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Sarcoidosis of the cardio–pulmonary systems

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ABSTRACT

Sarcoidosis is a multi-system disease with a wide range of phenotypes. Pulmonary involvement is the most frequently identified target for sarcoidosis and is responsible for the majority of deaths. Cardiac sarcoid is less commonly identified, may be occult, is significantly influenced by race, and can portend an unpredictable and sometimes fatal outcome. Sarcoidosis remains an enigmatic disease spectrum of unknown aetiology, frequently difficult to diagnose and with a variable disease course. This article summarises current views on the diagnosis and management of cardiopulmonary involvement.

KEYWORDS: Sarcoidosis, heart, lung

Introduction

Sarcoidosis is an inflammatory disease that most frequently targets the lungs and thoracic lymph nodes with a variety of presentations. While pulmonary involvement may be asymptomatic, it accounts for most deaths in patients diagnosed with sarcoidosis. Cardiac involvement is less common and may also be asymptomatic, but it can present with complete heart block, heart failure or sudden death. Furthermore, cardiac sarcoidosis can be difficult to diagnose, especially when occult or the sole site of involvement. There remains no unified theory on the aetiology of sarcoidosis and no reliable biomarker to identify its presence. Management is based on several guidelines but there remain large differences in opinion and the historical use of steroids remains the dominant choice. Sarcoidosis continues to fascinate with variable presentation that is influenced by occupation, gender and ethnicity, in addition to seasonal, familial and environmental clustering. This review focuses on thoracic organ involvement with an emphasis on developments in imaging and therapy.

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Pathophysiology

Sarcoidosis is a heterogeneous chronic inflammatory disorder, characterised by the presence of non-caseating granulomas. The inflammatory response is associated with the accumulation of $CD4^+$ T-lymphocytes at the active sites. In a minority of patients a chronic phase with fibrosis and organ damage ensues. Around 85% of patients will undergo spontaneous remission within two years of diagnosis.[1] Failure to regress within this period indicates the likelihood of a chronic course.[1]

It seems likely that genetically predisposed individuals develop a specific phenotype of the condition when exposed to one or more triggering antigens. A genetic component to susceptibility is supported by familial and racial clustering and disease concordance within monozygotic twins. The $CD4^+$ T-cell immune-mediated response in sarcoidosis has been linked to human leucocyte antigen (HLA) genes on the short arm of chromosome 6, with recognised effects on both susceptibility and the severity of disease.[2]

Within these HLA class II associations, a risk of chronic and severe pulmonary sarcoid is associated with alleles DRB1*12, DRB1*14 and DRB11*1501, while DRB1*0101 and DQB1*0501 appear protective against a mainly lung phenotype.[3,4] Cardiac involvement is most likely associated with the DQB1*0601 and DRB1*0803 alleles. A gene–environment interaction is indicated for HLA DRB1*1101 and occupational insecticide exposure for cardiac sarcoidosis. The same allele and exposure to molds and musty odours has been associated with isolated pulmonary sarcoidosis.[5]

Epidemiology

Sarcoidosis involves the lungs in more than 90–95% of patients,[6,7] while cardiac involvement is less common at 5% of cases.[6,8] Isolated extra-thoracic sarcoidosis is unusual at around 2% of cases. The pattern of organ system involvement is dependent on racial origin, and is influenced by referral bias and screening facilities. Scandinavians (typically Swedes and Danes) and African Americans are among those with the highest prevalence of disease.[3] However, the prevalence of cardiac involvement in Swedish patients with pulmonary involvement is considerably lower at 3.2%,[9] than the 21–58% quoted for Japanese patients,[10] who appear to have the highest prevalence of heart involvement. Post-mortem studies in both the UK and the USA suggest a higher prevalence of cardiac involvement at 19.5–28.0%, which is also the case in Japan at between 50–78%. In most studies, women have a higher

prevalence than men,[3] with an estimated lifetime likelihood of 1.3% and 1% respectively.[7] This gender discrepancy and an apparent reduced risk of sarcoidosis with cigarette smoking are unexplained. There are many reports of disease clustering within families, occupations and locations.[3,8,11]

