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Granulomatosis with polyangiitis – diagnostic difficulties?

Ziarniniakowatość z zapaleniem naczyń – problemy diagnostyczne?

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Słowa kluczowe: ziarniniakowatość z zapaleniem naczyń, przeciwciała ANCA, limfadenopatia.

Summary

Granulomatosis with polyangiitis (GPA) is characterized by necrotic vasculitis of the medium and small vessels, granuloma formation and presence of antineutrophil cytoplasmic antibodies against proteinase-3 in serum. The upper respiratory tract, lower respiratory tract and kidneys are usually involved in the disease. Atypical clinical presentation may generate problems. In this report we present a case in which the diagnosis of GPA was possible, but was verified during in further clinical observation.

We present the medical history of a 70-year-old woman with ocular symptoms, nasal discharge, progressive hearing impairment, craniofacial inflammatory infiltrates, lymphadenopathy, and microscopic haematuria in laboratory tests. Histopathology did not confirm GPA. cANCA tests were also negative. Finally, after mediastinoscopy and histopathological evaluation of the lymph nodes, the diagnosis of B-cell lymphoma was established.

Streszczenie

Ziarniniakowatość z zapaleniem naczyń (GPA) charakteryzuje się występowaniem martwiczego zapalenia małych i średnich naczyń krwionośnych z powstawaniem ziarniniaków i obecnością w surowicy przeciwciał skierowanych przeciwko proteinazie 3. Procesem chorobowym zajęte są przede wszystkim górne i dolne drogi oddechowe oraz nerki. Problem kliniczny stanowią przypadki o nietypowym przebiegu. W artykule przedstawiono przypadek kliniczny, w którym rozpoznanie ziarniniakowatości z zapaleniem naczyń wydawało się prawdopodobne, jednak z czasem zweryfikowano postawioną uprzednio diagnozę. Przedstawiono historię 70-letniej pacjentki, u której obserwowano zmiany oczne, patologiczną wydzielinę z nosa, postępujący niedosłuch, zmiany naciekowe w obrębie części twarzowej czaszki, limfadenopatię oraz erytrocyturię w badaniach laboratoryjnych. U chorej nie uzyskano potwierdzenia histopatologicznego GPA, powtarzane badania w kierunku obecności przeciwciał cANCA były negatywne. Ostatecznie po wykonaniu mediastinoskopii na podstawie badania histopatologicznego węzła chłonnego ustalono rozpoznanie chłoniaka z komórek B.

Introduction

Granulomatosis with polyangiitis (GPA) is associated with a characteristic presence of necrotic vasculitis of small and medium-sized blood vessels, accompanied by the formation of granulomas and serum presence of antibodies against proteinase 3 (cANCA, PR3-ANCA) [1]. The upper and lower respiratory tract and kidneys are organs that are especially affected by the disease [2]. The classification criteria of the American College of Rheumatology of 1990 are especially helpful to diagnose this disease [3]. They include: presence of ulcers in the oral cavity or pathologic nasal discharge, lesions observed in a radiological examination of the lungs (nodules, cavities, infiltrations), abnormalities in the urinary sediments (erythrocyturia > 5 hpf or presence of erythrocytic casts), and presence of granulomatous inflammation confirmed in a histopathological examination [4]. When at least 2 of these criteria are met, it is possible to make a diagnosis with the sensitivity of 88.2% and the specificity of 92% [4].

Various symptoms of GPA, especially in cases where typical clinical symptoms and immune disturbances are present, are usually not associated with diagnostic

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problems. Cases with an atypical course are a clinical problem. This paper presents a clinical case where the diagnosis of granulomatosis with polyangiitis seemed probable. However, due to a doubtful clinical picture the researchers were forced to search for other reasons for the abnormalities observed. Finally, the diagnosis made earlier was verified.

