Case Report

Mitral valve annular caseous calcification causing severe mitral valve stenosis and familial multiple lipomatosis: Case report and literature review

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Received 12 May 2016; revised 22 September 2016; accepted 25 September 2016; Available online 15 November 2016

Abstract

A 55-year-old male presented with severe mitral valve stenosis that was caused by a rare condition called caseous calcification of mitral valve annulus (CCMA). The condition was provisionally diagnosed by multi-imaging modalities, and the diagnosis was further established by histopathology. The patient required surgical excision of CCMA and mitral valve replacement. In addition, this patient exhibited a classical picture of another rare condition called familial multiple lipomatosis (FML). No such associations have been reported between the two rare conditions of CCMA and FML. Rare pathologies such as CCMA should be considered in the differential diagnosis of calcified mass involving mitral valve annulus with or without valvular dysfunction.

Keywords: Annular caseous calcification; Familial multiple lipomatosis; Mitral valve; Mitral valve dysfunction

Introduction

First condition: CCMA is a very rare degenerative process with unknown aetiology. The prevalence of CCMA in echocardiography laboratories (echo labs) was 0.6% in people with mitral valve annular calcification (MAC) compared with other populations who do not have MAC (0.06%) on transthoracic echocardiography (TTE) studies. On TTE, CCMA appears as a rounded calcified mass located at posterior aspect of mitral valve annulus with central echolucencies resembling liquefaction. These features could be delineated better by transoesophageal echocardiography (TEE). Recently, CCMA has been more recognizable by cardiac computed tomography (CCT) and cardiac magnetic resonance imaging (CMR). CMR is the diagnostic of choice for CCMA whenever diagnosis is questionable. Surgical removal of CCMA is unnecessary unless there is significant haemodynamic compromise of the mitral valve (MV).
Second condition: Familial multiple lipomatosis (FML) is a rare benign condition (incidence of 0.002%) that is frequently reported as an autosomal dominant condition.\textsuperscript{10} The condition is characterized by multiple subcutaneous lipomas that are typically located on the trunk and extremities. These lipomas vary in size from 1 cm to 10 cm and are well defined, encapsulated, rubbery, mobile and painless masses. FML is not associated with hyperlipidemia.\textsuperscript{11} In some patients, these masses cause disfigurement and discomfort with clothing, which require surgical removal. Histopathological examinations classically reveal mature adipose tissue.\textsuperscript{10–12}

Case presentation

A 55-year-old male was referred to our centre with rheumatic MV stenosis with paroxysmal atrial fibrillation. He had a cerebrovascular accident with full recovery. His symptoms were mainly shortness of breath and palpitation upon mild exertion with no other cardiac symptoms. The review of systems revealed no significant complaints apart from multiple masses under the skin growing in number and size over time. The first time these masses appeared was at the age of 18, and the largest 10 masses were removed 10 years prior to presentation. Some of the removed masses regrew again. His twin
brother and his son have the same skin lesions with no cardiac symptoms. The patient has no history of exposure to asbestos and no history of tuberculosis. His skin examination revealed multiple rubbery, mobile, non-fluctuant, and non-tender subcutaneous masses located on his trunk and extremities (Figure 1A). The masses range in size from 1 to 8 cm in diameter. He has also numerous pigmented spots that look like Café-au-lait spots on his trunk. A grade 3 mid-diastolic rumbling murmur was noted. Laboratory tests of renal function, liver function, calcium, phosphate, and parathyroid hormone were normal. Baseline TTE&TEE exhibited a large (29 mm) calcified multinodular mass involving posterior aspect of MV (Figure 2A and B) with an MV area of 0.9 cm². TTE three-dimensional (3D) multiplanar reconstructed (MPR) images exhibited echolucency areas inside the mass (Figure 2C). TTE exercise test confirmed the severity of MV stenosis. The largest subcutaneous mass was removed because it had caused discomfort with clothing, and histopathology revealed a classical picture of lipoma (Figure 1B). Therefore, the possibility of neurofibromatosis, which was entertained initially to explain both subcutaneous lesions and the intracardiac mass, was excluded. Since then, the patient has been diagnosed with FML based on family history and multiple lipomas. The TTE and TEE images of the cardiac mass was reassessed in depth to explore features of CCMA, namely, a calcified mass located at the posterior aspect of MV annulus with central echolucencies. For further confirmation before cardiac surgery, CMR (Figure 3A–E) and CCT (Figure 4A–G) were performed. Both proved CCMA radiological features. CMR delineated a fibrous calcified capsule, and CCT demonstrated dense calcification at the periphery and hypodense areas at the centre suggestive of liquefied materials. Extracardiac and pleural calcifications were noted on CCT. Initially, the patient requested to defer cardiac surgery as long as he could tolerate on medical therapy. Three years later, he presented with severe shortness of breath precipitated by fast atrial fibrillation. Repeated TEE showed partial reduction of CCMA size (largest diameter 18 mm), but MV stenosis remained the same (Figure 2D). At this time, the patient agreed to undergo urgent cardiac surgery. During surgery, the CCMA mass along with most of the subvalvular apparatus related to posterior commissure were excised (Figure 5A). Semi-liquid whitish material (toothpaste like) was extracted from the mass. A 27-mm metallic valve was implanted. Histopathology of the calcified mass was consistent with CCMA (Figure 5B). No evidence of rheumatic fever pathology was noted. The patient was subsequently discharged in a good condition.

