Cent. Eur. J. Med. • 8(1) • 2013 • 107-116
DOI: 10.2478/s11536-012-0095-8

VERSITA

Central European Journal of **Medicine**

Cardiac sarcoidosis: A review on the work-up and management

Case Report

Boris Solun[1], Dana Marcoviciu[1], Yulia Belnik[1], Tamar Azran[1], Dror Dicker[1], Yosef Perek[2], Orly Goitein[3]

1 Department of Internal Medicine D, Hasharon Hospital, affiliated to the Sackler School of Medicine, Tel-Aviv University Petah Tikva, 7 Keren Kayemet St., 49100, Israel

2 Department of cardiology, Rabin Medical Center, Hasharon Hospital, affiliated to the Sackler School of Medicine, Tel-Aviv University Petah Tikva, 7 Keren Kayemet St., 49100, Israel

3 Diagnostic Imaging, Sheba, Tel Hashomer, Israel

Received 30 July 2012; Accepted 18 September 2012

Abstract: Sarcoidosis is a multisystem granulomatous disease of unknown etiology and with variable presentation. Skin, lymph nodes, lungs, eyes and the central nervous system are mostly involved. Cardiac sarcoidosis (CS) is a rare condition with clinical manifestations in about 5% of patients. Since it increases the risk of acute cardiac failure, ventricular arrhythmia, conduction disturbances and even sudden death, it aggravates markedly the prognosis. The early diagnosis of CS is difficult, requiring the use of diagnostic tools such as electrocardiographic monitoring, two-dimensional echocardiography, radionuclide scan, cardiac magnetic resonance imaging, positron emission tomography and endomyocardial biopsy. Once the diagnosis of CS is established, there is a need for early corticosteroids treatment, with or without immunosuppressive therapy, to prevent deterioration of cardiac function. In patients with refractory ventricular tachyarrhythmia, markedly reduced left ventricular ejection fraction and high risk of sudden death, prophylactic insertion of a pacemaker or implantable defibrillator is recommended. We had the opportunity to treat a patient with CS and to review the currently accepted diagnostic and treatment approach.

Keywords: *Cardiac sarcoidosis • Conduction disturbances • Corticosteroids*

1. Introduction

Sarcoidosis has been first described by Hutchison, a British dermatologist, in 1869 [1]. A few decades later, Boeck reported on a patient with compact skin nodules, resembling sarcoma lesions, designated as multiple benign sarcoid of the skin. Sarcoidosis is a multi-system disease of unknown cause with variable presentation and characterized by noncaseating granulomas formation. Although it affects predominantly the lungs, eyes and skin, almost any body organ may be involved. Sarcoidosis affects annually 20 per 100.000 individuals of all races and all ages, but it is more prevalent and severe in blacks [2,3].

Beginning the 20th century, the incidence of cardiac involvement in sarcoidosis gradually increases and has been associated with poor prognosis. The occurrence of CS in the US is approximately 20-27%, whereas in Japan it riches 58% [4]. The heart may be affected at any stage of the disease, even without evidence of systemic involvement. Different types of arrhythmias and conduction disturbances resulting from granulomatous infiltrations in the conduction system or in the ventricular wall are the most common cardiac manifestations that may terminate in death [5].

2. Case report

A 51 year-old white woman of Indian descent presented at the Emergency Department with long-standing history of weakness, palpitations and dyspnea. Three months previously, she was admitted to the hospi-

* *E-mail: bsolun@gmail.com*

tal because of precordial pains, positive markers for cardiac damage and signs of non-ST elevated myocardial infarction on the electrocardiogram. However, coronary angiography revealed no evidence for coronary artery disease. One month later, she experienced episodes of recurrent palpitations and she was readmitted. On physical examination, she was conscious, well oriented, without pallor, cyanosis or edema. She was a febrile with no symptoms of respiratory distress. Her blood pressure was 126/59 mm Hg with no signs of postural hypotension. Pulse rate was 51/min. and regular. On chest auscultation, there were decreased breath sounds on the right lung base. S1, S2 were normal without murmurs. The abdomen was soft and non-tender, the bowel sounds were normal and the liver and spleen were not palpable. Lymph nodes were not detected in the cervical, supraclavicular, axillary or inguinal areas.

An electrocardiogram showed complete A-V block (Fig. 1). 24-hour Holter monitoring revealed bouts of non-sustained ventricular tachycardia (VT) and therefore treatment with 2.5 mg Concor® (Bisoprolol fumarate - Merck Ltd) was started. Chest radiography revealed left hilar lymphadenopathy with right lung low zone opacity (Fig. 2). However, on CT angiography bilateral pleural effusions were noted - small on the left side and moderate on the right (Fig. 3). A trans-thoracic echocardiogram showed a well preserved left ventricle systolic function with mild hypertrophy, mild mitral regurgitation, mild to moderate tricuspid regurgitation, and mild to moderate pulmonary hypertension (Fig. 4). Hemoglobin was 14.6 g/dL, white blood cell count, 9300/μL, platelet count- 345/μL, Erythrocyte Sedimentation Rate (ESR) – 30 mm. Peripheral blood film showed mild hypochromia. Serum angiotensin- converting enzyme level was within our laboratory range, blood glucose- 102 mg/dL, urea-31 mg/dL, creatinine- 0.8 mg/dL, total protein level- 7.1g/dL, albumin- 4.6 g/dL, serum glutamic oxaloacetic transaminase (SGOT) - 36.2 U/L, serum glutamic pyruvic transaminase (SGPT) - 64 U/L, alkaline phosphatase- 86 U/L, serum calcium- 9.7 mg/dL, serum sodium- 143 meq/L, serum potassium- 4.84 mEq/L.

A cardiovascular magnetic resonance (CMR) examination revealed multiple foci of myocardial damage in the antero-lateral, inferior-apical wall and in the mid-septum (Fig. 5).

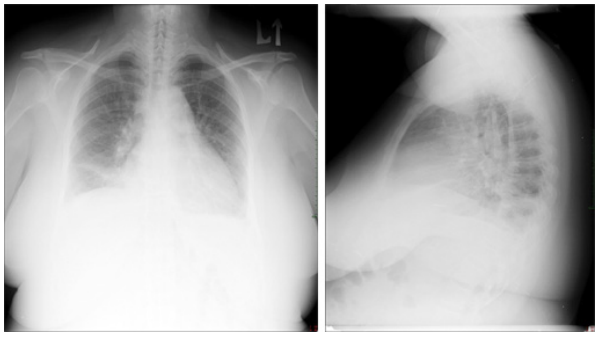

Figure 2. Chest radiography showing left hilar lymphadenopathy with right lung low zone opacity.

