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CLINICAL CASE OF RELAPSING POLYCHONDRITIS

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Abstract

Relapsing polychondritis is a rare systemic inflammatory disease of cartilage resulting in structure changes of cartilage until its disappearance. The analysis of the present data on pathogenesis, different clinical manifestations and methods of treatment is performed. The own clinical observation of relapsing polychondritis is described.

Keywords: Relapsing Polychondritis, Diagnostic, Treatment

Relapsing polychondritis (RPC) is a rare systemic disease with an undulating course, presumably of an autoimmune nature, characterized by periodic exacerbations of the inflammatory process in cartilage tissues, leading to their destruction. RPC was first described by Jaksch-Wartenhorst in 1927. This disease can be found under the names systemic chondromalacia, panchondritis, chronic atrophic polychondritis.

To date, about 800 cases of RPC have been described in the world, with about 30 new patients appearing annually. According to the Mayo Clinic, the incidence of the disease is 3.5 cases per 1 million population. Men and women get sick with the same frequency; people of any race can get sick, but more often whites (Caucasians) [1].

To date, the etiological factor of the disease has not been identified. There are indications of an autoimmune mechanism of development, which is confirmed by the discovery in patients during a period of high activity of the process of a large number of antibodies to type II collagen in the blood, and in damaged cartilage tissue, immunofluorescence detects deposits of IgG, IgA, IgM and C3. The fact that a feature of the autoimmune process is damage to cartilage has led researchers to the hypothesis that cartilage-specific antibodies occupy a central place in the pathogenesis of RPC. Circulating immune complexes (CIC) to cartilage-specific collagen types II, IX and XI were detected in 30-70% of patients with RPC. The most characteristic are antibodies to type II collagen, which are present in the acute phase of the disease and their level clearly correlates with the activity of the disease. However, these antibodies cannot be considered specific for RPC, since they are also detected in rheumatoid arthritis (RA). Antineutrophil antibodies are also important in pathogenesis. The role of infectious agents as a trigger for the development of autoimmune disorders cannot be ruled out [2, 3].

Clinical manifestations of RPC vary in location, severity and duration. All types of cartilage can be involved in the pathological process: elastic cartilage of the ear and nose, hyaline cartilage of joints, cartilaginous tissue of the tracheobronchial tree, as well as other structures rich in proteoglycans: eyes, inner ear, blood vessels.

Nasal chondritis is observed in 82% of patients. The cartilaginous septum of the nose is affected, which is manifested by its saddle-shaped deformity. This is the result of long-term inflammation of the cartilage tissue of the nose, in which the collapse of the cartilage and the

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collapse of the nasal bridge occur. However, this symptom may appear during the first attack of the disease. In addition, nasal congestion, rhinorrhea, nosebleeds, and a painful feeling of fullness in the bridge of the nose are noted. Sometimes nasal inflammation is clinically hidden; pain does not always accompany the development of nasal deformity.

Most patients (84% of cases) experience inflammatory changes in the ears. Soreness, swelling, induration, and a violet-erythematous coloration of the outer ear appear, not affecting the lobe. The inflammatory process is usually two-sided: if at the beginning of the disease one ear is affected, then the contralateral or both ears subsequently become inflamed. The attacks can last from several days to several weeks and sometimes end spontaneously. Prolonged and repeated episodes of inflammation lead to a gradual decrease in cartilage tissue and deformation of the auricle. The ear becomes flabby, drooping, shapeless - "cauliflower-shaped ear." Inflammation can involve retroauricular soft tissues, the auditory canal, and structures of the middle and inner ear, causing auditory and vestibular disorders [4, 5].

A variety of eye symptoms occur in 1/2 of patients. They are caused by inflammation of the connective tissue membrane of the eye. Proptosis develops (displacement of the eyeball forward and downward) with chemosis, periorbital edema, and ophthalmoplegia. Cases of scleritis or episcleritis, non-granulomatous uveitis, conjunctivitis, sicca keratoconjunctivitis, retinopathy (microaneurysms, hemorrhages, exudates), venous and arterial thrombosis of the retina, and ischemic neuropathy of the optic nerve have been described.

Articular syndrome in RPC varies from arthralgia to monoarthritis or polyarthritis involving large and small joints and parasternal joints. The classic manifestation of arthropathy in RPC is asymmetric, non-erosive, non-deforming arthritis that resolves spontaneously or with nonsteroidal anti-inflammatory drugs (NSAIDs). Involvement of the sternocostal joints can lead to chest pain and limited respiratory excursion [1].

Damage to the cardiovascular system occurs in 25% of cases of RPC. Aortic insufficiency most often develops due to expansion of the aortic root, which distinguishes it from aortic insufficiency in other rheumatic diseases. Less common are mitral insufficiency, pericarditis, arrhythmias and disorders of the cardiac conduction system. Cases of myocardial infarction have been described.