**Discussion**

Initially, the pathology of the calcified mass that caused severe mitral valve stenosis was ambiguous and represented a clinical challenge. The mass had a benign behaviour with regard to its size. A wide range of differential diagnosis for intracardiac benign tumours with calcifications was considered, such as myxoma, fibroma and calcified amorphous tumour of the heart.\(^6\) Lipoma was unlikely given severe calcification. The diagnosis of CCMA in our patient was
evident by multi-imaging modalities and proved by histopathology.5 In experienced hands, TTE is considered sufficient to diagnose CCMA.9 Moreover, MPR of 3D images, a relatively new echo technology, has the ability to slice through CCMA and demonstrate interior echolucencies. CMR and CCT images displayed characteristic features of CCMA as described previously by several authors, namely, a calcified mass involving posterior mitral valve annulus with central liquefaction and peripheral calcified fibrous cap.1–5,9 Interestingly, in our patient, the CCMA mass had regressed in size significantly in 3 years, whereas MV stenosis severity was not altered. Spontaneous regression of CCMA size was previously reported.8 Compared with the reported cases of CCMA,1–5 our patient is the youngest and has the most severe affection of MV in form of severe mitral stenosis.

**Figure 4:** A, B and C: Non-enhanced cardiac computed tomography (CCT) of the chest, mediastinal window settings in four chambers, two chambers and short axis multi-planar reformatted images depict a heavily calcified mitral annulus mass. D, E and F: Bone window settings of the former planes show peripheral dense calcification and reduced density of the centre (liquefaction). G and H: Axial CCT with mediastinal window settings showing bilateral large calcified plaques of parietal and diaphragmatic pleura.

**Figure 5:** A: Excised MV correlates very well with 3D surgical view in Figure 2B. The arrow indicates obliterated posteriomedical commissure, and the star indicates MV opening. B: Histopathology reveals islands of a cellular eosinophilic material (stars) with scattered calcification (arrows) with surrounding fibrosis and chronic inflammatory cells consistent with features of CCMA.
Recognized causes of pleural calcification, such as TB and asbestosis, and other conditions that alter calcium and phosphate metabolism, such as renal failure and hyperparathyroidism, are absent in our patient. This fact might indicate that pleural (extracardiac) calcifications that exists in our patient share CCMA same pathogenesis, which is still unknown. Conversely, our patient’s family history and histopathology of the subcutaneous masses are consistent with FML. In some patients, these masses cause disfigurement and discomfort with clothing, which require surgical removal, as noted in our patient. FML is inherited, and CCMA is an acquired degenerative process with unknown aetiology. These two rare conditions have coexisted in our patient. Could FML predispose an individual to CCMA? Are they coincidental? We do not know. To answer this question, most available medical search engines were searched (Wiley Online Library, Science Direct, MEDLINE®, and PubMed). No reported link between the two conditions was identified. This case report suggests the need for researchers to look for a possible association between FML and CCMA whenever they encounter these conditions in the future.

Conclusion

Rare pathologies such as CCMA should be considered in the deferential diagnosis of calcified mass involving mitral valve annulus with or without valvular dysfunction. We report for the first time FML coexisting with CCMA with an unclear association.

Conflict of interest

The author has no conflict of interest to declare.

Consent

Informed consent was obtained from the patient for publication of this case report and accompanying images.

Authors’ contribution

The author testifies that he is the sole contributor of the article. He rendered all the efforts to produce the article, starting from the idea, midline research, collecting the data, and writing the manuscript. He has acknowledged the support of his colleagues who provided him with some images and took care of the patient. He informs that the article is free from unacceptable quoting. He has revised and corrected the manuscript and is solely responsible the article content.

Acknowledgements

The author thanks Dr Amal Sakrana (radiologist), who provided him with CT and MR images, Dr Ibrahim Farah (Cardiac surgeon), who performed the surgery and provided him with surgical specimen images, Dr Alisisi Ghassan H. (G. surgeon), who performed excision of subcutaneous lipoma, and Dr Ahmad Ahijili (pathologist), who provided him with pathology images.

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How to cite this article: Alatawi FO. Mitral valve annular caseous calcification causing severe mitral valve stenosis and familial multiple lipomatosis: Case report and literature review. J Taibah Univ Med Sc 2017;12(2):169–173.