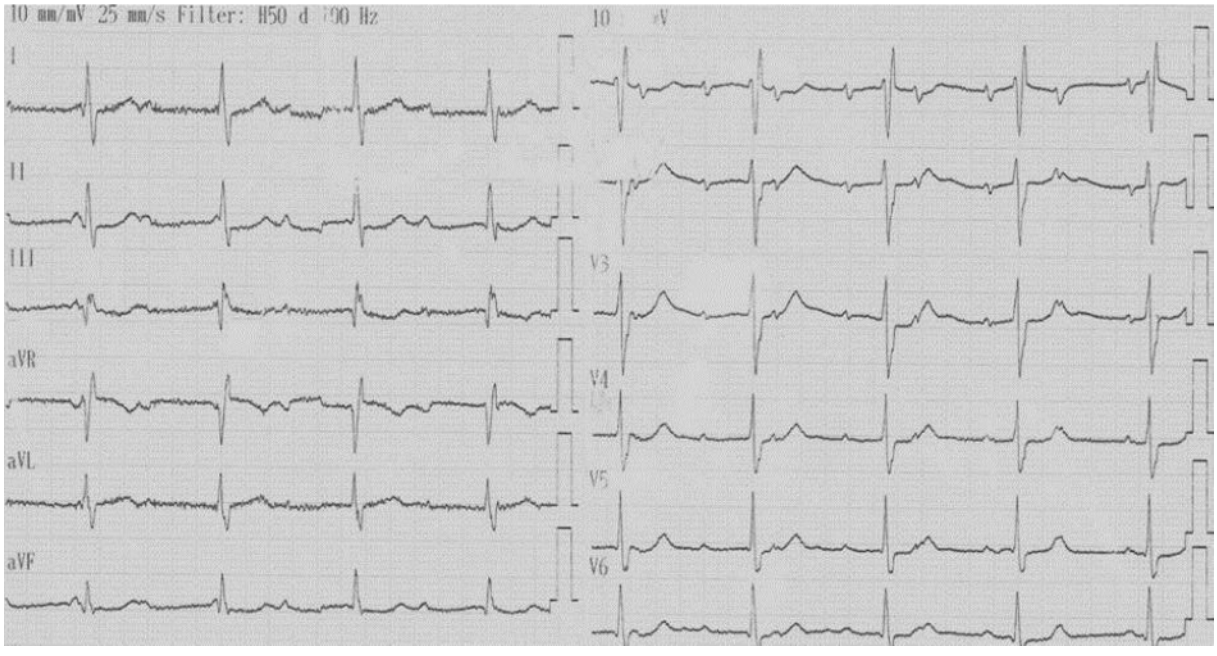

Figure 1. 12-lead ECG on admission showing a 3-d degree heart block.

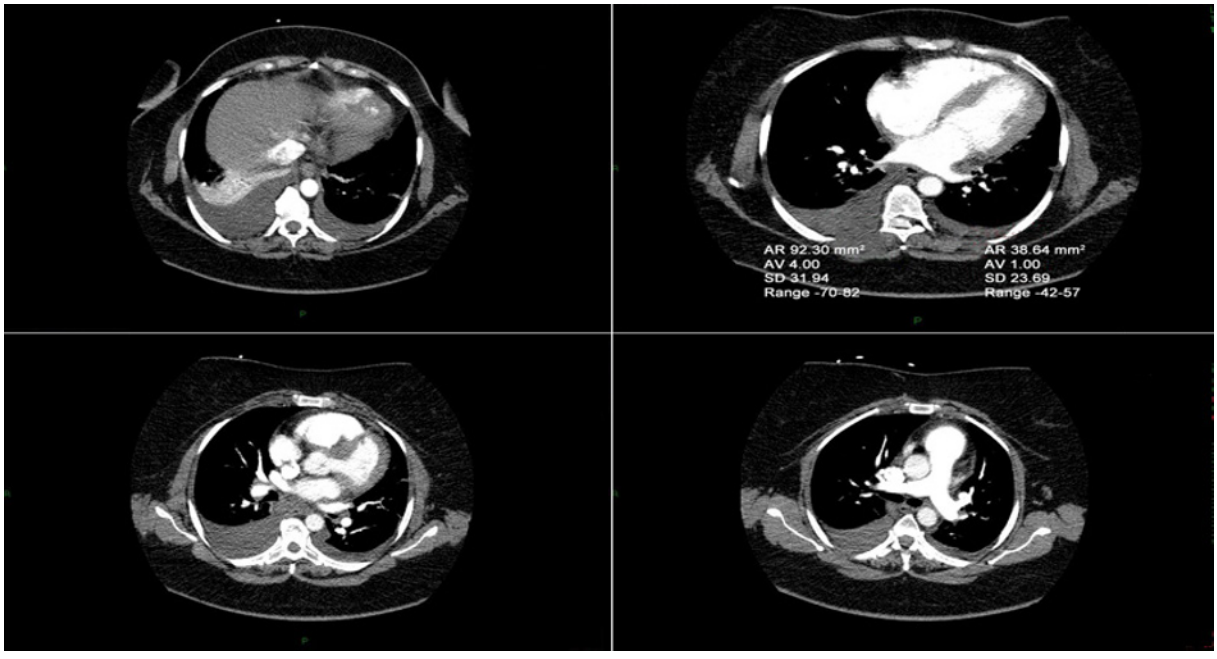

Figure 3. CT angiography showing bilateral pleural effusions - small on the left side and moderate on the right.