Respiratory tract involvement is the most severe and prognostically significant manifestation of RPC. Limited airway involvement may be asymptomatic. When inflammation is localized in the area of the larynx and trachea, a nonproductive cough, dysphonia, wheezing, inspiratory shortness of breath, hoarseness, and pain in the area of the thyroid cartilage or the anterior wall of the trachea appear. When the bronchi of the 1st and 2nd order are affected, the clinical picture resembles bronchial asthma. In the early stages of the disease, swelling and proliferation of inflammatory tissue into the lumen of the trachea, pharynx, subpharyngeal space, and larynx predominate. Subsequently, contractures develop due to fibrotic changes, cartilaginous support decreases, which leads to dynamic collapse of the airways during forced inhalation and exhalation. Shortness of breath develops with little physical exertion, a painful cough, and repeated intercurrent infections occur. In severe cases, swelling of the larynx and epiglottis can

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lead to severe increasing shortness of breath, wheezing, asthma attacks, or respiratory failure requiring emergency tracheostomy. Inflammatory processes in the respiratory tract, periodically exacerbating or persistent, lead either to tracheal stenosis or to dynamic collapse of the respiratory tract due to melting of the cartilaginous rings of the trachea and bronchi.

Kidney damage manifests itself in the form of focal proliferative glomerulonephritis, segmental necrotizing glomerulonephritis, which can lead to uremia.

Gastroenterological symptoms: dysphagia due to damage to the pharyngeal cartilage.

Damage to the central nervous system: persistent headache, neuropathy of cranial nerves (II, VI, VII, VIII pairs), seizures, encephalopathy, hemiplegia and ataxia.

The diagnosis of the disease is made taking into account clinical and laboratory data according to diagnostic criteria developed by McAdam in 1976.

To establish a diagnosis of RPC, three or more diagnostic criteria must be met:

- Recurrent chondritis of both ears;
- Nonerosive inflammatory polyarthritis;
- Chondritis of nasal cartilage;
- Inflammation of the tissues of the eyeball (conjunctivitis, keratitis, scleritis/episcleritis and/or uveitis);
- Chondritis of the cartilages of the larynx and/or trachea;
- Damage to the cochlea and/or vestibular apparatus, manifested by sensorineural hearing loss, tinnitus and/or dizziness.

There are no pathognomonic laboratory and instrumental tests for the diagnosis of RPC. Laboratory data are nonspecific and reflect the course of the inflammatory process: increased erythrocyte sedimentation rate (ESR), leukocytosis, thrombocytosis, chronic anemia and increased levels of α- and γ-globulins in the blood serum. Low titers of rheumatoid factor and antinuclear antibodies may be detected. In most patients, ESR is an accurate indicator of disease activity [1].

A biopsy of cartilage tissue is recommended only in extreme cases due to the high likelihood of subsequent wound infection and poor healing. The morphological picture implies foci of fibrosis and necrosis of cartilage tissue against the background of granulation-type inflammation. When performing an immunofluorescence study, class G immunoglobulins are detected, as well as signs of activation of the complement system, including C3D, C4d and C5b-9. At the same time, it is reported that soft tissue biopsy is informative - signs of leukocytoplastic or granulomatous type of vascular damage are revealed [6].

The goal of treatment is to reduce the severity of the symptoms of the disease and prevent cartilage destruction.

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Due to the fact that RPC is a very rare disease, no controlled studies of treatment options have been conducted. The main method of treatment at present is glucocorticoid therapy (GCS). In the acute phase of the disease, prednisolone is prescribed up to 60 mg per day. If the effectiveness is insufficient, the dose of the drug can reach 100 mg per day. Cytostatic drugs are also used: azathioprine, metatrexate, cyclophosphamide, cyclosporine A. There are reports of the effectiveness of the anti-leprosy drug dapsone, which suppresses the lysosomal activity of polymorphonuclear leukocytes. In recent years, the possibility of using genetically engineered biological drugs from the group of tumor necrosis factor inhibitors (infliximab, etanercept), antibodies to diabetes (20 (rituximab) has been widely discussed in the literature. Descriptions of isolated cases of the effectiveness of the use of these drugs are provided, but no specially organized studies have been conducted due to the rare occurrence of the disease [1, 7, 8].

We present a striking case of RPC in a patient observed in the 1st clinic of the Tashkent Medical Academy (TMA).

Clinical case. Patient D, 43 years old, was admitted to the cardio-rheumatology department of TMA on January 30, 2022 with complaints of redness, swelling of both ears, decreased hearing, pain when swallowing, dry cough, hoarseness, redness of the eyes and decreased vision, pain and swelling in small joints of the hands, knees, ankles, dizziness, loss of appetite, weight loss, general malaise.

