Respiratory Medicine Case Reports 12 (2014) 41–43

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

# Two cases of culture proven *Mycobacterium tuberculosis* presenting with a broad-complex tachycardia and non-caseating granulomas

Z. Farah*, V.E. Beasley, M. Berry, R.K. Coker, O.M. Kon

*Hammersmith Hospital, Imperial College Healthcare Trust, London, UK*

*Keywords:*
Tuberculosis
Arrhythmias
Endobronchial ultrasound
Cardiology arrhythmia-therapy

A B S T R A C T

Tuberculosis is a leading cause of death worldwide. It affects pulmonary and extra-pulmonary sites with a multitude of differing presentations. In this report, we describe two cases in which TB causes myopericarditis and presents with a broad-complex tachycardia that did not respond typically to standard anti-arrhythmic therapy; a very rare presentation with limited description in the literature. Both patients required extensive investigation culminating in identifying lymph nodes amenable to biopsy under endobronchial ultrasound guidance. It was not until both patients received anti-tuberculous chemotherapy alongside anti-arrhythmic management that any improvement to their condition was witnessed. Therefore, we recommend that the clinician should have a high index of suspicion for TB in any patient presenting with a broad-complex tachycardia that is not responding to standard first line management, especially if the patient is from a high risk background. We recommend an active diagnostic pursuit, and lymph node biopsy under endobronchial ultrasound guidance.



## Case one

A previously fit and well 38 year-old gentleman, originally from India presented with palpitations and chest pain. His electrocardiogram showed ventricular tachycardia with 1 mm ST elevation in V1, V2 and aVL. The troponin-I was elevated at 0.27 ug/L. He was cardioverted with amiodarone, and then transferred for Primary Coronary Intervention, which showed normal, right dominant arteries.

An echocardiogram showed a mildly dilated left ventricle with basal anteroseptal akinesis/myocardial thinning with moderate overall systolic impairment. A cardiac magnetic resonance (CMR) scan showed pericardial enhancement and an enlarged mediastinal lymph node suggesting myopericarditis or sarcoidosis. A computed tomography (CT) scan of the thorax, abdomen and pelvis showed right apical scarring with associated pretracheal and subcarinal lymphadenopathy, raising the possibility of tuberculosis.

A cardiac biopsy was performed but the samples were inconclusive with no features of myocarditis or granulomas. Acid fast bacilli (AFB) were not cultured.

He developed a global pericardial effusion that required pericardiocentesis and drainage. The blood stained pericardial fluid showed mildly increased neutrophils, macrophages and mesothelial cells. Fluid was negative for bacteria, fungi, AFB, malignant cells and granulomata.

Prior to discharge, an implantable cardioverter-defibrillator (ICD) was inserted alongside commencing amiodarone and bisoprolol.

Outpatient investigations included reactive TB-ELISPOT tests further raising the suspicion of TB. On ultrasound he had an enlarged right cervical lymph node which was biopsied, showing necrotising granulomatous inflammation but no organisms. His pretracheal and subcarinal lymphadenopathy were sampled via endobronchial ultrasound (EBUS). A trans-bronchial biopsy showed non-necrotising granulomas with a negative TB Polymerase Chain Reaction (PCR). However after 16 days, a fully sensitive *Mycobacterium Tuberculosis* was finally cultured, providing the final diagnosis. He subsequently commenced six months of quadruple anti-tuberculous treatment. He remains under cardiology and respiratory follow-up.

## Case two

A 25 year-old Asian gentleman presented with intermittent chest pain at rest and palpitations. He was morbidly obese with well-controlled asthma, smoking two cigarettes daily. His

* Corresponding author. Tel.: +44 203 312 1344; fax: +44 203 312 1613.
*E-mail addresses:* z.farah@doctors.org.uk, helen.crawford@imperial.nhs.uk, onn.kon@imperial.nhs.uk (Z. Farah).

http://dx.doi.org/10.1016/j.rmcr.2013.10.003
2213-0071/

presenting electrocardiograph showed T-wave inversion in V2–V4 with a positive Troponin-I of 0.099 ug/L. Coronary angiography showed unobstructed coronaries. Post procedure he had short episodes of a narrow complex tachycardia, which settled with bisoprolol. An echocardiogram showed good overall systolic function. He was discharged with outpatient follow-up.

He re-presented three weeks later with progressive dyspnoea. An echocardiogram demonstrated a severe cardiomyopathy with significantly impaired left ventricular function (ejection fraction 33%) and an associated stage 1 diastolic dysfunction. Electrocardiography detected a sustained monomorphic broad complex tachycardia. Electrophysiological study was unremarkable.