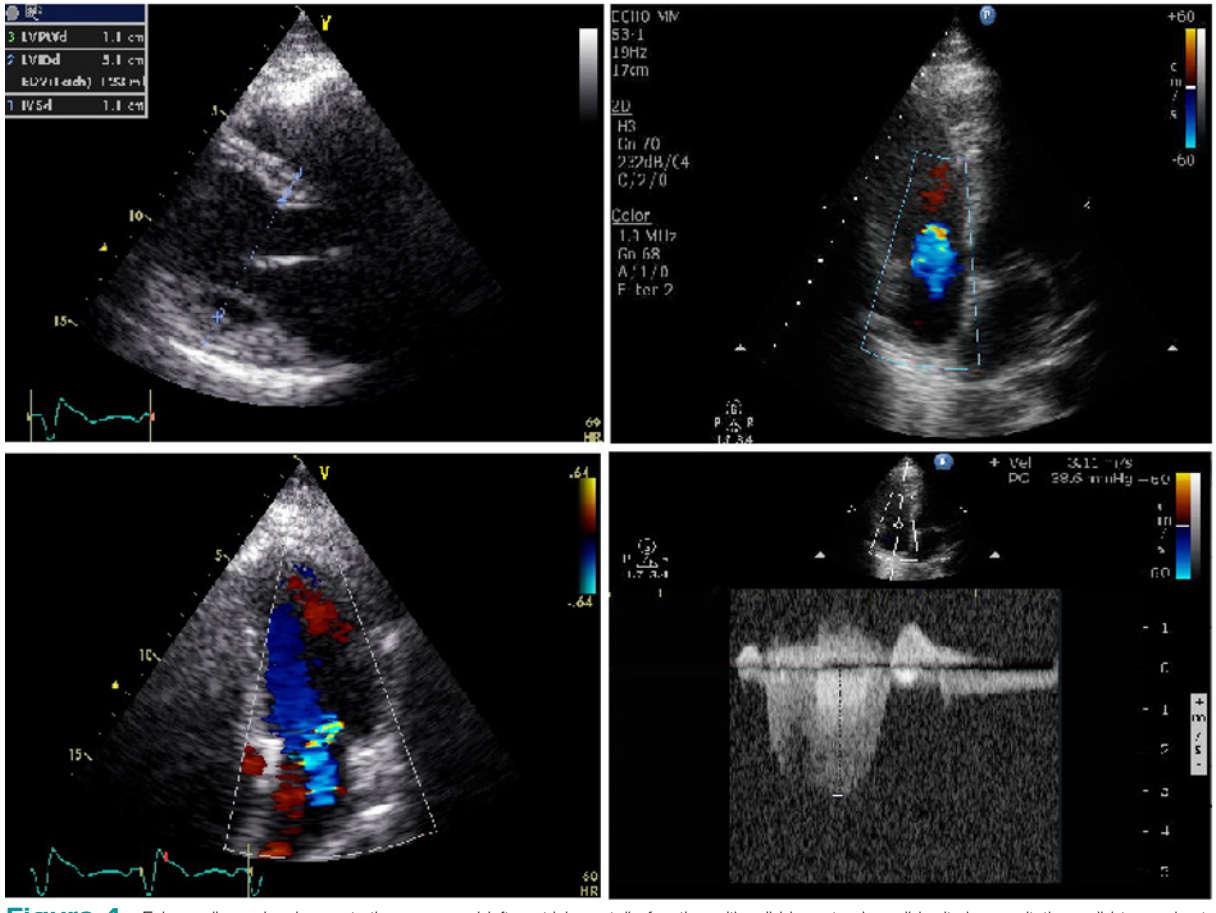

Figure 4. Echocardiography demonstrating preserved left ventricle systolic function with mild hypertrophy, mild mitral regurgitation, mild to moderate tricuspid regurgitation, and mild to moderate pulmonary hypertension.

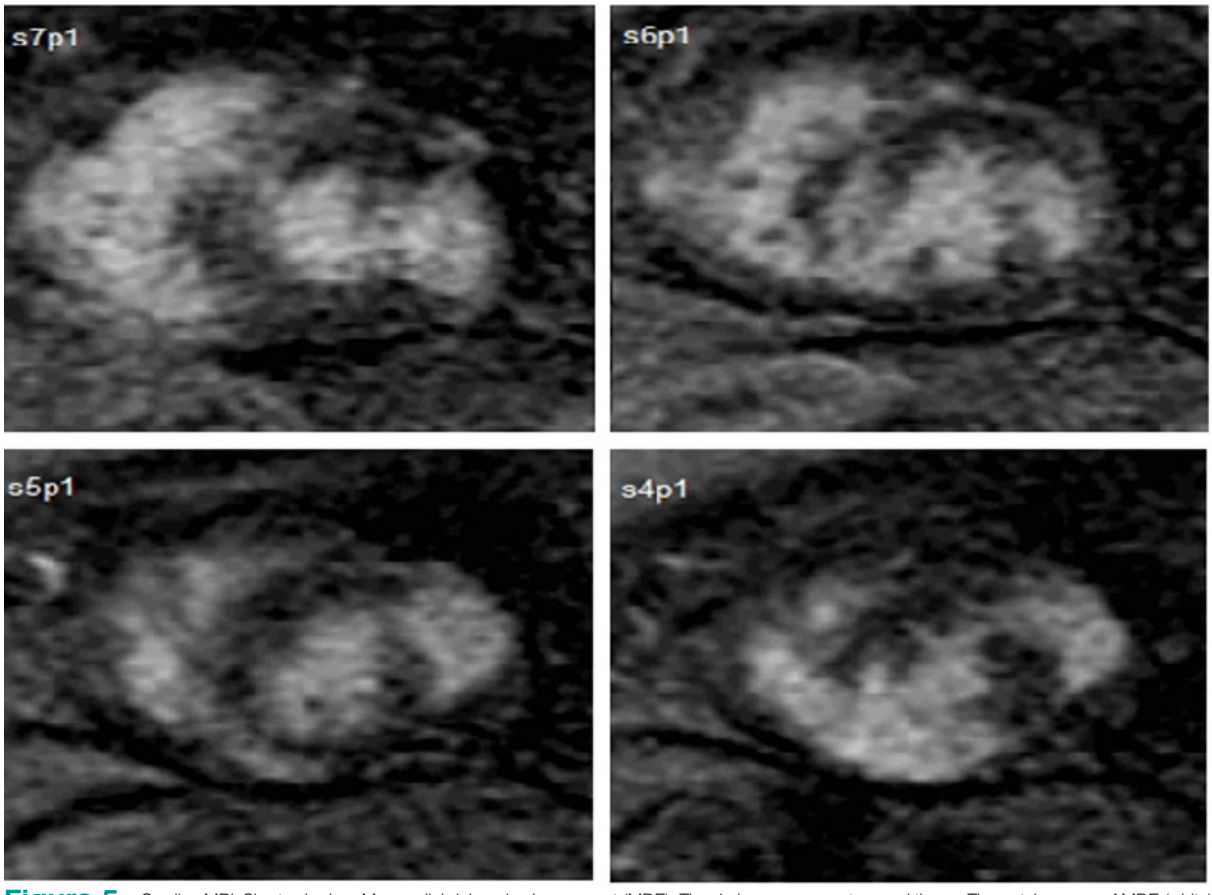

Figure 5. Cardiac MRI. Short axis view. Myocardial delayed enhancement (MDE). The dark areas present normal tissue. The patchy areas of MDE (white) depict areas of cardiac involvement in both lateral wall and septum.