Clinical features of individual organ involvement

Lungs

Patients with pulmonary involvement are often asymptomatic with lung or mediastinal node involvement identified on an incidental chest radiograph. Shortness of breath and a dry cough are the commonest respiratory symptoms, variably associated with malaise, fever, arthralgia and non-specific chest discomfort. Haemoptysis and clubbing are rare, with crackles on auscultation heard in less than 20% of cases.[6] Significant long-term disability, arising from irreversible pulmonary fibrosis and resulting in respiratory insufficiency, occurs in 3–20% of patients. Less commonly the airways, including the larynx, trachea and bronchi may be involved, with bronchiectasis an uncommon but well-recognised consequence. The development of pulmonary hypertension is multifactorial, with contributions from interstitial lung disease, granulomatous vasculitis, pulmonary venous stenosis, and both right and left heart involvement.[11]

Heart

Similar to pulmonary involvement, cardiac disease may be asymptomatic or can present with palpitations, presyncope or syncope, or symptoms of cardiac failure. Chronic heart failure occurs in around 30% of chronic cases.[12] Sarcoid granulomas show a predilection for the basal interventricular septum and inferolateral free wall of the left ventricle. The most common cardiac presentation results from infiltration of the conduction system with around a third of patients presenting with atrioventricular block. In the early inflammatory phase of the disease, there is myocardial oedema which can result in conduction abnormalities. Later in the disease, granulomatous development and fibrosis can lead to myocardial thinning, aneurysm formation and ventricular arrhythmias.

Diagnosis

Without a specific disease biomarker, sarcoidosis can prove difficult to diagnose. Serum levels of angiotensin-converting enzyme (SACE), derived from epitheliod cells of the granulomata and activated macrophages, are frequently elevated during active disease. However, SACE levels are non-specific, being elevated in other granulomatous diseases. Although unhelpful diagnostically, changes in SACE titres may still be used to follow treatment response. An excess of immunoglobulin (hypergammaglobulinaemia) may occur due to a B-cell 'proliferation' and routine bloods may indicate elevated inflammatory markers, along with hypercalcaemia and hypercalciurea. None of these tests are in themselves diagnostic. The Kveim test, a measure of response to injected human sarcoid 'reagent', is no longer used in the UK, due to concerns relating to the potential to transmit infection.

Algorithms for the diagnosis of cardiac or pulmonary sarcoidosis require using a combination of disease exclusion, histology and International guidelines (Fig 1). Non-caseating granulomas in sarcoidosis have recently been demonstrated to contain abundant serum amyloid-A (SAA), which may disrupt the clearance of an antigen within granulomata. Levels of SAA have been found to correlate with disease activity in patients with pulmonary involvement and may represent a potential biomarker for the disease.[13]

Pulmonary involvement

Pulmonary sarcoid is often first suspected from a chest radiograph showing bilateral hilar lymphadenopathy with or without lung parenchymal involvement. Chest radiograph appearances are grouped into five stages (Table 1), although these findings are now best demonstrated on high-resolution computerised tomography (CT) scans, which form the reference standard in clinical practice. Spontaneous resolution occurs in 55–90% with stage I disease, 40-70% with stage II and 10-20% with stage III.[14] Several advanced imaging modalites, including CT, magnetic resonance imaging (MRI), nuclear isotope perfusion imaging and positron emission tomography (PET), are available. Their combined use, supported by international recommendations,[15] can be used to identify and follow the disease course (Table 2).

