REVIEW

PERICARDITIS: DIAGNOSIS AND MANAGEMENT

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Abstract: *Pericarditis represents the inflammation of the pericardial sac and is probably the most common disease involving the pericardium. When the fluid accumulation becomes hemodynamically significant (the effusion is large or the rate of accumulation is too fast), the fluid can compress the cardiac chambers, determining cardiac tamponade. This pathology can be isolated or a cardiac manifestation of a system disease. Pericarditis may result from infectious, non-infectious, and idiopathic etiologies. European Society of Cardiology guidelines recommend 2 out of 4 criteria for the positive diagnosis of pericarditis: chest pain, pericardial rub, ECG changes or increase of pericardial effusion. Echocardiography represents the most important imaging method in pericarditis. It is used for quantification of pericardial effusion and monitoring its evolution over time. Cardiac magnetic resonance is used in cases of unclear echocardiographic images, suspicion of myocardial involvement and in patients with multiple recurrences. The sequence – late gadolinium enhancement – of cardiac magnetic resonance has a sensitivity of 94% and can assure information about the severity of pericardial inflammation. The most important treatment in acute pericarditis is anti-inflammatory therapy, which should continue until symptom relief. Most patients recover completely. Recurrent pericarditis occurs in 30% of cases not treated adequately.*

Keywords: *pericarditis, echocardiography, anti-inflammatory drugs.*

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Introduction

Pericarditis represents the inflammation of the pericardial sac and is probably the most common disease involving the pericardium [1]. It may be associated with pericardial effusion, which can be serous, hemorrhagic or purulent. When the fluid accumulation becomes hemodynamically significant (the effusion is large or the rate of accumulation is too fast), the fluid can compress the cardiac chambers, determining cardiac tamponade.

This pathology can be isolated or a cardiac manifestation of a system disease [2].

Pericarditis may result from infectious, non-infectious and idiopathic etiologies (Table 1,2). Sometimes, constrictive pericarditis can follow the initial pericarditis after months or years by the process of pericardial thickening [3][4].

ETIOLOGY

Table 1. Infectious causes of pericarditis

Viruses	Coxsackie viruses A, B; Echovirus; Adenoviruses; Parvovirus B19; HIV; Ebstein-Bar virus; Cytomegalovirus; Influenza
Bacterias	Mycobacterium tuberculosis (most frequent), Coxiella burnetii, Meningococcus, Pneumococcus, Staphylococcus, Streptococcus
Fungi	Histoplasma, Coccidioides, Candida, Blastomyces
Parasites	Echinococcus, Toxoplasma

Table 2. Non-infectious causes of pericarditis

Neoplasms	Metastasis
Connective tissue diseases	lupus erythematosus, rheumatoid arthritis
Metabolic disorders	Uremia, myxedema
Post-cardiac injuries	Dressler syndrome, post percutaneous intervention (transcatheter aortic valve implantation), post cardiac surgery (especially coronary artery bypass)
Blunt trauma	
Drugs-rare	procainamide, hydralazine, isoniazid, ipilimumab, nivolumab

CLASSIFICATION

The classification of pericarditis is resumed in Tables 3,4.

Table 3. Classification of pericarditis

Acute	Pericardial syndrome is diagnosed corresponding with 2 of 4 criteria
Incessant	➢ 4-6 weeks but < 3 months
Recurrent	Recurrence of pericarditis after a first episode of pericarditis after 4-6 weeks or longer
Chronic	➢ 3 months

Table 4. Classification of pericarditis depending on fluid type

Serous
Purulent
Fibrinous
Caseous
Hemorrhagic

POSITIVE DIAGNOSIS

European Society of Cardiology guidelines recommend 2 out of 4 criteria for the positive diagnosis of pericarditis [5]:

1. Chest pain

Chest pain with a rapid onset represents the cardinal symptom of acute pericarditis [6]. The pain is usually central, very severe, worsened with inspiration (pleuritic) and alleviated by sitting up and leaning forward (positional) [7]. Sometimes the chest pain can radiate to neck, arms, left shoulder or trapezius muscles if the phrenic nerve is inflamed [8].