An endomyocardial biopsy was performed, revealing areas of myocyte loss and destruction associated with an inflammatory cell infiltrate including giant cells, lymphocytes, histiocytes and occasional eosinophils. Granulomas were not identified. Pathology interpreted these changes as a giant cell myocarditis, for which he received a 3-day course of anti-thymocyte globulin and was commenced on oral prednisolone at a daily dose of 1 mg/kg. An ICD was also inserted.

Owing to his body habitus CMR was not possible. Thoracic and abdominal CT-scan demonstrated significant lymphadenopathy. He proceeded to positron emission topography (PET), showing PET-avid lymphadenopathy in the right paratracheal and subcarinal regions. A TB-Elispot interferon gamma-release assay was reactive. A mantoux test was similarly positive (16 mm). His LDH however, was elevated at 325 IU/L. The differential diagnosis included both lymphoma and tuberculosis.

He underwent an EBUS biopsy of his right peribronchial lymph node, showing non-necrotising granulomas and a negative TB-PCR. However after 18 days, the culture grew *M. tuberculosis*, finally confirming the diagnosis. He therefore commenced anti-tuberculosis therapy for six months, while continuing prednisolone. Following four months of steroid and TB treatment his ventricular function showed significant improvement. A repeat cardiac biopsy showed resolving inflammation with re-organisation of the myocardium, suggesting a response to the combination of TB treatment and immunosuppression. It remains unclear as to whether there was a degree of TB myocarditis underlying his initial presentation. He remains under cardiology and respiratory follow-up.

## Discussion

*M. tuberculosis* (TB) is a leading cause of death worldwide. The latest WHO report states that there were 9.4 million new cases of, and 1.7 million deaths caused by TB in 2009 [1]. The 21st century has witnessed growing challenges in the ongoing battle against TB. Human immunodeficiency virus, the increased use of immunosuppressive medications, and the emergence of multi and extremely drug resistant mycobacterium infections have created an evolving and new climate of complexity in the management of this pandemic [2]. However, what remains unchanged is the multitude of diverse TB presentations.

TB most commonly infects the pulmonary system [3]. The most frequently affected extra-pulmonary sites are the abdomen, lymph nodes and central nervous system. The cardiovascular system is only rarely involved with the pericardium being most susceptible. Myocardial, endocardial, valvular and coronary arterial involvement is extremely uncommon. Cardiac tuberculosis deserves a special mention due to its potential to cause sudden cardiac death (SCD) secondary to tachyarrhythmia [4], or the development of pericardial effusions and tamponade.

In this report, we describe TB presenting as a sustained monomorphic ventricular tachycardia (SMVT): a phenomenon that has very limited description in the literature. Liu et al. 2012 review the association between cardiac tuberculosis and SCD, emphasising that this is a diagnosis confirmed on post mortem [5]. This highlights the importance of considering tuberculosis early in a patient with a susceptible background and symptoms not responding to gold-standard management [4].

Thachill et al., 2011 describe 14 cases of SMVT with preserved ventricular function that responded poorly to radiofrequency ablation. These patients underwent CMR, PET and cardiac perfusion scans to investigate an alternative diagnosis. Significant lymphadenopathy became apparent, raising the possibility of TB or sarcoidosis. In select cases endomyocardial biopsies were performed to seek a histopathological diagnosis and tissue for TB culture [6]. The importance of searching for lymphadenopathy is highlighted in this study whereby even in those patients without cardiac inflammation on CMR, mediastinal nodes were found on PET. With our second patient, it was only upon PET scanning that we found right paratracheal and subcarinal lymphadenopathy.

Thachill et al., 2011 [6] and Koplan et al., 2006 [7] describe a VT recurrence rate of 100% in patients receiving only anti-arrhythmics and radiofrequency ablation. Recurrence was significantly reduced from *"6.5 VTs/patient-year to 0.6 VTs/patient-year"* by introducing disease-specific therapy [6]. In both our patients, treatment consisted of antiarrhythmic drugs, quadruple anti-tuberculous medication and the implantation of an ICD, with successful outcome.

Interestingly, in both patients there was predominance of right-sided signs including right paratracheal lymphadenopathy or right apical scarring suggestive of old TB. It is proposed that TB myocarditis arises from three possible routes of spread: direct infection from the pericardium, haematogenous seeding, or through lymphatic spread. The case report by Khurana et al., 2007, in agreement with Maeder et al., 2003 [8] suggests that there may be an anatomical predilection to the right-sided mediastinal lymph nodes *"making the right side of the heart the most vulnerable area of the myocardium owing to the potential for direct spread"* [9]. Further investigation is necessary to determine whether this is a true association or coincidental.