Historically, a formal diagnosis was considered to require histological evidence of non-caseating granulomas and the exclusion of likely alternative diagnoses; typically tuberculosis, lymphoma, malignancy and fungal infections.[15] When biopsy is required, mediastinal lymph nodes may be sampled by transbronchial needle aspiration, by mediastinoscopy or more recently using endobronchial ultrasound-guided biopsy. Alternatively, endobronchial or transbronchial lung biopsies may be diagnostic. Gallium-67 scanning, used historically by some clinicians to identify an optimal biopsy site, has largely been supplanted by PET scans which detect areas of active disease, but does not possess the specificity to diagnose pulmonary sarcoidosis. In atypical pulmonary sarcoidosis, video-assisted thorascopic lung biopsy and open lung biopsy are occasionally required. When bronchoscopy is performed, endobronchial and transbronchial lung biopsies should both be performed as

Table 1. Chest radiographic staging of pulmonary and thoracic lymphoid involvement.

Stage	Observation
0	Normal chest radiograph
I	Bilateral hilar lymphadenopathy ± paratracheal lymphadenopathy. Despite no evidence of parenchymal infiltration, granulomas may be seen on lung biopsy
II	Bilateral hilar lymphadenopathy plus lung parenchymal infiltration
III	Pulmonary infiltration without hilar lymphadenopathy
IV	Pulmonary fibrosis, with evidence of honey-combing, hilar retraction, bullae, cysts and emphysema

