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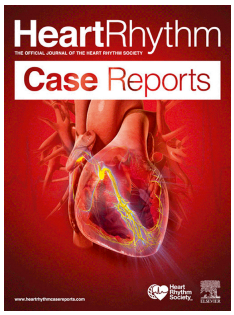

Syncope on exertion in a young male

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Syncope on exertion in a young male

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Introduction

Cardiac sarcoidosis is a rare immunological disease causing heart involvement in 5% of the patients [1]. Cardiac sarcoidosis may manifest clinically as a cardiomyopathy with impaired left ventricular function or tachy- or bradyarrhythmias [2]. On autopsy, cardiac granulomas can be found in approximately 25% of patients. The most common location for granulomas and scars is the left ventricular free wall, followed by the intraventricular septum, often with involvement of the conduction system [3, 4].

Case report

We report the case of a 34-year-old-man presenting with a history of recurrent syncope on exertion. At rest, 12-lead ECG showed first-degree AV-block with undisturbed intraventricular conduction (fig. 1A). On exercise treadmill testing (fig.1 B), second-degree AV-block with two-to-one AV-conduction occurred with increasing workload at 100W suggesting infra-hissian block (fig. 1C). Long-term ECG monitoring one day later demonstrated intermittent third-degree AV-block (fig. 1D). Echocardiography showed both mildly impaired RV and LV function (RVEF=47%, LVEF=54%) but normal diameters and mild tricuspid regurgitation. As the etiology of the underlying heart disease remained unclear, cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) was performed (fig. 2).

Cardiac MR imaging revealed moderately reduced left ventricular (LV) global systolic function (LVEF=45%) with sharply demarcated intramyocardial enhancement within the mid-anterior septal segment, corresponding to the region of the bundle of His (fig. 2A). In addition, remote native T1 and T2 mapping values were elevated, consistent with the presence of myocardial inflammation. Together with bihilar lymphadenopathy

on CMR, the findings were highly suggestive of cardiac involvement in a patient with systemic sarcoidosis. Subsequent bronchoalveolar lavage revealed an increased CD4/CD8 lymphocytes ratio, and lung and paratracheal lymphnode biopsy provided the histological proof of non-caseating granuloma. Subsequently, a two-chamber pacemaker was implanted and the patient started on high dose steroid therapy (1mg per kg bodyweight per day) [5]. Two months after therapy initiation, pacemaker interrogation showed predominantly physiological AV conduction with only occasional need for ventricular pacing. On repeated cardiac MRI, myocardial native T1 and T2 were almost normalized with less late gadolinium enhanced myocardium (figure 2B).

Discussion

Progressive AV-nodal conduction disturbances are a hallmark of cardiac sarcoidosis [1, 2]. The present case illustrates the importance of a multidisciplinary approach to establishing the diagnosis of this disease entity. Collaboration between electrophysiologists, MRI specialists and pulmonologists enables a timely diagnosis and appropriate therapy.

Diagnosis. Cardiac sarcoidosis should be suspected in young and middle-aged patients (<50 years) presenting with unexplained syncope in the setting of AV-conduction abnormalities and/or ventricular arrhythmias with or without heart failure [1-2, 5]. All patients with extra-cardiac sarcoidosis are recommended to be actively screened for cardiac involvement by electrocardiography and echocardiography [1, 5]. Although there are no pathognomonic diagnostic criteria to date; abnormal thinning or thickening of the septal wall, wall motion abnormalities not corresponding to a coronary region and systolic or diastolic dysfunction as well as pericardial effusion might be present in cardiac sarcoidosis [1, 2]. If either a patient´s history or

electrocardiography or echocardiography is positive for cardiac sarcoidosis, further diagnostic testing with cardiac MR imaging is recommended due to a HRS consensus statement of 2014 [5]. Apart from myocardial thickening and/or wall motion abnormalities, enhanced T1 and T2 signal as markers for inflammation and edema [4] can be found in the setting of sarcoidosis, especially in an early, clinically silent stage. Furthermore, late gadolinium enhancement might visualize granuloma or scarring, often found in a patchy distribution [4]. Compared to FDG-PET, cardiac MRI was considered to be of better specificity but worse sensitivity. Newer observational studies found that an optimal MRI technique adjudged by an expert cardiologist and radiologist can yield a sensitivity of 100% to diagnose cardiac sarcoidosis [1]. Endomyocardial biopsy can confirm cardiac involvement in systemic sarcoidosis, but due to the disseminated granulomatous infiltration, only 25% of cardiac biopsies in patients with cardiac sarcoidosis are positive [3]. That is why extra-cardiac biopsies e. g. from pulmonary lymph nodes or lung tissue are preferred in patients with systemic sarcoidosis. If only a cardiac manifestation is suspected, an image guided endomyocardial biopsy (e.g. with CMR or 3D voltage map) is recommended by current consensus statements [5]. To establish the risk of sudden cardiac death, an electrophysiological study can be performed as a IIb class recommendation in patients with LVEF > 35%, despite optimal medical therapy and a period of immunosuppression if there is still evidence of active inflammation [5]. A small prospective study of 75 patients with cardiac sarcoidosis undergoing extensive programmed ventricular stimulation (PES) demonstrated, that event-free survival in patients with inducible ventricular arrhythmia on PES is significantly lower.

