

# Mitral valve rheumatoid nodule complicated by infective endocarditis

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## SUMMARY

We report a case of a 73-year-old male with rheumatoid arthritis presented with acute abdominal and back pain and rapidly developing multiorgan failure. A positive blood culture (*Staphylococcus aureus*, *Candida* species) followed by transoesophageal sonography established a diagnosis of mitral valve infective endocarditis.

At the autopsy, the heart examination revealed fibrinous pericarditis and multiple small vegetations on the mitral valve. The mitral valve itself showed no significant damage. Surprisingly, the histological examination of the mitral valve showed granulomatous inflammation with central fibrinoid necrosis and peripheral palisade of histiocytes, with occasional giant cells and lymphocytic inflammatory infiltrate - findings consistent with a rheumatoid nodule. Infective vegetations were overlying the nodule.

Due to its relative frequency, a possibility of cardiac involvement by rheumatoid arthritis and its potential infective complications should be considered in patients with appropriate history and clinical symptoms.

**Keywords:** rheumatoid arthritis – rheumatoid nodule – infective endocarditis – mitral valve

## Revmatoidní uzel mitrální chlopně komplikovaný infekční endokarditidou

### SOUHRN

Popisujeme případ 73-letého muže s revmatoidní artritidou hospitalizovaného pro akutní bolest břicha a zad, jehož stav rychle progredoval do multiorgánového selhání. Pozitivní hemokultura (*Staphylococcus aureus*, *Candida* species) následovaná transesofageální sonografií svědčila pro infekční endokarditidu mitrální chlopně.

Při pitvě jsme na srdci našli jednak fibrinózní perikarditidu, jednak mnohočetné drobné vegetace na mitrální chlopni. Mitrální chlopně samotná makroskopicky nevykazovala známky poškození. Mikroskopické vyšetření mitrální chlopně však překvapivě prokázalo granulomatózní zánět s centrální fibrinoidní nekrózou a periferní palisádou histiocytů s několika rozptýlenými obrovskými mnohojadernými buňkami a lymfocytárním infiltrátem – nález konzistentní s diagnózou revmatoidního uzlu. K povrchu tohoto uzlu lnuly infekční vegetace.

Na postižení srdce při revmatoidní artritidě by kvůli jeho relativně častému výskytu a potenciálním infekčním komplikacím mělo být pomýšleno u všech pacientů s relevantní anamnézou a klinickými symptomy.

**Klíčová slova:** revmatoidní artritida – revmatoidní uzel – infekční endokarditida – mitrální chlopně

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Rheumatoid arthritis (RA) is a multifactorial chronic systemic autoimmune disease predominantly affecting joints and causing progressive disability, premature death and socioeconomic burdens (1). Global prevalence of RA is 460:100 000, but varies according to geographical location, and is increasing, especially in industrialized countries (2, 3). RA arises more frequently in women than men and can affect patients of any age (4).

Rheumatoid arthritis is characterized by synovial inflammation and synovial hyperplasia, cartilage and bone destruction and autoantibody production (i.e. ACPA – anti-citrullinated protein antibody) (5). RA affects small and large joints of extremities, spine and axial joints. In a poorly controlled or severe disease, there is a risk of extraarticular manifestations, even though its incidence is decreasing due to new and effective

treatment possibilities with disease-modifying anti-rheumatic drugs (DMARDs) (6)(5).

Heart involvement in RA is relatively common, mostly in form of fibrinous pericarditis. Formation of heart rheumatic nodules is however only rarely reported in the literature and their complication by infectious endocarditis as described in this report is exceptional (7).

## CASE DESCRIPTION

We report an autopsy case of a 73-year-old male with second type diabetes mellitus, diagnosed with seropositive rheumatoid arthritis two years prior to his death and treated with corticosteroids. The patient further developed a pulmonary rheumatoid nodule which was biopsied seven months before his death. No cutaneous rheumatoid nodules were described. The patient presented with acute abdominal and back pain at the current admission, with a rapid development of a multiorgan failure. Following positive blood culture (*Staphylococcus aureus* and *Candida* species), the transoesophageal sonography was performed, establishing the diagnosis of mitral valve infective endocarditis. A conservative approach was chosen due to the clinical condition of the patient. Acute ischemia of distal ileum

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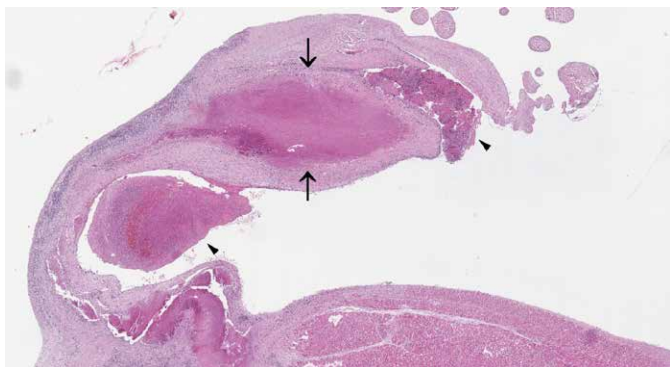
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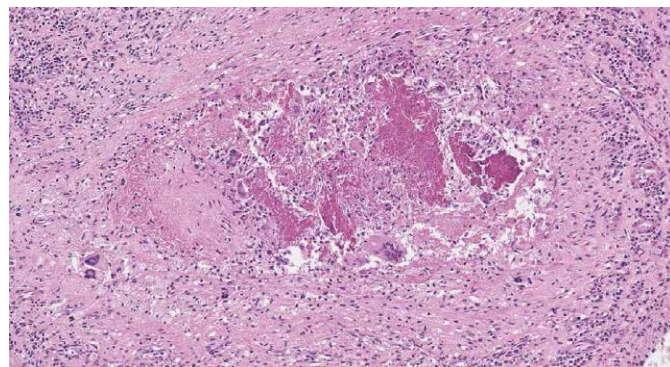
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**Fig. 1.** Low power view of the mitral valve with rheumatoid nodule (between arrows) and infective vegetations (arrowheads). HE, magnification 17x.



