspid, pressure gradient - 5 mm Hg | –                         |
| Mitral valve                                   | Minimal regurgitation, maximal pressure gradient - 3 mm Hg | –                         |
| Tricuspid valve                                | Minimal regurgitation maximal, pressure gradient - 3 mm Hg | Minimal regurgitation |
| Pulmonary artery                               | Normal size             | –                         |
| Pulmonary valve                                | Minimal regurgitation, pressure gradient - 5 mm Hg | –                         |
| Left atrium                                    | 33 mm                   | 36 mm                     |
| Right atrium                                   | Not expanded            | Normal                    |
| Left ventricle (LV):                           |                         |                           |
| LV end-diastolic size                          | 45 mm                   | 39 mm                     |
| LV end-systolic size                           | 28 mm                   | 22 mm                     |
| LV ejection fraction                           | 68%                     | 76%                       |
| The interventricular septum                    | 9 mm                    | –                         |
| The posterior wall of the LV                   | 9 mm                    | –                         |
| LV regional contractility                      | No hypokinesia zones    | –                         |
| LV diastolic function                          | E/A - abnormal pattern  | Normal                    |
| Right ventricle                                | 22 mm                   | –                         |
| Right ventricular free wall thickness          | 4 mm                    | –                         |
| Systolic pulmonary artery pressure             | 35–40 mm Hg             | –                         |
| Pericardium:                                  | large effusion          | Minimal effusion          |
| LV posterior wall                              | 37 mm                   | 0.8 mm                    |
| LV apex                                       | 24 mm                   | 0 mm                      |
| Right ventricular free wall                    | 35 mm                   | 0 mm                      |
| Right atrium                                   | 22 mm                   | 0 mm                      |
| Atrial septum                                  | intact                  | No signs of collapse      |
| Ventricular septum                             | intact                  | –                         |
| Pleural cavities:                              |                         |                           |
| The left echonegative space                    | 12 mm                   | No effusion               |
| The right echonegative space                   | 34 mm                   | –                         |
| Vena cava inferior                             | 22 mm, collapses on inspiration less than 50% | –                         |
**Fig. 3.** Computed tomography images of lymph nodes enlargement (arrows) in anterior mediastinum.

**Fig. 4.** Micropreparations of lymph nodes No. 17,133,366 (edge part). A) A- giant multi-core cells, B- healthy tissue; B) Granulomas with accumulation of epithelioid cells of macrophages on the periphery (giant multi-core cells) - A- giant multi-core cells, B- healthy tissue; C) Micropreparations of lymph nodes No. 17,133,366 (central part); Granuloma with accumulation of epithelioid cells in the center macrophages - A - focal lymphocytic infiltration, B- healthy tissue D) Pericardial micropreparations №27,133,366 of focal lymphocytic infiltration - A - focal lymphocytic infiltration, B- healthy tissue.

The diagnosis of sarcoidosis is usually established by clinicoradiological findings of lymphadenopathy with or without pulmonary involvement, or pulmonary only involvement, supported by histological findings of non-caseating epithelioid cell granulomas [1]. The lymphadenopathy in sarcoidosis is usually bilateral hilar and right paratracheal, while isolated mediastinal lymphadenopathy is a rare finding [17]. Hilar lymphadenopathy is usually established by chest radiography, while CT is superior for diagnosis of mediastinal lymphadenopathy and parenchymal involvement [17].

Mediastinal lymphadenopathy was detected by CT in 88% of histologically proven cardiac sarcoidosis cases manifesting as dilated cardiomyopathy and in all cases with arrhythmias, undergoing radiofrequency ablation and ICD placement [7,18]. The case with cardiac tamponade and mediastinal lymphadenopathy was also reported [11].
Our patient had signs of mediastinal lymphadenopathy on CT, but our case was distinguishable by presence of pericardial lymphadenopathy on CT, mimicking pericardial mass and confirmed intraoperatively.

For histological diagnosis of cardiac sarcoidosis, endomyocardial biopsy may be used, though biopsies of mediastinal lymphadenopathy guided by CT or PET imaging have been shown to be accurate [6,19].

We could not find studies with pericardial lymphadenopathy and cardiac sarcoidosis proven by histological analysis of pericardial lymph node. Examination of specimen of pericardial lymph node demonstrated findings associated with sarcoidosis. There was only one report on presence of multiple nodules in pericardium of a patient with cardiac tamponade, in whom biopsy of pericardium demonstrated non-caseating granulomas [8].

We undertook open-heart surgery due to presence of pericardial mass on CT and large pericardial effusion. The intervention revealed the enlarged pericardial lymph node suspected by CT, which was excised and sent together with pericardial specimens for histological examination that revealed non-caseating granulomas specific for cardiac sarcoidosis.

Treatment of sarcoidosis with signs of large pericardial effusion, usually includes pericardiocentesis, drainage and corticosteroids therapy [4,5,11,20]. In very rare cases of constrictive pericarditis, pericardectomy is indicated [9]. Treatment of cardiac sarcoidosis is based on use of corticosteroids, but immunosuppressive therapy may be required 5,11]. Therapy of cardiac sarcoidosis with involvement of myocardium and arrhythmias and conduction disturbances are ablation of ventricular tachycardia source, ICD implantation for secondary prevention of sudden cardiac death and pacing [7,14].

3. Conclusion

This is the first case reporting increased CA-125 levels associated with pericardial effusion with signs of tamponade, pericardial and mediastinal lymphadenopathy in cardiac sarcoidosis, established by histological analysis of pericardial lymph node specimen. One should keep in mind that cardiac sarcoidosis may present as massive pericardial effusion, with signs of tamponade and pericardial lymphadenopathy mimicking pericardial mass, mediastinal lymphadenopathy and elevated CA-125, mimicking malignancy.

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Consent

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Author contribution

(1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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