Treatment. Due to the scarcity of data, it is still unknown whether only patients with myocardial inflammation and signs of active sarcoidosis or all patients with

sarcoidosis, even in clinically silent stages, should be treated. There are no randomized, prospective data on treatment with corticosteroids. A recently initiated randomized-controlled trial, the CASTOR study, had to be closed due to a lack of funding. Small cohort studies report improvement in AV-conduction as well as in left ventricular function in patients with initially severely depressed LVEF (< 35%), but no regeneration in patients with moderately impaired LVEF under immunosuppressive therapy with corticosteroids [1-2]. The current expert consensus paper recommends immunosuppression as a class IIa recommendation in patients with AV-block typ II (Mobitz) or higher as well as ventricular ectopy or (non-) sustained ventricular arrhythmia and/or evidence of active myocardial inflammation [5]. Initially, a daily dose of 30-40 mg is recommended, requiring close monitoring. Treatment response should be evaluated after 1-3 months and steroid dose be tapered to 5-15mg daily for 9-12 months [1]. In cases of relapses, methotrexate has been successfully used to skimp steroid doses [1]. In patients with depressed LV function, initiation of heart failure therapy including ACE-inhibitors, ARBs or aldosterone antagonists might be useful. An ICD implantation is recommended as a class I indication for patients with cardiac sarcoidosis and either documented sustained ventricular arrhythmias, a history of survived cardiac arrest or LVEF < 35% [5]. An ICD can be useful (class IIa recommendation) in patients with unexplained syncope, indication for permanent pacing or positive electrophysiological study [5]. In patients with moderately impaired LV-function (36-49%) or impaired RV-function (< 40%) an ICD may be considered (class II b recommendation), if signs of active myocardial inflammation persist despite immunosuppression and optimal heart failure therapy [5]. In the latter group, a temporary protection with the wearable cardioverter-defibrillator (WCD) might be indicated during risk stratification.

Prognosis. Cardiac sarcoidosis is generally associated with a less favorable outcome in patients with systemic sarcoidosis [1-5]. Nonetheless, a recent Finnish study demonstrated a 10-year survival of 92.5% in patients with cardiac sarcoidosis due to modern heart failure therapy including active transplant surgery [1]. The magnitude of LV dysfunction is considered to be a strong prognostic marker [1, 2, 4]. With rising CMR technology and research, the extent of myocardial LGE might be a more important prognostic factor compared to LV-function [1]. Native T1- and T2-values proved to be excellent screening markers in patients with systemic sarcoidosis and silent cardiac involvement [4].

Conclusions

Although cardiac sarcoidosis is a rare disease, young people with a history of syncope and complete heart block should be actively screened to initiate early treatment. Cardiac MRI seems to be a suitable, non-invasive diagnostic tool to monitor myocardial involvement.

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Figure legend

Figure 1

ECG at 25mm/s paper speed at rest (panel A), at exercise 50 W (panel B), at exercise 100 W (panel C) and during Holter monitoring (panel D).

Figure 2

Cardiac MR on initial presentation (panel A) and during follow-up (panel B).

Yellow arrows showing late gadolinium enhancement, red arrows showing pacemaker induced artefacts.