In some cases, if oppressive pain appears, it can be difficult to differentiate it from myocardial ischemia. In addition to differential diagnosis, if the chest pain is pleuritic, but it does not improve when sitting up, it is usually correlated with respiratory disease [9].

2. Pericardial rub

Pericardial rub can be auscultated on the left sternal border while the patient is leaning forward. The sound is determined by the friction between the two pericardial layers during atrial, ventricular systole and ventricular diastole [10]. It is recommended to be listened multiple times as the pericardial friction rub can appear and disappear intermittently and on different positions (lateral decubitus at end expiration).

The most specific pericardial rub is the triphasic type. However, sometimes, the third component can be absent. Moreover, it is necessary to differentiate the pericardial rub from the pleural rub which may produce a similar sound, by asking the patient to hold his breath while auscultating [11].

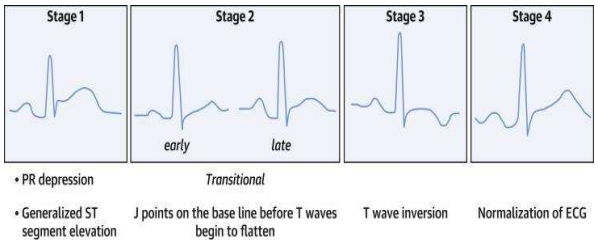
3. Electrocardiogram (ECG) changes

ECG changes combine 4 stages over more weeks. In stage I, diffuse changes occur on ECG like concave up ST segment elevation, reciprocal ST depression in AVR and PR segment elevation in AVR. Stage II appears after a few weeks and distinguishes normalization of ST and PR segments. Stage III and IV are characterized by T wave inversions and T wave normalization (Figure 1) [12].

Differential diagnosis should be made with acute coronary syndrome where ST elevation is localized in some leads and is concave down (opposed to pericarditis).

However, 40% of patients present atypical ECG changes and, sometimes, PR depression is the only sign [12].

Figure 1. ECG changes in pericarditis [13].



4. New/ Worsening pericardial effusion

Additional investigations:

- *Inflammatory biomarkers*

No specific markers for pericarditis are available. CRP, ESR and leucocytes are high in 80% of acute pericarditis, but they are not sensitive or specific. In case of elevated troponin I or T, myocardium is involved, determining myopericarditis [14]. High-sensitivity CRP is associated with high risk of recurrent pericarditis [15].

- *Echocardiography*

Echocardiography represents the most important imaging method in pericarditis. It is used for quantification of pericardial effusion and monitoring its evolution over time (small < 10mm, moderate 10-20mm, large 21-25mm, very large > 25mm), determining complications such as tamponade or constrictive pericarditis and helping to perform pericardiocentesis. Transesophageal echocardiography is necessary when transthoracic echocardiography is suboptimal [16].

- *Cardiac computed tomography*

Cardiac computed tomography is preferable because of its short acquisition time and high spatial resonance. In cases of pericarditis, enhancement of thickened pericardium can be determined immediately after the intravenous administration of contrast. As an advantage, cardiac computed tomography is very sensitive for determining pericardial calcification, but, on the other hand, the pericardium is better viewed where it is surrounded by fat [17].

- *Cardiovascular magnetic resonance*

CMR is used in cases of unclear echocardiographic images, suspicion of myocardial involvement and in patients with multiple recurrences [18]. The sequence – late

gadolinium enhancement – of CMR has a sensitivity of 94% and can assure information about the severity of pericardial inflammation [19].

Normal pericardium is non-vascularized, consequently late gadolinium enhancement is minimal or absent in this condition. On the other hand, acute pericarditis is correlated to neovascularization, late gadolinium enhancement helping at identifying cases with high risk of complications and reduced rate of remission [20].