FDG-positron emission tomography (PET) revealed diffuse enhanced FDG uptake in the left ventricle and presence of mediastinal lymph nodes (Fig. 6). An endomyocardial biopsy showed non-necrotizing granulomatous myocardiopathy compatible with the diagnosis of sarcoidosis (Fig. 7). To prevent complete A-V block, an automatic implantable cardioverter-defibrillator (ICD DDD) was inserted. The patient was given 1mg/kg prednisone daily with clinical improvement expressed by good functional activity and lack of episodes of ventricular tachycardia.

3. Discussion

Although the clinical manifestations of CS are not frequent (in only 5% of patients) autopsy examination indicates that myocardial lesions are found in 20-60% of the cases with sarcoidosis. It is notable that CS is not an entirely benign condition. In Japan, CS is a leading cause of sudden death in patients with sarcoidosis, whereas in the US it is the second most prevalent cause of mortality after respiratory failure [6]. Recognition of cardiac involvement in sarcoidosis may be difficult because of non-specific clinical manifestations, and limitations in sensitivity and specificity of the diagnostic tests. Clinical manifestations, such as atrioventricular or intraventricular conduction disturbances, ventricular ectopy, congestive heart failure and sudden cardiac death are frequent. Congestive heart failure occurs in 30 % of the cases [7]. Sarcoidosis affects almost all parts of the heart including pericardium, myocardium and endocardium in descending manner. The most affected sites are the left ventricular free wall, septum, papillary muscles, right ventricle and the atria. As a result, sarcoidosis mimics others cardiovascular conditions, such as pericarditis, acute coronary syndrome and even acute myocardial infarction. Valvular insufficiency leading to congestive heart failure may be due to papillary muscle involvement [5,7]. There are no clinical manifestations specific for CS. Patients' complaints such as dyspnea, palpitations or syncope are associated with heart failure or arrhythmias.

Since 1993 the Japanese Ministry of Health and Welfare (JMHW) guideline have has been used widely for diagnostic purposes [8]. However, since the diagnostic tests and procedures in this guideline are of low specificity and sensitivity, additional diagnostic tests, including

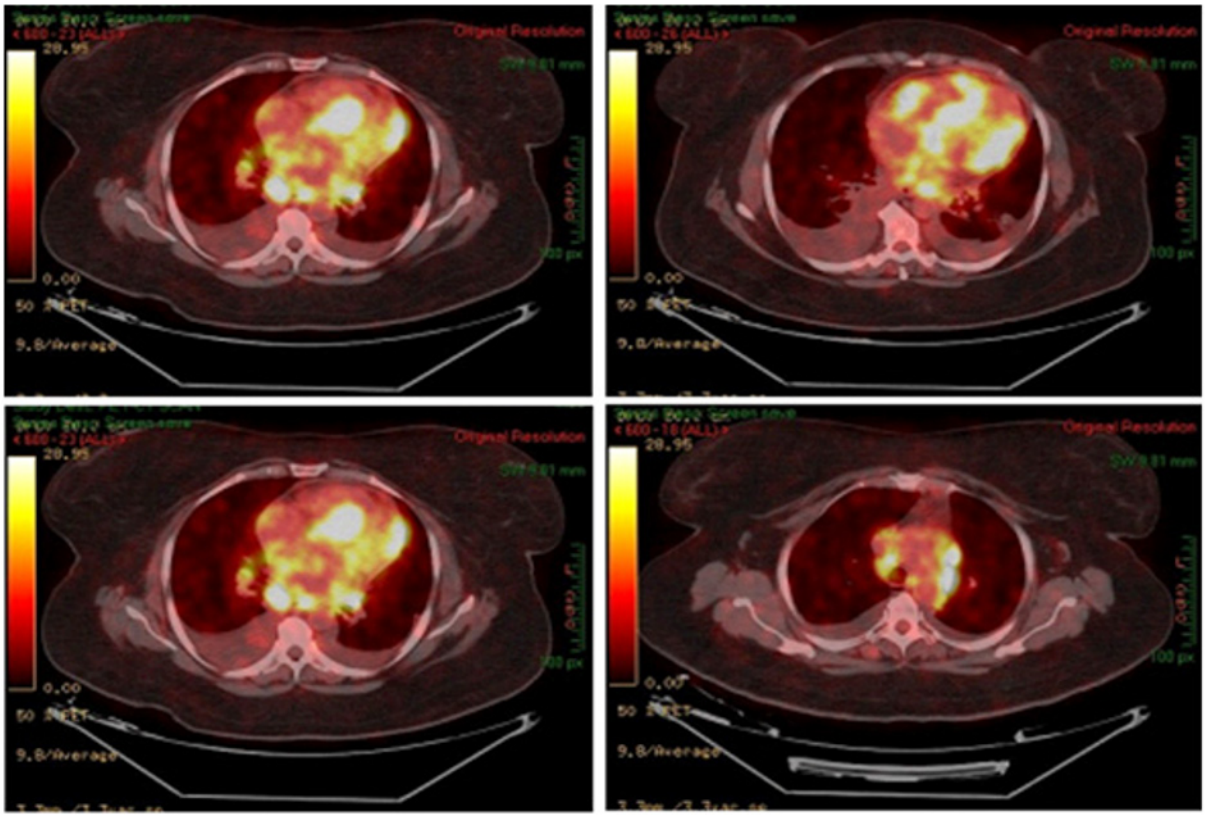

Figure 6. PET/CT shows diffuse 18FDG uptake in the mediastinum, septum and left ventricle.