From his medical history, he considers himself sick since October 2021, when a cough and hoarseness appeared. She received outpatient treatment, but there was no effect from the treatment. In January, swelling and redness of the ears appeared, after 10 days there was swelling of the joints and pain, redness of the eyes and decreased vision. The patient received inpatient treatment for 3 days in the clinic of TMA with the diagnosis: “Diffuse connective tissue disease. Bilateral chondroperichondritis of the auricles, acute sensorineural deafness of the first degree. Chronic fibrinous-plastic uveitis. The following treatment was carried out: ceftriaxone per 1g once a day, rhinoxyl nasal spray 0.1% - 10.0 3-4 drops in each nasal passage, dexamethasone 0.4% - 1 ml IM 1 time No. 3. After improvement of her condition, the patient was referred to the rheumatology center of the TMA and hospitalized in the cardio-rheumatology department. On examination: the general condition is moderate, consciousness is clear. Body type: asthenic type. The skin is pink. Subcutaneous fat tissue is poorly developed. There is no edema, the right axillary lymph node is enlarged. The eyeballs were of normal shape, the sclera were hyperemic, and decreased vision was noted. The ears are swollen, hyperemic, and painful on palpation, hearing is reduced. The nose is deformed like a saddle. Pain, swelling and tenderness when moving in both small joints of the hands, right elbow, right knee, ankle joints. There is vesicular breathing in the lungs, no wheezing. On auscultation, heart sounds are rhythmic and muffled. Blood pressure 110/80 mmHg. Pulse at rest is 96 per minute, rhythmic. The abdomen is soft and painless. The liver is not palpable. Diuresis is free and painless.

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Blood test: hemoglobin – 102 g/l, erythrocytes – 3.6 x 1012/l, leukocytes – 11.8 x 109/l, ESR – 20 mm/hour. Dynamics: hemoglobin – 85 g/l, erythrocytes – 2.8 x 1012/l, leukocytes – 6.2 x 109/l, ESR – 10 mm/hour. Coagulogram: hematocrit - 32%, fibrinogen - 7.87, PTI 91, Thrombotest - 7 degrees.

HbsAg - negative, RW - negative, HVC - negative, TIV - negative. SRB-6 (negative), ASLO – 250.

General urine analysis: protein - 0.099%, epithelium. 7-8/1, leukocytes. 11-15/1, red blood cells. 2-3/1. Dynamics: protein - 0.033%, epithelium. 0-1/1, leukocytes. 2-3/1, red blood cells. 0-1/1.

ECG: sinus tachycardia. Heart rate 112, incomplete blockade of the right bundle branch, metabolic changes in the myocardium.

Chest X-ray: no changes.

MSCT (soft tissues of the neck and chest organs): CT scan did not reveal any signs of pathological formations in the soft tissues of the neck. Uniform narrowing of the glottis should be combined with clinical findings and laryngoscopy data. Chronical bronchitis. Adenopathy of the mediastinal lymph nodes. Pericarditis. Ultrasound (liver, kidneys): echo signs of inflammation of the left kidney.

Currently, there are no standards for the treatment of RPC. A combination of NSAIDs with colchicine and corticosteroids is used. Clinical observations have shown that GCS suppress the activity of the disease, but do not reduce the frequency of relapses, and ¾ of patients require constant therapy with prednisolone at an average daily dose of more than 25 mg, but some patients show resistance to GCS.

Our patient was started on treatment with prednisolone at a dose of 30 mg/day per os, and symptomatic therapy was carried out. Already on the second day of taking prednisolone, an improvement was noted: pain in the joints decreased significantly, scleral injection, cyanosis and swelling of the ears decreased, and body temperature normalized. The patient underwent 3-day pulse therapy: 1st and 3rd days - solumedrol 1.0 g intravenously, 2nd day solumedrol 1.0 g in combination with cyclophosphamide. Over time, ESR decreased and Hb increased. The liver function tests showed some improvement. The patient was discharged with improvement and was recommended to take a dose of prednisolone 30 mg/day under the supervision of a rheumatologist.

Thus, the rapid and pronounced clinical and laboratory effect of GCS treatment confirms the diagnosis of RPC. We think that this disease is little known to doctors of other specialties and the given literature review and description of a clinical case will be useful.

RPC is an urgent disease. It takes 10 months from diagnosis to death. Up to 20 years. The most dangerous manifestations of the disease, in addition to damage to the respiratory tract (56%), is the involvement of the cardiovascular system in the inflammatory process (24%), with the development of aortitis, aortic aneurysm, arterial thrombosis, aortic and mitral valve insufficiency, conduction blocks and myocardial infarction, vasculitis .

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Poor prognostic signs are: onset at a young age, systemic vasculitis, early saddle nose deformity, anemia in the elderly. A large study conducted at the Mayo Clinic found that in a group of 112 patients, the 5-year survival rate was 74% and the 10-year survival rate was 55%. The main causes of death were infectious diseases and systemic vasculitis, 15% of patients died from damage to the respiratory tract and heart. The rarity of the disease and the low awareness of doctors of various specialties encourage patients and specialists dealing with the problem of cancer to unite.

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