In addition, CMR can be used in patients suspected with constrictive pathophysiology and unclear echocardiography images [21].

TREATMENT

The most important treatment in acute pericarditis is anti-inflammatory therapy, which should continue until symptom relief.

- Nonsteroidal anti-inflammatory drugs

The therapy consists of Ibuprofen 600mg every 8 hours, Indomethacin 25-50mg every 8 hours or Naproxen 500-1000mg every 12 hours for 3 days-2 weeks. Aspirin 500-1000mg every 6-8 hours should be used in patients with coronary artery disease [22]. Side effects consist of high risk of gastrointestinal ulcers, arterial hypertension and kidney failure [23].

- Colchicine

Colchicine blocks tubulin polymerization, inhibiting inflammasome formation and cytokine release, having an essential anti-inflammatory effect [24]. It is efficiently associated with aspirin or other NSAID in acute (3-6 months) or recurrent pericarditis, decreasing recurrences in half. The recommended dose is 0.6mg for weight >70kg and 0.5mg for weight <70kg. Side effects are represented by gastrointestinal intolerance (most frequent), myelosuppression, aplastic anemia (rare) and neuromuscular toxicity. It is contraindicated in patients with severe renal impairment and pregnant women [25].

- Corticosteroids

Corticosteroids are used as second- or third-line treatment. Some studies enhanced the fact that they are associated with a higher risk of recurrence. Low-dose corticosteroids are more beneficial than high-dose corticosteroids, reducing hospitalizations, treatment failure and risk of adverse effects [26].

However, corticosteroids should be used when there is an unfavorable response to another anti-inflammatory therapies or for some indications as pericarditis associated with autoimmune disease [27].

- Antimicrobial therapy

According to the etiology of the pericarditis, specific treatment is indicated. The most common pathogens are staphylococcus aureus and streptococci [28]. Other pathogens are: Propionibacterium acnes and Mycobacterium tuberculosis. The treatment of tuberculous pericarditis consists of multidrug therapy: rifampicin, isoniazid, pyrazinamide and ethambutol for less <2 months, followed by rifampicin and isoniazid for 4-6 months, with or without prednisolone, in order to eradicate Mycobacterium tuberculosis and to prevent the evolution to constrictive pericarditis [29].

- Pericardiocentesis

Emergent pericardiocentesis is recommended in patients diagnosed with cardiac tamponade.

Pericardiocentesis is also performed in patients with moderate-large pericardial effusion without hemodynamic compromise.

Diagnostic pericardiocentesis can be recommended in case of infectious etiology.

Basic chemistry, PCR and fluid cultures should be made from bacterial, fungal and tuberculosis pericardial fluid to determine the exact etiology and initiate the correct treatment [30].

Purulent effusions are associated with high mortality.

Pericardiectomy should be considered in case of failure of tuberculous pericarditis treatment [31].

PROGNOSIS

Most patients recover completely. Recurrent pericarditis occurs in 30% of cases not treated adequately. Constrictive pericarditis evolves in less than <1% of patients. Cardiac tamponade is relatively rare and appears associated with malignancy and infectious causes [32].

CONCLUSIONS

Pericarditis is a common etiology of chest pain which can be easily diagnosed by ECG and echocardiography. The most cases are idiopathic. The correct use of anti-inflammatory treatment significantly reduces the risk of recurrence and alleviates the evolution of the disease. The complete understanding of the pathogenesis of pericardial syndrome remains difficult.

Author Contributions:

L.B.G. conceived the original draft preparation. L.B.G., A.I.N., R.I.D., V.M.M., C.C.D. were responsible for conception and design of the review. L.B.G., A.I.N., R.I.D., V.M.M. and C.C.D. were responsible for the data acquisition. L.B.G. was responsible for the collection and assembly of the article/published data, and their inclusion and interpretation in this review. L.B.G., A.I.N., R.I.D., V.M.M., C.C.D. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

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