

similarity is one reason that CAP and prick skin tests produced many positive results in patients without clinical manifestations of *Anisakis* sensitivity.

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Hypereosinophilic syndrome presenting as acute myocardial infarction

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Key words: acute myocardial infarction; hypereosinophilic syndrome.

● **HYPEREOSINOPHILIC** syndrome is a leukoproliferative disorder characterized by a sustained overproduction of eosinophils. The distinctiveness of the syndrome, in addition to eosinophilia, is its marked predilection to damage specific organs, including the heart.

A 63-year-old woman was admitted to our hospital because of new onset anginal pain. She had a history of asthma treated with inhaled steroids, which had replaced oral steroids for the last 2 months.

Physical examination on admission was unremarkable, while laboratory tests revealed marked eosinophilia ($14.7 \times 10^9/l$) and elevated creatine kinase isoenzyme (CPK), which was later followed by elevated lactate dehydrogenase (LDH). Electrocardiography showed ST depressions in the lateral wall. Low-molecular-weight heparin, β -adrenergic receptor blockers, and ACE inhibitors were administered, while the presumptive diagnosis was acute myocardial infarction. Initial investigation including blood smear, stool examination, serum vitamin B₁₂ level, and chest radiography were all within normal limits, while serum IgE level was markedly elevated (1247 IU/l). On the second and third hospital days, the patient was asymptomatic with marked hemodynamic stability. Two I.V. boluses of high-dose steroids were given. On the fourth

hospital day, sudden pulmonary edema, hypotension, and new left-bundle branch block were noticed. While supported by mechanical ventilation, the patient was transferred to the intensive care unit. Echocardiogram showed left ventricle hypertrophy, severe systolic dysfunction due to posterior and basal hypokinesia, and a small pericardial effusion. Cardiac catheterization demonstrated normal coronary arteries.

The patient deteriorated with further hemodynamic compromise and died a few hours later. Postmortem bone-marrow aspiration and biopsy demonstrated 30% mature eosinophils characterized by hypersegmentation and pale granules. Myocardial biopsy showed heavy eosinophilic infiltration between myocardial fibers, with patchy myocardial necrosis.

The cardiac involvement in our patient was attributed to fulminant and atypical presentation of HES. Cardiac manifestations are common and usually are manifested late in the course of the disease, but, as a presenting symptom or sign, they are rare (1). The presenting manifestation of HES usually tends to be more insidious and present for months or longer. The most common symptoms include tiredness, cough, breathlessness, muscle pain, angioedema, rash, fever, and visual disturbances, all of which were absent in our patient (2). Our patient's initial evaluation suggested myocardial ischemia, which was not confirmed by cardiac angiography. HES was diagnosed on the basis of the characteristic histopathology findings.

The damage to the heart in HES ranges from early necrosis to subsequent thrombosis and fibrosis. Eosinophilic-mediated heart damage can evolve through three stages. The first is an acute necrosis stage in which the duration of the illness is short. This stage is not recognized clinically and is usually diagnosed at autopsy. The

The clinician should be alert when hypereosinophilia is found.

damage to the endocardium and myocardium is caused by infiltration of eosinophils and lymphocytes. The second is a late thrombotic stage found in those with a mean 10-month duration of eosinophilia. In this stage, formation of thrombi along the damaged endocardium is typical. The third is the late fibrotic stage encountered in those with illness for about 2 years. Progressive scarring develops, and it may lead to entrapment of chordae tendineae, with development of mitral or tricuspid valve regurgitation and endomyocardial fibrosis producing restrictive cardiomyopathy. The cardiac involvement in HES is often presented at the later thrombotic or fibrotic stages (3).

It may be hypothesized that the progress of HES in this patient was the result of discontinued oral steroid treatment for asthma, which had been administered for a long time. The patient was a new immigrant in Israel; therefore, her previous blood count results could not be retrieved.

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Functional polymorphism in the gelatinase B gene and asthma

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Key words: asthma; metalloproteinase; MMP; polymorphism.

● ATOPIC diseases can be perceived as dynamic ailments where chronic inflammation and remodeling of tissues play a role assisted by a family of Zn²⁺- and Ca²⁺-dependent endopeptidases called matrix metalloproteinases (MMPs). Gelatinase B (also known as MMP-9) is one of the MMPs, and its increased levels were found in sputum or bronchoalveolar fluid in asthmatic patients (1). MMP-9 levels were correlated with the number of macrophages and neutrophils (2). The coding gene is situated on chromosome 20q11.2–13.1, a genetic position which has been shown to be linked to bronchial hyperresponsiveness and specific sensitization (3, 4). The results of a previous study (5) suggest that a 9-bp sequence containing the C–1562-T polymorphic site is an important regulatory element. This C–to-T substitution results in a higher promoter activity of the T-allelic promoter. This idea was supported by the higher level of serum MMP-9 found in individuals with the T/T genotype (5). Our study aimed to determine whether this functional polymorphism is important in relation to the etiopathogenesis of atopic asthma.

Caucasian subjects of Czech nationality (*n*=138) were included in this study. We studied 59 patients (35 men and 24 women), aged 24.0 ± 11.6 years, with atopic asthma (eventually in combination with other atopic diseases – allergic rhinitis and atopic

dermatitis). The control group included 79 subjects (43 men and 36 women), aged 28.3 ± 8.1 years without clinical symptoms of any atopic diseases.

Atopy was defined as the presence of at least one of the following signs:

- 1) positive skin prick test (greater than or equal to 3 mm above negative control) to one or more common antigens
- 2) positive specific IgE levels (>0.35 kU/l, by ELISA, DPC, Germany)
- 3) raised total IgE level (greater than 150 IU/ml in nonsmoking adults, Boehringer), as described previously (6).

Asthma was defined according to the American Thoracic Society criteria (7).

All the subjects gave written informed consent to participation in the study. The study was approved by the Ethics Committee, Medical Faculty, Masaryk University, Brno, Czech Republic.

After DNA extraction, the polymorphism (C–1562-T) in the gene for MMP-9 was detected by our modification of the PCR method based on the published SSCP technique (5). The genotype of the individual was evaluated as homozygote [CC], 329 bp; heterozygote [CT], 144, 185, and 329 bp; or homozygote [TT], 144 and 185 bp.

Among the healthy population, the frequencies of the C and T alleles were 0.861 and 0.139; the distributions of the CC, CT, and TT genotypes were 75.9%, 20.3%, and 3.8%, respectively. Among the asthmatics, the frequencies of alleles C and T were 0.856 and 0.144; the distributions of the CC, CT, and TT genotypes were 74.6%, 22.0%, and 3.4%, respectively. No statistically significant differences in the frequencies of the alleles or genotypes were found between asthmatics with low or high values of the pulmonary function tests or between patients with high or low levels of the total serum IgE (data not presented).

MMPs comprise a family of enzymes that play a role in the tissue remodeling and repair associated with inflammation.