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REVIEW

Eosinophilic cardiac disease: Molecular, clinical and imaging aspects

Cardiopathie à éosinophiles : aspects moléculaires, cliniques et en imagerie

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Summary Eosinophilia may be responsible for cardiac injuries of widely varying severity, from acute myocarditis to endomyocardial fibrosis. In this review, we present both the molecular mechanisms that are responsible for these lesions and their clinical and paraclinical aspects. Numerous aetiologies can lead to severe eosinophilia, but these are mainly represented by hypersensitivity reactions, rheumatological diseases and hypereosinophilic syndrome. Because cardiac involvement may be extremely severe, echocardiography should be always performed in the context of eosinophilia and appropriate therapeutics should be started rapidly in order to limit the progression of the disease.

Abbreviations: CT, computed tomography; DRESS, drug rash with eosinophilia and systemic symptoms; ECG, electrocardiography; ECP, eosinophil cationic protein; ECPA, eosinophilic coronary periarteritis; EDN, eosinophil-derived neurotoxin; EMF, endomyocardial fibrosis; EPO, eosinophil peroxidase; FP, FIP1L1-PDGFRA; GM-CSF, granulocyte macrophage colony-stimulating factor; HES, hypereosinophilic syndrome; Ig, immunoglobulin; IL, interleukin; L-HES, lymphocytic hypereosinophilic syndrome; MBP, major basic protein; MRI, magnetic resonance imaging.

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Myocardite à éosinophiles ;
Syndrome DRESS

Résumé Une hyperéosinophilie peut être responsable de lésions cardiaques dont la sévérité est très variable, allant de la myocardite aiguë jusqu'à la fibrose endomyocardique. Nous présentons, à travers cette revue de la littérature, les mécanismes moléculaires qui entraînent ces différentes lésions ainsi que leurs aspects cliniques et paracliniques. Si de nombreuses étiologies peuvent être responsables d'hyperéosinophilie, les réactions d'hypersensibilité, les maladies rhumatologiques et le syndrome d'hyperéosinophilie en sont les principales causes. Parce que l'atteinte cardiaque peut être extrêmement sévère, une échocardiographie doit être systématiquement réalisée en cas d'hyperéosinophilie et un traitement approprié doit être débuté rapidement afin de limiter la progression des lésions.

Introduction

Eosinophilic cardiac disease is a relatively rare condition that was first described in 1936 by Wilhelm Löffler, who called it 'fibroplastic parietal endocarditis with blood eosinophilia' [1]. Also known as Löffler's endocarditis, eosinophilic endomyocardial fibrosis (EMF) is an uncommon cause of restrictive cardiomyopathy. In fact, several types of cardiac damage may be encountered in the context of eosinophilia, from acute myocarditis to EMF. All result from toxicity of infiltrating eosinophils into cardiac tissue. The aim of this review is to present both the mechanisms that underlie these lesions and their clinical aspects, imaging features and specific treatments.

Physiology and pathophysiology of eosinophils

Eosinophils are normally found in the blood and in certain tissues. These granulocytes are involved in normal antimicrobial immunity [2]. They have surface proteins for immunoglobulin (Ig)E binding to IgE antigen complexes by which phagocytosis and release of granules is triggered. Indeed, when stimulated, eosinophils possess the ability to elaborate substances that are toxic to a wide variety of parasites that are too large to phagocytose [3]. Their usual location in the body (respiratory tract, gastrointestinal tract and skin) is therefore explained by this antiparasitic activity. They measure 12—15 μm in diameter and are characterized by a bilobed nucleus and numerous eosin-staining specific granules in their cytoplasm [4]. These granules contain high concentrations of hydrolases and cationic and basic proteins [5,6] (Fig. 1 [7]).

Production and kinetics

Along with the other polymorphonuclear leukocytes, eosinophils are produced by the bone marrow, where they represent up to 6% of the resident nucleated cells [8]. Under the influence of several cytokines, the haematopoietic stem cells gradually differentiate into eosinophilic myelocytes and then into mature eosinophils (Fig. 1). This maturation process takes approximately 8 days. The main cytokines responsible for the increase in eosinophil number are granulocyte macrophage colony-stimulating factor (GM-CSF), interleukin (IL)-3 and IL-5. IL-5 — produced by T helper 2 lymphocytes — is specific for the production of eosinophils and is considered to be their major growth factor [9]. It is also involved in survival, chemotaxis and degranulation. Eosinophils remain in the peripheral blood for 8—12 hours before migrating preferentially to certain tissues where they are concentrated: the respiratory tract, the gastrointestinal tract, the skin and the urogenital tract (in females). Eosinophils survive for 1—2 weeks unless apoptosis is prevented by cytokines (GM-CSF, IL-3, IL-5) [8].

Composition

The cytoplasm of eosinophils is filled with many eosin-staining specific and non-eosinophilic granules. As eosinophils are involved in the inflammation process and in innate and adaptive immunity, the specific granules are capable of inducing tissue damage and dysfunction by degranulation following activation by an immune stimulus. They contain cationic proteins: major basic protein (MBP), eosinophil cationic protein (ECP), eosinophil-derived neurotoxin (EDN) and eosinophil peroxidase (EPO) [9] (Fig. 1). These proteins have several effects including production of free radicals, cell necrosis and apoptosis induction. These eosinophilic constituents are very deleterious to the endothelial cells and are capable of activating platelets and impairing the anticoagulant effects of thrombomodulin [10]. Finally, the endocardium appears to be very sensitive to the release of these cardiotoxic agents, especially MBP and ECP [11].

Definition of eosinophilia

Eosinophils are present in the blood in small numbers: the normal count of circulating eosinophils is $\leq 350/mm^3$, for both adults and children. Mild eosinophilia is defined by a level of 500—1500 eosinophils/mm^3. A count of 1500—5000 eosinophils/mm^3 is considered as moderate and > 5000 eosinophils/mm^3 is a significant eosinophilia [8].