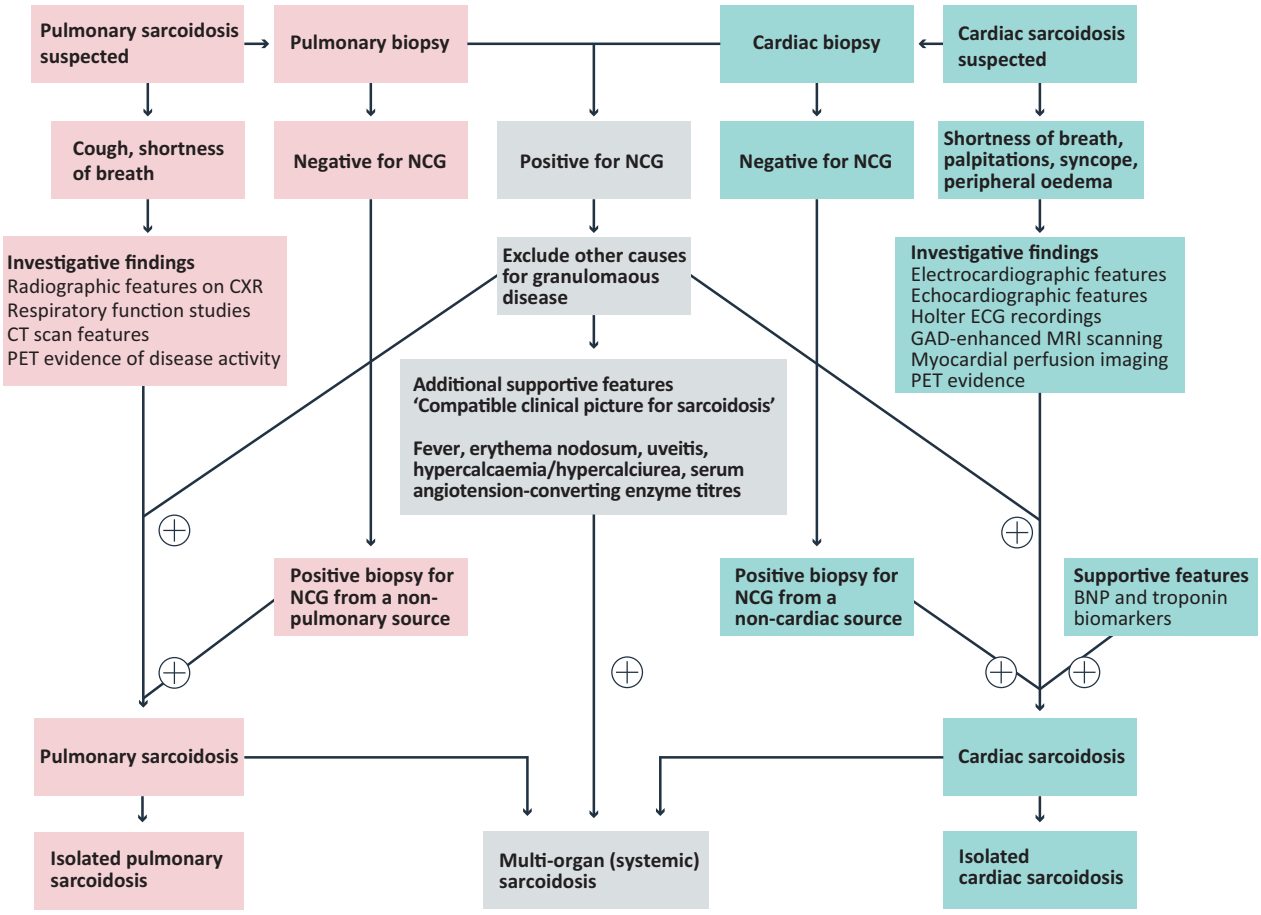

Fig 1. Algorithm for the diagnosis of cardio-pulmonary sarcoidosis. BNP = brain natriuretic peptide; CT = computerised tomography; CXR = chest X-ray; ECG = electrocardiogram; GAD = gadolinium; MRI = magnetic resonance imaging; NCG = non-caseating granuloma; PET = positron emission tomography.

the combined diagnostic yield is 80–90%. Bronchoalveolar lavage should also be performed as a lymphocytosis may provide important diagnostic support, as well as evidence for active disease.

However, the historical view that a biopsy is required, except in relatively uncommon cases with classical acute sarcoidosis (Lofgren's syndrome), is increasingly questioned. In many cases, demographic, clinical and imaging features (especially high-resolution CT findings) together present a classical picture of sarcoidosis, and the likelihood that the diagnosis will change with the performance of biopsy is exceedingly low. There is growing consensus that in this context, the decision on whether to proceed to biopsy should be influenced by the wishes of the patient. If biopsy is not performed, careful follow-up is essential to ensure that ongoing disease behavior is typical of sarcoidosis in the next 6–12 months. The presence of typical systemic features, including arthralgia (most commonly involving the ankles), erythema nodosum and/or uveitis, increases the threshold for strongly recommending a semi-invasive biopsy procedure. In impending European Respiratory Society/World Association of Sarcoidosis and other Granulomatous disease (WASOG) guidelines, it is likely that the approach summarised above will be integrated into diagnostic recommendations. However, it should be stressed that a less invasive approach than recommended historically required clinician expertise at a level available at sarcoidosis centres.

Cardiac involvement

An endomyocardial biopsy, demonstrating non-caseating granuloma in the absence of alternative diagnoses, confirms cardiac sarcoidosis. In practice, a positive extra-cardiac biopsy and supportive evidence from cardiac imaging (usually cardiac MRI, with or without FDG-PET scans) will usually suffice.[15] Several advanced imaging modalities, including CT, MRI, nuclear isotope perfusion imaging and PET are available. Their use, supported by international recommendations,[15] can be combined to identify and provide invaluable prognostic information (Table 2). Making a histological diagnosis of heart involvement is complicated by the patchy distribution of myocardial infiltration, particularly early in the disease. Furthermore, endomyocardial biopsies involve the right ventricular free wall and apex of the interventricular septum, whereas granulomas are most frequently located in the left ventricular free wall and base of the septum. It follows that a negative cardiac biopsy does not exclude the diagnosis and some centres do not support cardiac biopsies.[30]

Table 2. Advanced imaging modalities: advantages and disadvantages in their use with cardiopulmonary sarcoidosis.