**Fig. 2.** Rheumatoid nodule – fibrinoid necrosis with palisading histiocytes, giant cells and lymphocytic inflammation. HE, magnification 116x.

and proximal colon developed later, requiring surgical removal of the affected intestine. The patient died 12 days after the admission due to refractory septic shock with multiorgan failure.

After patient's death, a standard autopsy was performed at our department. The main findings consisted of severe atherosclerosis of the aorta and state after previous proctocolectomy, right lung lower lobe resection and partial resection of the diaphragm with pleural adhesions. Small infarcts in the spleen and right kidney were also present. The heart showed fibrinous pericarditis and multiple small vegetations on the mitral valve at the autopsy, while the mitral valve itself showed no significant damage.

The histological examination identified granulomatous valve inflammation with central fibrinoid necrosis and peripheral palisade of histiocytes, with occasional giant cells and lymphocytic inflammatory infiltrate – findings consistent with rheumatoid nodule in rheumatoid arthritis. Infective vegetations were overlying the nodule (Fig.1, Fig.2). Special stains (Gram, Grocott, Ziehl-Neelsen) were negative. Another rheumatoid nodule with identical morphology was further identified in pleural adhesions of the right lung.

## DISCUSSION

The involvement of the cardiovascular system in rheumatoid arthritis is relatively common, and it is associated with increased mortality. The involvement includes fibrinous pericarditis (most commonly), cardiomyopathy, myocarditis, cardiac amyloidosis, coronary vasculitis, arrhythmias and valve disease, but also congestive heart failure and ischemic heart disease (8). Furthermore, chronic inflammation or the influence of some chronic therapies can promote and accelerate atherosclerotic plaque development or additionally increase vascular vulnerability (9).

Patients with rheumatoid arthritis can present with both infective (7) and non-infective (sterile, non-bacterial thrombotic) endocarditis (10), with treatment-related immunosuppression being a possible contributing factor. The symptomatic manifestation of cardiac rheumatoid nodules is rare, although between 30 – 50 % of patients with systemic rheumatoid arthritis do have any other kind of cardiovascular involvement (11). There are few well documented cases of rheumatoid nodules of the cardiac valves in the literature, some of them causing acute coronary syndrome or cerebral stroke in case of embolization (11) or causing valvular insufficiency (12). Complication in form of infective endocarditis developing at the background of such a damaged valve is however exceedingly rare (7) and can be potentially fatal, as in our case.

Other extraarticular organ manifestations of RA include keratitis, pulmonary involvement: granulomas (rheumatoid nodules), interstitial lung disease, constrictive or follicular bronchiolitis, bronchiectasis (13); serositis (pleuritis, pericarditis), small vessel vasculitis, cutaneous manifestations, such as classic cutaneous nodules, but also pyoderma gangrenosum, interstitial granulomatous dermatitis, Felty syndrome (14); and neurologic manifestations (1)(1). Central and peripheral nervous system is usually affected due to small vessel vasculitis, joint damage or drug toxicity. Microvascular cerebral damage is associated with the development of the Alzheimer's disease and vascular dementia (15).

The exact etiology of rheumatoid nodules is not known (16). Classic rheumatoid nodules commonly occur in genetically predisposed patients with severe, seropositive arthritis (16). Homozygosity for HLA-DRB1\*0401 makes RA patients susceptible to involvement of major organs (17). Studies of cytokine composition suggest that the nodule is probably due to a Th-1-mediated inflammatory mechanism (18). Subcutaneous nodules could be also associated with previous trauma (19). Methotrexate therapy or other systemic therapies can paradoxically induce or exacerbate nodule formation (20). Cardiac valvular nodules may arise on any cusp or valvular ring, but are most commonly described on the mitral and aortic valve (21).

Incidence of infective endocarditis is annually estimated between 15 to 80 cases per million persons in population-based studies and it is markedly increased in patients with valve prostheses or with prior infective endocarditis. Impaired valvular endothelium is a predisposing factor for vegetation formation (22) and apparently played a role in our case as well. Affected patients are older and the most frequent responsible microorganism is *Staphylococcus* sp. (23). Infective endocarditis as a complication of intracardiac rheumatoid nodule is only exceptionally reported (7).

According to a study of Meune et al. RA is associated with 60 % increase in risk of cardiovascular death in comparison to general population and the standardized mortality ratio remains unchanged over the past decades (9, 24). RA patients have also twice the risk of myocardial infarction compared to general population (15). Compared to the healthy population, the mortality rate is higher in patients with rheumatoid arthritis and cardiovascular and other systemic complications remain a major challenge (25). Thus, reduction of cardiovascular mortality should be considered one of the main targets in RA management (9, 24). Suspicion of rheumatoid nodules and their potential infective complications should be also considered in patients with rheumatoid arthritis and cardiac or systemic symptoms.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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