A further consideration is whether the TB could be a bystander in our second case. The presenting features included a dysrhythmia and severe cardiomyopathy with significantly impaired left ventricular function, which dramatically improved following the introduction of anti-tuberculous medication. The case report by Everett et al. in 2013 suggests that in our second case, the primary diagnosis was that of giant cell myocarditis, rather than TB myocarditis as we speculate here [10]. The report suggests that it was only once the patient was subjected to immunosuppression that latent TB was reactivated. Even if true, the patient was high risk for tuberculosis given his ethnicity, and therefore, actively searching for tuberculosis early was warranted. It was not until the patient received anti-tuberculous medication alongside the standard management that his ventricular function improved.

The optimal investigative modality for diagnosing TB early is yet to be determined. Perhaps as Thachill et al. recommend, a combination of varied imaging techniques in conjunction with histopathological analysis from endomyocardial and/or lymph node biopsies will provide a higher diagnostic yield [6]. In situations where an endomyocardial biopsy is inconclusive, as with our first patient, it is crucial to investigate for lymphadenopathy using PET scanning or CMR to identify potential lymph nodes to biopsy using EBUS [11]. In both our patients, it was not until EBUS-guided lymph node biopsies were performed that a final diagnosis of TB was reached. As in our second patient, it is vital to analyse the biopsy for histology and PCR genetic testing as well as culture since the outcome may only be positive in one mode of analysis.

Khurana and Shalhoub 2008 highlight the importance of serial CMR imaging to reveal lymphadenopathy [9]. CMR can also demonstrate the best endomyocardial areas to biopsy. However, where serial MR imaging is contraindicated following ICD insertion, Uusimaa et al. suggest the use of LV-cineangiography, $^{201}$TI single-photon-emission computed tomography, or multi-slice computed tomography [11].

In conclusion, we describe two cases of tuberculosis presenting as sustained monomorphic ventricular tachycardia. In both, standard anti-arrhythmic therapies were unsuccessful and it was only once anti-tuberculous chemotherapy was commenced alongside ICD insertion that any clinical improvement was witnessed. The diagnosis of TB myocarditis is a difficult one to make. It requires a high index of suspicion from the clinician and an active diagnostic pursuit. This must include a multitude of imaging techniques with the aim of identifying lymph nodes amenable to biopsy via EBUS, or the use of endomyocardial biopsy. It is possible that this condition has been historically underdiagnosed but the improvements in diagnostic tools may now allow us to fully appreciate the impact of this rare manifestation of a common global disease.

## References


[1] WHO global tuberculosis control report 2010. Summary. Cent Eur J Public Health 2010;18:237.
[2] Small PM. Tuberculosis: a new vision for the 21st century. Kekkaku 2009 Nov;84(11):721–6.
[3] Fanning A. Tuberculosis: extrapulmonary disease. CMAJ 1999;160:1597–603.
[4] Liu A, Hu Y, Coates A. Sudden cardiac death and tuberculosis – how much do we know? Tuberculosis (Edinb) 2012 Jul;92(4):307–13 [Epub 2012 Mar 8].
[5] Behr G, Palin HC, Temperly JM. Myocardial tuberculosis. Br Med J 1977;1:951.
[6] Thachill A, et al. Monomorphic ventricular tachycardia and mediastinal adenopathy due to granulomatous infiltration in patients with preserved ventricular function. J Am Coll Cardiol 2011;58:48–55.
[7] Koplan BA, Soejima K, Baughman K, Epstein LM, Stevenson WG. Refractory ventricular tachycardia secondary to cardiac sarcoid: elective trophysiologic characteristics, mapping, and ablation. Heart Rhythm 2006;3:924–9.
[8] Maeder M, Ammann P, Rickli H, Schoch OD. Fever and night sweats in a 22-year-old man with a mediastinal mass involving the heart. Chest 2003;124:2006–9.
[9] Khurana R, Shalhoub J, Verma A, Assomull R, Prasad SK, Kooner JS, et al. Tubercular myocarditis presenting with ventricular tachycardia. Nat Clin Pract Cardiovasc Med 2008;5:169–74.
[10] Everett R, et al. Chest pain and palpitations: taking a closer look. Circulation; 2013 [In Press].
[11] Uusimaa P, Ylitalo K, Anttonen O, Kerola T, Virtanen V, Pääkkö E, et al. Ventricular tachyarrhythmia as a primary presentation of sarcoidosis. Europace 2008;10:760–6.