Uses and advantages	Disadvantages
CT > Standard for identification of lung parenchymal disease, mediastinal, hilar and paratracheal lymphadenopathy and can help identify high-yield sites for biopsy. > LGE with ECG-gated CT may be of benefit in patients with suspected heart involvement and implanted devices (unable to undergo MRI).[16] > CT plays a key role in a condition where sarcoidosis may mimic other diseases.[17] Also of use with atypical chest radiograph appearances and in identifying complications of mycetoma and pulmonary hypertension.	LGE for characterisation of myocardial involvement less optimal compared to MRI. High radiation dose.
MRI > Enables characterisation of myocardium and identifies wall thinning and motion abnormalities.[18] > Identifies supportive evidence of lymphadenopathy. > LGE identifies areas of inflammation and/or fibrosis and potentially smaller areas than seen on nuclear perfusion studies.[19] > Demonstation of LGE may have a significantly adverse prognostic implication.[20,21]	Prohibited in patients with implanted devices unless certified 'MRI conditioned'. Sub-optimal for pulmonary assessment.
Nuclear isotope perfusion imaging > SPECT using gallium-67 or thallium-201. Gallium-67 is highly specific for lung, lymph node and cardiac sarcoidosis and may be used to monitor response to therapy.[22] > Positron-emitting radiopharmaceuticals include those labelled with fluorine-18 or gallium-68. > All of the above can be combined with X-ray CT for more precise anatomical definition. > Myocardial perfusion scintigraphy with thallium-201, technetium-99 or rubidium-82 may be used to identify scarring and particularly useful when combined with evidence of inflammation.[23]	Gallium-67 has a low sensitivity and a high radiation burden.
PET > Fluorine-18 labelled FDG uptake has a high sensitivity and specificity for detection of inflammatory damage from myocardial sarcoidosis.[24] > Quantification of FDG activity improves diagnostic accuracy,[25] allows assessment of disease progression[26,27] and prognosis.[28]	

CT = computerised tomography; ECG = electrocardiogram; FDG = 2-fluorodeoxyglucose; LGE = late gadolinium enhancement; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = Single photon emission tomography.

Electrocardiographic features are non-specific but include bundle branch block, ventricular ectopy, second- and third-degree AV block and less commonly a pseudo-infarction pattern, prolonged QT-interval, sinus node dysfunction and prominent U-waves. Electrocardiograms (ECGs) are a simple and rapid tool to help in screening for cardiac involvement.[31] Many clinicians use Holter ECG recordings to detect and monitor cardiac sarcoidosis. A 2014 consensus statement indicated that 71% of experts would select Holter monitoring in screening for cardiac involvement.[32] Implantable loop recorders, particularly the latest generation devices, which are injectable and allow remote monitoring, can aid in the detection of arrhythmias.

Echocardiographic appearances are variable with features of cardiac sarcoidosis, including interventricular thinning, regional wall motion abnormalities, aneurysmal distortion, left ventricular dilatation and/or global dysfunction. Thickening of the interventricular septum is less common, suggesting an early pre-fibrotic stage, associated with inflammation, oedema and granuloma formation. Increased myocardial echogenicity is also less common and consistent with infiltration.

Diastolic dysfunction is seen with initial interstitial inflammation, when systolic function may still be normal. Subsequent injury and fibrosis can then progress to systolic abnormalities. Since features may mimic ischaemic heart disease and usually occur in a young adult population, coronary angiography should always be considered. Around half of experts (52%) would use ECGs to screen, and over 87% as part of any work-up in assessing suspected heart involvement.[31]

Management

As a significant proportion of patients will be asymptomatic with either pulmonary or cardiac sarcoidosis, a general rule is to institute therapy when organ function is threatened.[33] When asymptomatic, a clinician must decide whether treatment (ie long-term steroid therapy or immunosuppressives) would cause more harm than the disease process itself. This is a complex decision when there is a possibility of an unpredictable sudden cardiac death on the background of a disease with a high chance of spontaneous remission.[1,34] Patients who remain untreated will need a careful monitoring regime to check for progression of symptoms or organ dysfunction. Corticosteroids remain the first line of therapy for sarcoidosis (Table 3),[35] although it should be emphasised that they, along

Table 3. Summary of the initial and long-term management of pulmonary and cardiac sarcoidosis.