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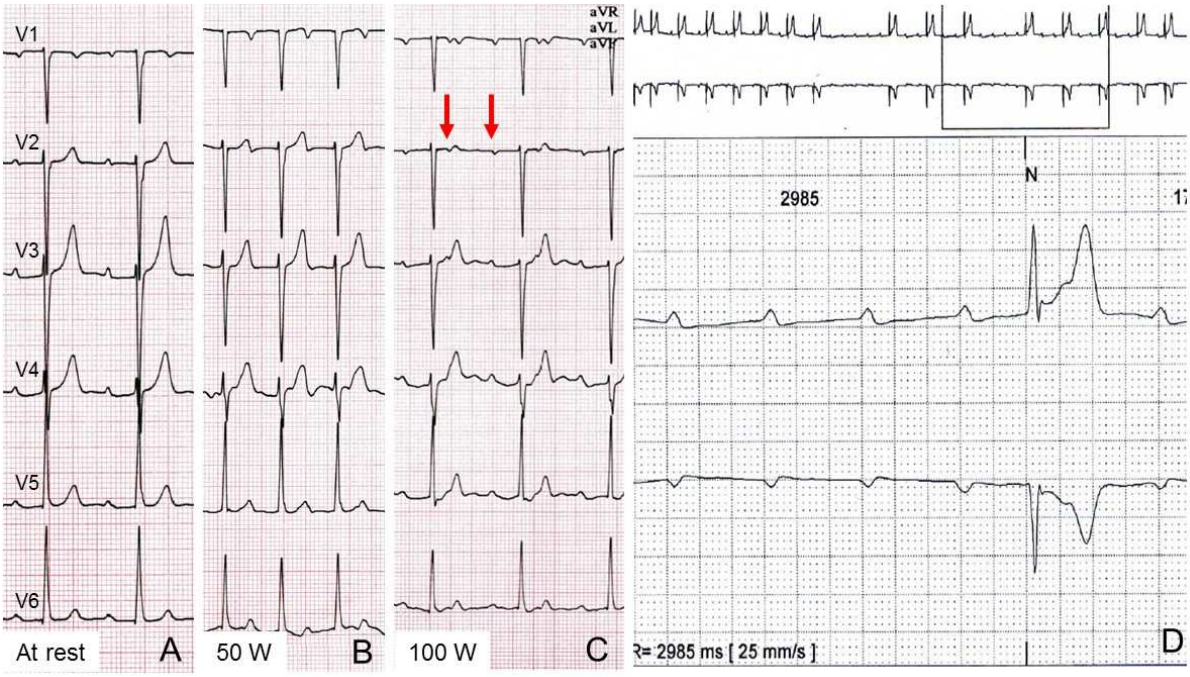

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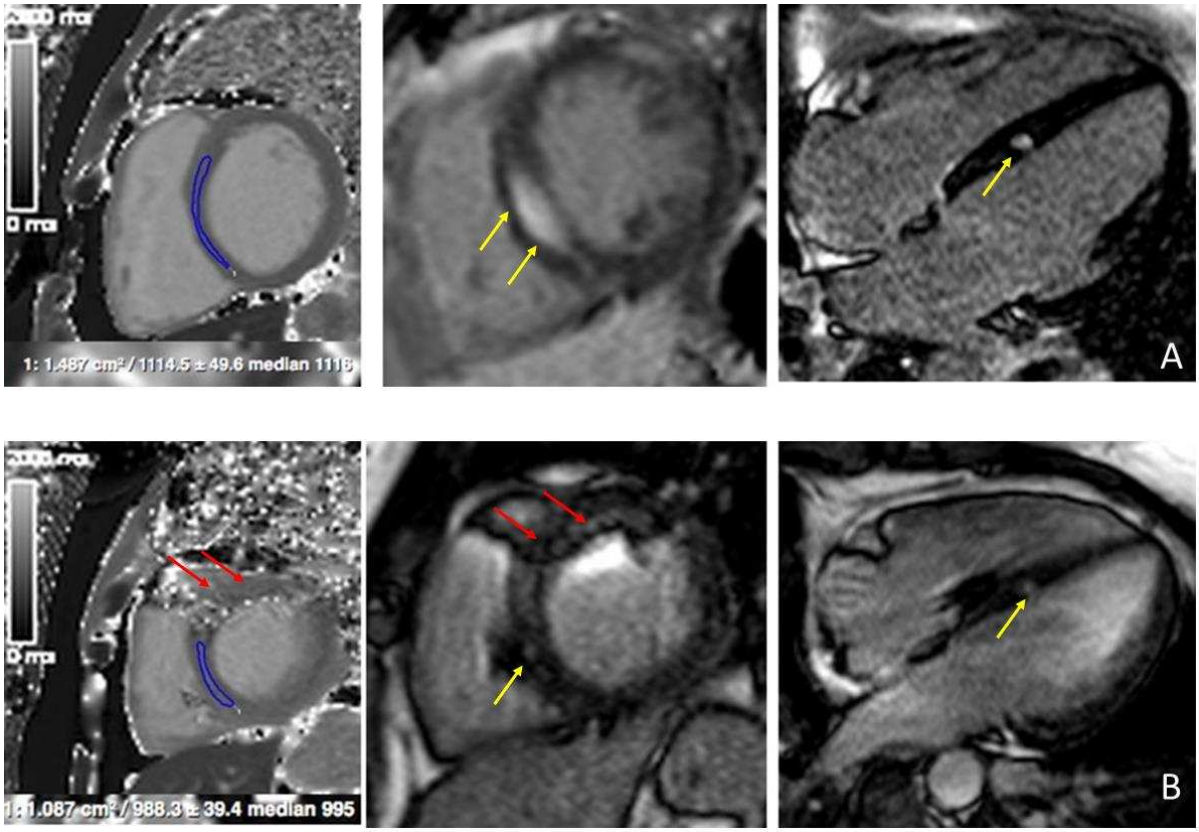

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Key Teaching Points

- Young patients with syncope, especially on exertion, should undergo provocative exercise testing
- Inflammatory cardiac disease might be the cause for transient complete heart block
- Cardiac magnetic resonance imaging is a suitable tool to monitor myocardial involvement on first presentation and during follow-up

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