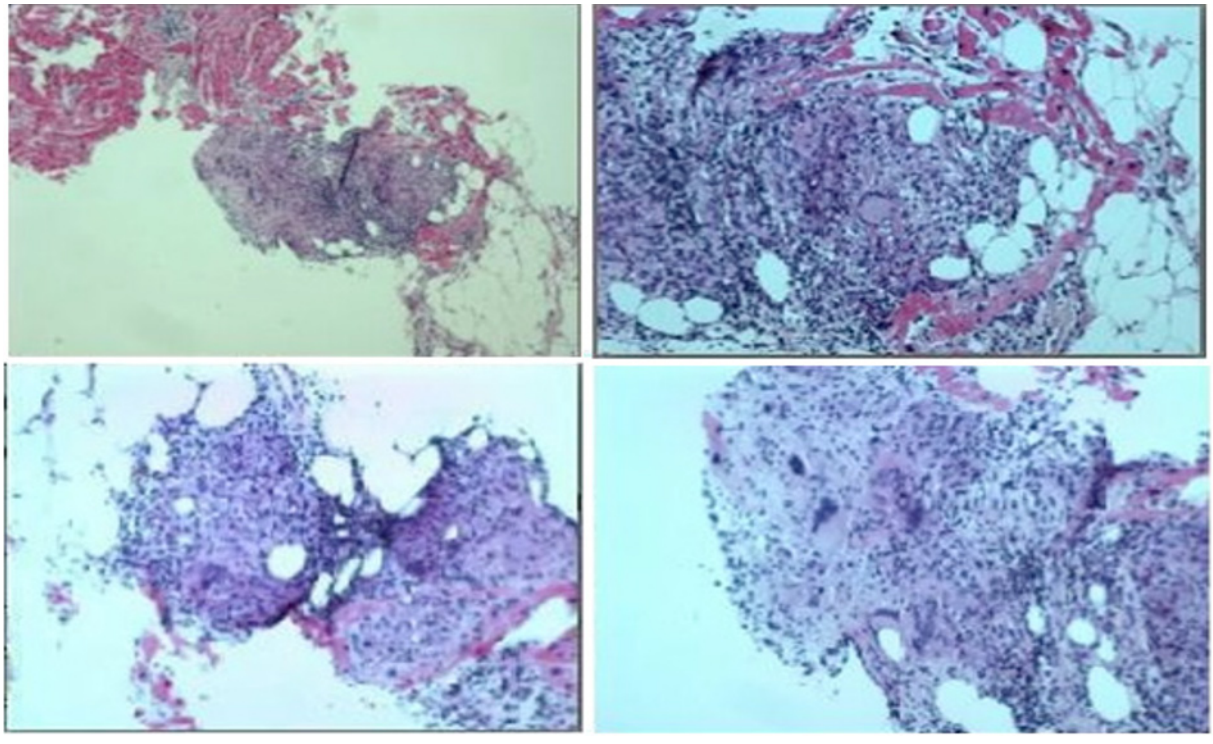

Figure 7. Endomyocardial biopsy demonstrates granulomatous infiltration of the myocardium. (hematoxylin-eosin staining, original magnification 40x).

PET CT and cardiac MRI, allow to establish the diagnosis of cardiac involvement [9]. Following a Delphi study with two round questionnaires, sarcoidosis experts reached a consensus that the best management approach to the disease should be based on the medical history, physical examination, 12-lead ECG, echocardiogram, Holter monitoring, FD PET CT scan, cardiac MRI and treatment with steroids. On the other hand, the role of signal-average ECG in screening, the optimal prednisone dose, the question about using of steroid- sparing drugs, and duration of treatment - are still areas of uncertainty [10]. The revised guidelines for the diagnosis of CS published by Japanese Society of Sarcoidosis and other Granulomatous Disorders in 2006 are particularly useful in patients with sarcoidosis in whom cardiac involvement is suspected and in contrast to previous guidelines they include cardiac MRI but still not PET CT [11,12].

Electrocardiographic conduction abnormalities, such as atrioventricular block, bundle branch block, premature ventricular contractions or ventricular tachycardia are well known findings in patients with suspected or confirmed CS. Conduction disturbances and bundle branch blocks, either complete or incomplete, are the most common arrhythmias with a prevalence ranging from 12% to 62%. Supraventricular arrhythmias, sinus node dysfunction, pseudo Q- wave infarction, long QT intervals or U waves, have been less frequently observed [13]. Homsi et al. have found that the sensitivity and specificity of a fragmented QRS complex on 12-lead ECG as a marker of myocardial scar were higher by 100% and 80% respectively in comparison with gadolinium cardiac magnetic resonance imaging [14]. 24-hour Holter monitoring is useful and may detect abnormalities even when ECG at rest is normal. Suzuki et al. reported that Holter monitoring is associated with a diagnostic sensitivity and specificity of 67% and 62% respectively and provides a convenient and non- expensive tool for noninvasive screening of cardiac involvement in sarcoidosis [15].

Trans-thoracic echocardiography is a helpful imaging tool for confirming the diagnosis of CS. The echocardiographic features vary widely and include the presence of abnormal thickening or thinning of the septum, left ventricle dilatation and systolic or diastolic dysfunction, pericardial effusion, valvular abnormalities and ventricular aneurysms. A typical, but uncommon lesion, is the thinning of the basal anterior septum. Rarely, signs of hypertrophic cardiomyopathy have been described. However, these findings are usually difficult to detect [16,17]. The echocardiographic abnormalities are directly related to the disease's stage and may be undetectable in its early phases. It is notable that there is no correlation between the ECG and echocardiographic findings [13].