Organ	Clinical features	Initial therapy	Chronic therapy
Lungs	CXR stage I and asymptomatic	Observation	Observation
	Cough, wheezing	Inhaled corticosteroids	
	CXR stage II–IV; dyspnoea with FEV1 or FVC <70%	Prednisolone at 20–40 mg/day for 1–3 months.	Tapering of dose to 5–10 mg/day after initial 1–3 months. Treatment continues for 9–12 months before reassessment (and possible discontinuation) Steroid-sparing therapies: > Methotrexate 5–25 mg/week, with folic acid > Azathioprine 50–200 mg/day > Leflunomide 10– 20 mg/day Lung transplantation
	Refractory pulmonary sarcoidosis	Infliximab 3–5mg/kg as a stat intravenous dose.	Infliximab 3–5mg/kg intravenously at 2 weeks, then monthly Lung transplantation Rituximab has also shown potential
Heart	Asymptomatic with preserved LV systolic function	Disease monitoring	Disease monitoring: implantable loop recorders, regular echocardiography, baseline cardiac MRI
	Complete heart block	Prednisolone Conventional pacemaker/ICD	Conventional pacemaker/ICD
	Ventricular fibrillation, tachyarrhythmias	Beta-blocker therapy (caution if no device) Intravenous methylprednisolone for resistant ventricular arrhythmias. ICD	Amiodarone, sotalol ICD
	Reduced left ventricular ejection fraction (<35%)	Prednisolone ACE inhibitors, AII-blockers, mineralocorticoid receptor antagonists, beta-blockers	Prednisolone with steroid-sparing therapies: > methotrexate > cyclophosphamide > azathioprine > hydroxychloroquine Conventional heart failure pharmacotherapy (ACE inhibitors, AII-blockers, mineralocorticoid receptor antagonists, diuretics, beta blockers) CRT-D
	Refractory cardiac sarcoidosis	Infliximab, (contraindicated in NYHA class III–IV heart failure)	Infliximab 3–5mg/kg intravenously at 2 weeks, then monthly.

ACE = angiotensin-converting enzyme; AII = angiotensin II receptor; CRT-D = cardiac resynchronisation therapy defibrillator; CXR = chest X-ray; EP = electrophysiology; FEV1 = forced expiratory volume in 1 sec; FVC1 = forced vital capacity; ICD = implantable cardiac-defibrillator; LV = left ventricular; MRI = magnetic resonance imaging; NYHA = New York Heart Association.

with all other pharmaceuticals used to treat sarcoidosis, do not have Food and Drug Administration or European regulatory authority approval. The second-line choice for both pulmonary and cardiac sarcoidosis is methotrexate.[31,35] There are no randomised controlled trials of steroid efficacy. While the WASOG consensus statement agrees with the initial use of steroids,[6,35] the long-term benefits and specifically the prevention of progression of fibrosis have not been proven.[36] This is also the opinion of the British, Australian, New Zealand and Irish Thoracic Societies.[37] Thus decisions to persist with therapy in the longer term must be individualised. Long-term treatment is more likely to be needed when disease is severe (and there is an imminent risk of disability) and also if major fibrotic diseases are associated with inflammatory flares when therapy is reduced. Average statements encompassing all sarcoidosis patients (stressing absence of evidence for prolonged treatment) do not apply when disease is overtly severe and progressive, and stabilisation is achieved with initial intervention. However, the dangers of overtreatment must be kept constantly in mind in less severe disease. Patients with sarcoidosis are frequently young and many are females of childbearing age. This demands considerable scrutiny when using immunosuppressants, biological agents and corticosteroids, sometimes over prolonged periods.[34]

