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# Recurrent pericarditis — diagnostic and therapeutic implications

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Exudative pericarditis is the cause of 5% of admissions to accidents and emergency departments with chest pain being the presenting complaint in most of these cases [1]. This problem is encountered by doctors practicing surgical and non-surgical specialities, including pulmonology.

The principal causes of exudative pericarditis include malignancy, infections, connective tissue diseases and other autoimmune diseases, traumatic injuries and iatrogenic factors [2–4].

Tsang et al. [5] analysed a population of patients hospitalised at surgical and non-surgical wards of Mayo Clinic undergoing pericardiocentesis between 1979 and 2000 and found a predominance of malignancy-related, postprocedural and postoperative pericarditis. The authors demonstrated an increased incidence of postprocedural and postoperative pericarditis in the 1990s versus 1980s. Cornily et al. [6] investigated the causes of cardiac tamponade in patients hospitalised at non-surgical wards between 1991 and 2005 at the University Hospital of Brest, France, and established malignancy as the primary cause of tamponade (65%), followed by viral causes (10%) and iatrogenic causes (3%) associated with intrapericardial bleeding secondary to anticoagulant treatment.

Recurrences are one of the problems in patients with pericarditis. Tsang et al. [5] reported the highest likelihood of recurrent effusion in the group of patients who did not receive pericardial drainage following pericardiocentesis, in cases with malignancy-related aetiologies, and in patients with large drained volumes (exceeding 400 ml).

In developing countries, tuberculosis may be a cause of recurrent pericardial effusion. Shahbaz

and Fatimi [7] observed tuberculous pericarditis in 50% of patients with recurrent pericardial effusion hospitalised between 1994 and 2001 in Karachi, Pakistan. Due to the diverse symptomatology of tuberculous pericarditis (exudative, recurrent exudative, exudative-constrictive, constrictive forms) it is important that the tuberculous aetiology is suspected in each patient originating from geographic regions where tuberculosis is highly prevalent (Sub-Saharan Africa and the Southeast Asia and Pacific region) [7, 8]. In these regions, tuberculosis often co-exists with HIV infection, which makes control and treatment particularly difficult [9]. Tuberculous pericarditis is also the likely cause of recurrent pericardial effusion in immunosuppressed patients [4].

In developed countries, there is an increasing percentage of patients with recurrent pericarditis of autoimmune aetiology [10]. This applies to patients with connective tissue diseases (rheumatoid arthritis, systemic lupus erythematosus, Sjögren syndrome, systemic sclerosis) [4], seronegative arthritides [11], autoimmune inflammatory bowel diseases [12] and postcardiotomy syndrome [4].

However, in the majority of cases of recurrent pericarditis, the aetiology cannot be established and these cases are labelled idiopathic. Recent studies suggest a contribution of autoimmune aetiology to some of the cases of idiopathic pericarditis [13–15]. Immune response may be triggered by infections (usually viral infections), although sometimes it assumes an autonomous nature. An argument to support this hypothesis is the presence of elevated levels of proinflammatory cytokines (interleukin[IL]-6, IL-8, tumour necrosis factor- $\alpha$ ) in the pericardial effusion and autoanti-

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bodies in the serum in many patients with recurrent pericarditis [13]. Caforio et al. [13] showed the presence of cardiac antibodies in the serum in 50% of patients with recurrent pericarditis, in 3% of patients with non-inflammatory cardiac conditions and in 1% of healthy volunteers [14]. Imazio et al. demonstrated antinuclear antibodies in the serum in most patients with recurrent pericarditis, at low titres (generally up to 160) without other signs of systemic disease [15].

It is also possible that genetic predispositions play a role in the pathogenesis of recurrent idiopathic pericarditis, as suggested, among others things, by the more frequent occurrence of recurrences in patients with specific patterns of histocompatibility antigens, the 10-percent contribution of familial recurrent pericarditis and the rare genetic conditions accompanied by pericardial effusion [13, 16, 17].

Another controversial topic is the management of recurrent idiopathic pericarditis. As current guidelines are lacking, experience from studies conducted in large groups of patients is of significant importance. The CORE (*Colchicine for REcurrent pericarditis*) study [18], whose results were published in 2005, showed that the addition of colchicine to standard anti-inflammatory treatment (acetylsalicylic acid) significantly reduced the frequency of exudative pericarditis recurrences with the absence of significant adverse effects. In 2008, Imazio et al. [19] showed low-dose prednisone (0.1–0.5 mg/kg) to be superior to high-dose prednisone (1 mg/kg) in preventing recurrences of exudative pericarditis. In 2010, the POPE (*POstpericardiotomy PEricarditis*) study demonstrated inefficacy of a non-steroid anti-inflammatory drug (diclofenac) in preventing recurrences of postoperative pericarditis [20]. Studies to assess the efficacy of colchicine in combination with glucocorticosteroids in this group of patients are ongoing [21].

While the completed studies have modified clinical practice, no new management standards in recurrent exudative pericarditis have been developed [22]. It is emphasised that glucocorticosteroids should not be used as first-line treatment, unless an autoimmune aetiology of pericarditis has been established [23].

Lazaros et al. [13] proposed an algorithm of treatment of subsequent recurrences of idiopathic pericarditis. They suggested that the first recurrence should be managed with non-steroid anti-inflammatory drugs at maximum doses in combination with colchicine, the second — with a low-dose glucocorticosteroid in combination with colchicine,

the third with an effective dose of a glucocorticosteroid in combination with colchicine and a non-steroid anti-inflammatory drug, and the fourth with an immunosuppressant. Ibuprofen remains the optimal non-steroid anti-inflammatory drug recommended in the 2004 guidelines, as it causes relatively mild adverse effects and does not impair coronary blood flow [4]. The most commonly used immunosuppressant is azathioprine. Picco et al. [24] described three cases of recurrent idiopathic pericarditis in children successfully managed with the IL-1b receptor antagonist anakinra.

While the experience of the past few years has significantly contributed to the evaluation and treatment of recurrent pericarditis, we continue to come across diagnostically and therapeutically difficult cases in clinical practice. These problems are illustrated by the paper by Biliska et al. [25] published in the present issue of “Pneumonologia i Alergologia Polska”.

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