Myocardial perfusion scintigraphy with single photon emission computed tomography (SPECT), the use of radiochemicals, such as thallium-201, Tc-99m-methoxy-isobutylisonitrile (Tc-99m-sestamibi) and gallium-67 are indicated when the diagnosis of cardiac sarcoidosis is suspected. The characteristic phenomenon that differentiates CS from coronary artery disease is the occurrence of an improvement or complete resolution of perfusion defects after pharmacological dilatation with dipyridamole or adenosine [18]. This phenomenon, known as "reverse distribution", may be due to focal microvascular vasoconstriction surrounding myocardial sarcoid granulomas, but it has not been fully elucidated. However, the reverse distribution is not specific for CS since it has been observed in other cardiomyopathies [19]. Gallium-67 scintigraph, being positive only in the active stage of the disease, reflects the activity of sarcoid granulomas. Gallium-67 scintigraphy well correlates with a better response to corticosteroid treatment [20,21]. Combined use of both 99-mTc sestamibi and gallium-67 increases the diagnostic feasibility for CS. However, the results of radionuclide scintigraphy should be interpreted with caution considering the lack of specificity of these tests [11,22].

New cardiac molecular imaging modalities, such as (18) F-fluoro-2- deoxyglucose positron emission tomography (18F-FDG PET), have made important contribution to the diagnosis of CS [23]. In a meta analysis Youssef et al. have evaluated the accuracy of 18F-FDG PET for diagnosis of CS. The authors reported estimated an overall sensitivity and specificity of 89% and 78% respectively [24]. An increased focal or diffuse pattern in FDG uptake in the myocardium reflects metabolic activity in the heart, related to sarcoid granulomas and inflammation. 18F-FDG PET is useful not only for early detection of sarcoidosis, but also serves for assessment of therapeutic efficacy in sarcoid patients with cardiac involvement [25,26].

Cardiac magnetic resonance imaging is a sensitive non-invasive diagnostic modality and it is considered to be the technique of choice for evaluation and diagnosis of CS [27]. Moreover, this method provides not only high resolution, but also three dimensional images of long–axis, short-axis and four-chamber views with reproducible measurements and lacks radiation exposure. Currently, cardiac MRI is of increasing use for assessment and quantification of myocardial stroke, ventricular volume and myocardial mass [28]. From MRI point of view, the CS findings may be divided into three stages i. e edema, granulomatous infiltration and scaring. At the early stage MRI reveals focal zones with increased signal intensity on T-2 weighted images and an early contrast enhancement within the myocardium due to inflammation associated edema [29]. Granulomatious in-

filtration appears as areas of high signal intensity at T-1 and T-2 weighted sequences with delayed contrast enhancement. These lesions are observed predominantly in the vicinity of the mid-myocardium and epicardium and rarely in the endocardium with a preference to the basal and lateral parts of the left ventricle and papillary muscles [30,31]. Myocardial scarring is usually patchy and it is not limited to vascular territories [30]. Several studies point to the high diagnostic accuracy of cardiac MRI with a sensitivity and specificity of 100% and 78% respectively [32]. Ohira et al. have shown that cardiac MRI has a better specificity, but a lower sensitivity than FDG-PET [33]. The value of MRI in evaluation of the prognosis of the disease is directly dependent on the degree of myocardial involvement [6,34,35]. Since a powerful magnetic field may affect defibrillator settings, MRI is not safe for patients with pacemakers and implantable defibrillators and is not recommended in those cases [36]. Areas of active inflammation and edema are visible on T2 -weighted imaging during the acute stage of the disease, and their visualization is useful when endomyocardial biopsy is indicated [11].

Endomyocardial biopsy was first introduced in 1962. The histological findings of noncaseating granulomas are almost pathognomonic for CS. Because of the patchy nature of the disease with frequent involvement of the basal intraventricular septum and the left ventricle free wall, false negative results are common [37,38]. Endomyocardial biopsy has a diagnostic yield ranging between 20-30% [39]. According to Diagnostic Standard and Guideline for Sarcoidosis of the Japanese Society of Sarcoidosis and other Granulomatous Disorders, early endomyocardial biopsy is recommended whenever the diagnosis of CS is suspected. It should be emphasized that negative biopsy results do not exclude the diagnosis [22].

The first line of the treatment in patients with CS should be corticosteroid administration. The initiation of early steroid therapy is mandatory for prevention of malignant arrhythmias and improvement of the left ventricular function. However, steroid therapy is less effective in the later stages of the disease [28]. There is no agreement upon optimal therapeutic regimens, dosage and duration of treatment, as well as whether asymptomatic patients require therapy [40,41]. While some clinicians have advocated high doses of corticosteroids (1mg/kg/d), the study of Yazaki et al. did not show any difference between patients receiving more than 40 mg/daily of prednisone and those with low initial prednisone dose (< 30 mg) [42]. Londner et al. recommend initial treatment with 0.5 to 1 mg/kg/d prednisone for 6 to 12 weeks with a gradual tapering every 6-12 weeks [43]. The use of steroid- sparing drugs is indicated when steroids are not effective or cause serious undesirable effects. Yet, there is minimal data and lack of control trials concerning alternatives to corticosteroids. Thus, methotrexate and azathioprine are indicated in selected patients who failed, or experienced adverse effects from corticosteroids treatment. If they are ineffective, especially in patients who have progressive disease, the available therapeutic armamentarium includes cyclophosphamide, leflunomide, hydroxychloroquine and chloroquine [44-47]. Newer approaches for treatment of severe cases include administration of thalidomide as a tumor necrosis factor α (TNF-α) antagonist and monoclonal antibodies such as infliximab or adalimumab [48]. Arrhythmias, especially of ventricular origin should be promptly treated. Amiodarone is the preferred drug, although it may cause of pneumonitis or pulmonary fibrosis. Pulmonary lesions due to amiodarone are indistinguishable from pulmonary sarcoidosis on chest X-ray examination and may aggravate patients' respiratory status. Beta- blockers should be used with caution since they may increase the incidence of heart block [30]. Considering these limitations, insertion of implantable cardioverter defibrillator may become mandatory in cases of refractory ventricular tachyarrhythmias, in those with markedly reduced left ventricular ejection fraction and in those at high risk of sudden death [1]. Generally, the indications for permanent pacing are similar to those in patients with advanced atrioventricular block and other bradyarhythmias [22]. In patients with CS with severe symptomatic ventricular arrhythmias with aneurysms, surgery is occasionally required. Cardiac transplantation is rarely indicated, and is reserved for younger patients with severe and intractable heart failure, or resistant ventricular tachycardia. Recurrence of sarcoidosis in transplanted hearts has been reported as early as 24 weeks to 19 months after the procedure. In this cases administration of high doses of corticosteroids is necessary to achieve complete resolution [41,49].