Pulmonary disease

Asymptomatic pulmonary disease usually does not require treatment, as severe and dangerously progressive involvement is almost always symptomatic. Nonetheless, it is essential that a distinction is made with regard to treatment goals between dangerous disease and unacceptable loss of quality of life. Optimal treatment decisions depend on a multidisciplinary assessment of symptom burden, lung function studies and high-resolution CT imaging.[17] Treatment of pulmonary sarcoidosis has been described as 'the six phases of therapy': initial dosage, tapering of dose to maintenance levels, maintenance dose, tapering off to discontinuation, monitoring and treatment of relapses. Oral steroids form the basis of management with several alternatives used in steroid-sparing roles. Inhaled steroids have been assessed for managing pulmonary disease but a Delphi study of sarcoidosis experts concluded that this should not form part of a routine recommendation.[35] The initial treatment dose of prednisolone recommended for pulmonary sarcoid, by the WASOG consensus statement, is for 20–40 mg/day (Table 3). The authors concluded that patients with progressive symptomatic disease, or asymptomatic disease with infiltrates on chest X-ray (CXR) and worsening lung function should be treated. Almost 10 years later, the British Thoracic Society (BTS) interstitial lung disease guideline supported withholding treatment in disease stages I–III with mild lung function abnormalities. They recommend oral steroid (prednisolone) at a dose of 0.5 mg/kg/day for 4 weeks and then reduced to a maintenance dose that controls symptoms and disease progression over 6–24 months.[37] Both WASOG and BTS guidelines suggest inhaled steroid may be used for 'airways disease' or 'symptom control of troublesome cough', respectively.

Exacerbations may be managed using 20 mg prednisolone for a median period of 3 weeks. Paramothayan and Jones conducted a meta-analysis of steroid use in pulmonary sarcoidosis and concluded that oral corticosteroids do improve CXR appearances and provide a small increase in vital capacity and diffusion capacity after 6–24 months of therapy. It was not clear whether there was any benefit after 24 months.[38] A recent study compared methotrexate to azathioprine which resulted in similar reductions in steroid dose and improvement in pulmonary function testing. However patients receiving azathioprine had more drug-related adverse events and higher rates of infection.[39] Leflunomide appears promising, while several anti-tumour necrosis factor-α antagonists, including infliximab, pentoxifylline, etanercept and golimumab, have provided variable success, with infliximab emerging as the most useful. Surprisingly, as sarcoidosis is usually considered a T-lymphocyte mediated inflammatory process, the B-lymphocyte monoclonal antibody, rituximab, also appears active in the treatment of pulmonary sarcoidosis. Cyclosporin A, cyclophosphamide and mycophenolate mofetil are not currently recommended. Sarcoidosis-associated pulmonary hypertension may be treated using the oral agents sildenafil and bosentan, along with the inhaled prostacyclin iloprost.[36] Patients with end-stage fibrotic lung disease, and likely pulmonary hypertension, will require domiciliary oxygen, and palliative care may be necessary if transplantation is not an option.

Lung transplantation is an unusual outcome in sarcoidosis, representing around 3% of transplant cases in the US. However, the outcome for lung transplantation, despite frequent recurrence in the allograft, is as good or better than for transplantation for other causes. The 1, 3 and 5 year survival rates for lung transplantation in sarcoidosis, reported by the United Network for Organ Sharing (UNOS 2011) is 83, 65 and 51% respectively.[40]

Cardiac disease

In contrast to the management of asymptomatic pulmonary disease, asymptomatic cardiac sarcoidosis is a contentious issue, due to the potential for life-threatening rhythm disturbances. Some centres will assess and monitor without treatment,[41] while others mandate therapy for such cases. In patients with established cardiac involvement and organ compromise, a consensus agreement recommended that an initial dose of 30–40 mg prednisolone be used (Table 3).[31] A Japanese study concluded that long-term survival for patients with cardiac involvement was similar at 40 mg or more prednisolone compared to 30 mg or less per day,[42] prompting some clinicians to use 30 mg/day. Some groups have advocated considerably higher dosages of prednisolone (1 mg/kg/day) be used initially[12] for up to 24 months.