4. Conclusion

Sarcoidosis is uncommon multisystem disease of unknown origin with an elusive diagnostic nature, affecting various body organs and thus contributes to protean manifestations. The possibility of CS should be considered in the differential diagnosis of unexplained cardiomyopathy or arrhythmias particularly in young adults. Early disease detection is essential given its grave prognosis. Currently, in the absence of any single test for CS identification, aggressive workup including combination of multiple diagnostic modalities and ECG, is the most accepted approach. 18F-FDG PET or CMR are valuable

tools for both initial diagnosis and follow-up. Endomyocardial biopsy should be carried out in highly suspected cases, although negative results do not deny the diagnosis. Early initiated corticosteroid treatment (with or without steroid-sparing agents) is mandatory since it improves patient' survival. Conduction abnormalities, such as complete heart block, and high risk of sudden cardiac death, especially if ventricular arrhythmias or reduced ejection fraction are present, require permanent pacemaker or internal cardiac defibrillator placement. Cardiac transplantation is rarely indicated and should be recommended to patients with refractory ventricular tachycardia or intractable heart failure.

Conflict of interests

The authors state that they have no conflict to interest.

Acknowledgments

We are grateful to Prof. M.Djaldetti for his help and editorial assistance in the preparation of the manuscript.

References

[1] Iannuzzi M.C., Rybicki B.A., Teirstein A.S. Sarcoidosis., N. Engl. J. Med., 2007, 357,2153-2165

[2] Dorfman T., Canales J., Farukhi I., McGuire D.K., Sarcoidosis masquerading as an acute coronary syndrome. Cardiol. Rev., 2005, 13, 256-259

[3] Pierre-Louis B., Prasad A., Frishman W.H., Cardiac manifestations of sarcoidosis and therapeutic options. Cardiol. Rev., 2009, 17,153-158.

[4] Sun B.J., Lee P.H., Choi H.O., Ahn J.M, Seo J.S, Kim D.H., et al., Prevalence of echocardiographic features suggesting cardiac sarcoidosis in patients with pacemaker or implantable cardiac defibrillator. Korean Circ. J., 2011, 41, 313-320

[5] Sohn I.S., Cardiac Sarcoidosis: Oldies but not goodies. Korean Circ J., 2011, 41, 296–298

[6] Patel M.R., Cawley P.J., Heitner J.F., Klem I, Parker M.A, Jaroudi W.A., et al., Detection of myocardial damage in patients with sarcoidosis. Circulation, 2009, 120, 1969–1977

[7] Nunes H., Freynet O., Naggara N., Soussan M, Weinman P, Diebold B., et al., Cardiac sarcoidosis. Semin. Respir. Crit. Care Med., 2010, 31, 428-441

[8] Hiraga H., Yuwai K., Hiroe M., Guideline for diagnosis of cardiac sarcoidosis: study report on diffuse pulmonary disease from the Japanese Ministry of Health and Welfare. 1993, 23-24

[9] Mitropoulos F.A., Floudas C.S., Kanakis M.A., Vaiopoulos G.A., Cardiac sarcoidosis. Thorac. Cardiovasc. Surg., 2009, 57,187-190

[10] Hamzeh N.Y., Wamboldt F.S., Weinberger H.D., Management of cardiac sarcoidosis in the United States: a delphi study. Chest., 2012,141,154-162

[11] Dubrey S.W., Falk R.H., Diagnosis and management of cardiac sarcoidosis. Prog. Cardiovasc. Dis., 2010, 52, 336-346

[12] Soejima K., Yada H., The work-up and management of patients with apparent or subclinical cardiac sarcoidosis: with emphasis on the associated heart rhythm abnormalities. J Cardiovasc Electrophysiol., 2009, 5,578-583

[13] Divakara Menon S.M., Chemello D., Morillo C.A., Sarcoidosis: yet another masquerader the cardiologist / electrophysiologist has to fight with. Indian Pacing Electrophysiol. J., 2010, 10, 479-485

[14] Homsi M., Alsayed L., Safadi B., Mahenthiran J., Das M.K., Fragmented QRS complexes on 12-lead ECG: a marker of cardiac sarcoidosis as detected by gadolinium cardiac magnetic resonance imaging. Ann. Noninvasive Electrocardiol., 2009,14, 319-326

[15] Suzuki T., Kanda T., Kubota S.,Imai S.,Murata K., Holter monitoring as a noninvasive indicator of cardiac involvement in sarcoidosis. Chest, 1994, 106, 1021-1024

[16] Petrović M., Vujisić-Tesić B., Boricić M., Spectrum of echocardiographic findings in patients with systemic sarcoidosis. Med. Pregl., 2005;58 Suppl 1:35-38

[17] Hyodo E., Hozumi T., Takemoto Y., Watanabe H., Muro T., Yamagishi H., et al., Early detection of cardiac involvement in patients with sarcoidosis by a non-invasive method with ultrasonic tissue characterisation. Heart, 2004, 90, 1275-1280

[18] Tellier P., Paycha F., Antony I., Nitenberg A., Valeyre D., Foult J.M., et al., Reversibility by dipyridamole of thallium 201 myocardial scan defects in patients with sarcoidosis. Am. J. Med., 1988, 85, 189-193

[19] Nery P.B., Leung E., Birnie D.H., Arrhythmias in cardiac sarcoidosis: diagnosis and treatment. Curr. Opin. Cardiol., 2012, 27,181-189

[20] Futamatsu H., Suzuki J., Adachi S., Okada H., Otomo K., Ohara T., et al., Utility of gallium-67 scintigraphy for evaluation of cardiac sarcoidosis with ventricular tachycardia. Int. J. Cardiovasc. Imaging, 2006, 22, 443-448

[21] Okayama K., Kurata C., Tawarahara K., Wakabayashi Y.,Chida K.,Sato A., Diagnostic and prognostic value of myocardial scintigraphy with thallium-201 and gallium-67 in cardiac sarcoidosis. Chest, 1995, 107, 330-334

[22] Sekhri V., Sanal S., Delorenzo L.J., Aronow W.S., Maguire G.P., Cardiac sarcoidosis: a comprehensive review. Arch. Med. Sci., 2011, 7, 546-554

[23] Ohira H., Tsujino I., Yoshinaga K., ^{18}F-Fluoro-2-deoxyglucose positron emission tomography in cardiac sarcoidosis. Eur. J. Nucl. Med. Mol. Imaging., 2011, 38, 1773-1783

[24] Youssef G., Leung E., Mylonas I., Nery P., Williams K., Wisenberg G., et al., The use of 18F-FDG PET in the diagnosis of cardiac sarcoidosis: A Systematic review and metaanalysis including the Ontario experience. J. Nucl. Med., 2012, 53, 241-248

[25] Mañá J., Gámez C., Molecular imaging in sarcoidosis. Curr. Opin. Pulm.Med., 2011,17, 325-331

[26] Sharma S., Cardiac imaging in myocardial sarcoidosis and other cardiomyopathies. Curr. Opin. Pulm. Med., 2009, 15, 507-512

[27] Tadamura E., Yamamuro M., Kubo S., Kanao S., Saga T.,Harada M., et al., Effectiveness of delayed enhanced MRI for identification of cardiac sarcoidosis: comparison with radionuclide imaging. A.J.R. Am. J. Roentgenol., 2005, 185, 110-115

[28] Penugonda N., Cardiac MRI in infiltrative disorders: a concise review. Curr. Cardiol. Rev., 2010, 6, 134-136

[29] Vignaux O., Cardiac sarcoidosis: spectrum of MRI features. A.J.R. Am. J. Roentgenol., 2005,184, 249-254

[30] Doughan A.R., Williams B.R., Cardiac sarcoidosis. Heart, 2006, 92, 282-288

[31] Smedema J.P., Truter R., de Klerk P.A., Zaaiman L., White L., Doubell A.F., Cardiac sarcoidosis evaluated with gadolinium-enhanced magnetic resonance and contrast-enhanced 64-slice computed tomography. Int. J. Cardiol., 2006, 112:261-263

[32] Smedema J.P., Snoep G., Marinus P.G., van Kroonenburgh M.P.,van Geuns R.J., Dassen W.R.,et al., Evaluation of accuracy of gadolinium enhanced cardiovascular magnetic resonance imaging for diagnosis and evaluation of cardiac function in patients with cardiac sarcoidosis. J. Am. Coll. Cardiol. 2005, 45, 1683-1690

[33] Ohira H., Tsujino I., Ishimaru S., Oyama N., Takei T., Tsukamoto E., et al., Myocardial imaging with 18F-Fluoro-2-deoxyglucose positron emission tomography and magnetic resonance imaging in sarcoidosis. Eur. J. Nucl. Med. Mol. Imaging, 2008, 35, 933-941

[34] Ichinose A., Otani H., Oikawa M., Takase K., Saito H., Shimokawa H., et al., MRI of cardiac sarcoidosis: basal and subepicardial localization of myocardial lesions and their effect on left ventricular function. A.J.R. Am. J. Roentgenol, 2008, 191, 862-869

[35] Matoh F., Satoh H., Shiraki K., Odagiri K., Saitoh T., Urushida T., et al., The usefulness of delayed enhancement magnetic resonance imaging for diagnosis and evaluation of cardiac function in patients with cardiac sarcoidosis. J. Cardiol., 2008, 51, 179-188

[36] Stone M.E., Salter B., Fischer A., Perioperative management of patients with cardiac implantable electronic devices.Br J Anaesth. 2011, 107, Suppl 1:i16-26.

[37] Uemura A., Morimoto S., Hiramitsu S., Kato Y., Ito T., Hishida H., Histologic diagnostic rate of cardiac sarcoidosis: evaluation of endomyocardial biopsies. Am Heart J. 1999,138, 299-302

[38] Schulte W., Kirsten D., Drent M., Costabel U., Cardiac involvement in sarcoidosis. Eur. Respir. J. Monogr., 2005, 10,130-139

[39] Sekiguchi M., Yazaki Y., Isobe M., Hiroe M., Cardiac sarcoidosis: diagnostic, prognostic, and therapeutic considerations. Cardiovasc. Drugs Ther., 1996, 10, 495-510

[40] Kim J.S, Judson M.A, Donnino R., Gold M., Cooper L.T Jr, Prystowsky E.N., et al. Cardiac sarcoidosis. Am. Heart J., 2009, 157, 9-21

[41] Schutt A.C., Bullington W.M., Judson M.A., Pharmacotherapy for pulmonary sarcoidosis: a Delphi consensus study. Respir Med. 2010, 104,717-723

[42] Yazaki Y., Isobe M., Hiroe M., Morimoto S., Hiramitsu S., Nakano T., et al., Prognostic determinants of long-term survival in Japanese patients with cardiac sarcoidosis treated with prednisone. Am. J. Cardiol., 2001, 88, 1006-1010

[43] Londner C., Zendah I., Freynet O., Carton Z., Dion G., Nunes H., et al., Treatment of sarcoidosis. Rev. Med. Interne, 2011, 32,109-113

[44] Chapelon-Abric C., de Zuttere D., Duhaut P., Veyssier P., Wechsler B., Huong DL., et al., Cardiac sarcoidosis: a retrospective study of 41 cases. Medicine (Baltimore), 2004, 83, 315-334

[45] Roberts S.D.,Wilkes D.S., Burgett R.A., Knox K.S., Refractory sarcoidosis responding to infliximab. Chest, 2003, 124, 2028-2031
[46] Deng J.C., Baughman R.P., Lynch J.P. III., Cardiac involvement in sarcoidosis. Semin. Respir. Crit. Care Med., 2002, 23, 513-527
[47] Baughman R.P., Costabel U., du Bois R.M., Treatment of sarcoidosis. Clin. Chest Med., 2008, 29, 533-548
[48] Baughman R.P, Lower E.E, Drent M., Inhibitors of tumor necrosis factor (TNF) in sarcoidosis: who, what, and how to use them. Sarcoidosis Vasc. Diffuse Lung Dis., 2008, 2, 76-89
[49] Greif M., Petrakopoulou P., Weiss M., Reithmann C., Reichart B., Nabauer M., et al., Cardiac sarcoidosis concealed by arrhythmogenic right ventricular dysplasia/cardiomyopathy. Nat. Clin. Pract. Cardiovasc. Med., 2008, 5, 231-236