The immediate prescription of corticosteroids may lead to recovery of atrioventricular nodal conduction and improve survival.[42] By contrast, the effect of corticosteroids against ventricular tachyarrhythmic events is variable, depending on whether the mechanism is related to myocardial scar formation or active inflammation. Adverse effects of steroid use include fluid retention, weight gain, diabetes and hypertension, and an increased risk of implanted devices becoming infected. Additionally, long-term steroid use might contribute to the development of ventricular aneurysms.

Several steroid-sparing alternatives (chloroquine, hydroxychloroquine, cyclosporine A, azathioprine, thalidomide, leflunomide, pentoxifylline and mycophenolate mofetil) and cytotoxic therapies (methotrexate and cyclophosphamide) are available in general for sarcoidosis. The most studied is methotrexate and, although cardiac efficacy is not established, a multinational group of experts have indicated that 80% of physicians consider methotrexate a first-choice second-line treatment.[31,35] The usual dose of methotrexate is 10–25 mg once weekly with a 5 mg folic acid supplement. Of the remaining drugs, cyclophosphamide, despite significant toxicity, has shown some success in cardiac sarcoidosis.

Aside from the management of the underlying disease process, patients with cardiac involvement will require drug and device-initiated protection from deteriorating myocardial function and serious rhythm disturbances (Table 3). Amiodarone and sotalol are the most frequent choice of antiarrhythmics, although ventricular arrhythmias are frequently resistant. Potential side effects of amiodarone include pneumonitis and pulmonary fibrosis, features indistinguishable from pulmonary sarcoidosis. Caution is required with the use of beta-blockers in patients without a device in case of precipitating heart block.

The recent Heart Rhythm Society consensus statement,[32] summarises the key recommendations for pacemakers, implantable cardiac defibrillators (ICDs), and cardiac resynchronisation therapy defibrillators (CRT-Ds) for patients with cardiac sarcoidosis. This topic is beyond the scope of the current article and the reader is advised to consult the

publication for more detailed guidance. Following the HRS consensus statement, it is likely that ICD and CRT-D devices will be the preferred option compared to conventional pacemakers for cardiac sarcoidosis patients presenting with heart block.

Heart transplantation for cardiac sarcoidosis is rare, but may be considered in young refractory cases, resistant ventricular tachycardia or intractable heart failure. In the UK, very few patients have undergone heart transplantation for a primary indication of sarcoidosis. Only 4 patients, 2 described as having sarcoidosis cardiomyopathy and a further 2 with a diagnosis of sarcoidosis, are recorded by UK Transplant [personal communication]. In all cases it is unclear as to whether the diagnosis was made pre-transplant (ie endomyocardial biopsy) or subsequently on the explanted heart.

Psychosocial aspects

The psychological aspects of this potentially chronic and life-threatening disease cannot be underestimated. Treating patients with a disease that is difficult to diagnose, unpredictable in outcome and with no proven long-term therapy presents many issues for the clinician. Patient and family education, monitoring drug compliance and complications will help reduce the chance of relapses and hospital admission. As with all chronic diseases, a clear 'management plan' and an individualised 'support package' can improve overall care. Involvement in research studies and information about patient support groups is also important.

Conclusion

Sarcoidosis affecting the thoracic organs illustrates the conundrum of this disease spectrum. While in the majority of patients the disease may spontaneously resolve, in some the outcome will be life changing or fatal. With no disease biomarker, the diagnosis may rely on satisfying international definitions for organ involvement. Significant progress has been made diagnostically using advanced imaging techniques, with combinations of CT, MRI, PET and perfusion studies. Treatment is still largely dependent on corticosteroids with the occasional use, usually in combination with steroid, of a small selection of immunosuppressive agents.

Learning points

- Corticosteroids remain the first-line treatment for both pulmonary and cardiac sarcoidosis.
- The management of isolated and/or asymptomatic cardiac sarcoidosis remains contentious.
- Complex device therapy (ICD and CRT-D) may be indicated for selected cardiac sarcoidosis patents with heart failure or those with an increased risk of ventricular arrhythmias.■

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