Case report

A 70-year-old female patient with arterial hypertension and type 2 diabetes mellitus treated with insulin presented to her GP due to conjunctival redness and a feeling of sand under her eyelids. Conjunctivitis was initially diagnosed, followed by glaucoma. However, complaints did not regress after standard therapy. One month later the patient developed tinnitus, a sensation of pulsation and hypoacusis in her left ear, watery nasal discharge, dry oral cavity, and pain and edema of her right knee. Antibiotic therapy was started but no improvement was observed. Based on the clinical picture and ENT examination (swelling of the mucosa of the inferior nasal conchae with hemorrhage, hyperplasia of the mucosa in the nasopharyngeal cavity and in the subvocal region of the larynx, exudative otitis media on the left side) granulomatosis with polyangiitis was suspected. A general urine analysis revealed erythrocyturia and acanthocytes. A computed tomography scan of the ears revealed inflammatory changes of both mammillary processes, more advanced on the left side, and inflammation of the left tympanic cavity. Magnetic resonance imaging of the facial skeleton revealed streak-like tissue infiltrations in the temporal and subtemporal areas changing into nodular thickening of the upper eyelids. Small nodules of the same morphology were also observed inside the orbital cavities along the surface of both parotid glands. Computed tomography of the chest revealed the presence of concentric thickening of the tracheal and bronchial walls, as well as lesions in the lymph nodes forming pockets in the mediastinum and in both pulmonary hila. Enlarged lymph nodes were also present in both axillary fossa, and in the supra and subclavicular areas (with dimensions up to 20 × 13 mm).

The clinical picture suggested GPA; however, there were still doubts with regard to the diagnosis. The serum tests were negative for ANCA, and laboratory inflammation markers were low (ESR 4 mm/h, CRP 1.02 mg/l). Complete blood count revealed: leukocytes 4.56 (neutrophils 47.4%, lymphocytes 44.5%, monocytes 5.7%, eosinophils 2%, basophils 0.2%), erythrocytes 5.07 M/µl, platelets 115 K/µl. The serum protein levels were at the lower limit of the normal range (6.6 g/dl). There were no anti-cardiolipin or anti-nuclear antibodies.

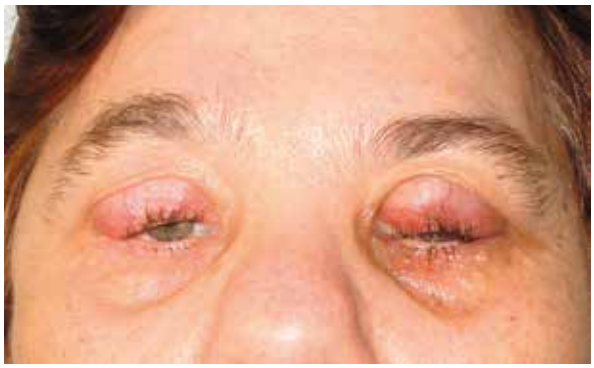

Fig. 1. Infiltrates of the eyelids and nose.

During diagnostic tests, tissue specimens from the eyelids and nasopharyngeal cavity were collected, but no significant histopathological lesions were visualized. A specimen from the area of the left parotid gland revealed chronic, active, predominantly lymphocytic, non-specific inflammatory infiltration located mainly in the gland stroma. No features of GPA or sarcoidosis were observed.

The patient's general status gradually deteriorated. The swelling of the face, eyelids (Fig. 1), and hard and soft palate increased. Bilateral hypoacusis progressed, and symptoms of chronic sinusitis were still present. Dry cough appeared and effort tolerance was impaired (signs of respiratory tract obstruction appeared above the lung fields). For life-saving reasons a decision was made to administer a methylprednisolone infusion (500 mg IV), and then to continue oral steroids (methylprednisolone at a dose of 16 mg/d).

Subjective and clinical improvement was observed. However, a unanimous diagnosis was still not made. Mediastinoscopy was performed, and mediastinal lymph nodes were collected for a histopathological evaluation. The result obtained was small B-cell lymphoma. The patient was referred for further hematological treatment.

Summary

Granulomatosis with polyangiitis is a rare systemic connective tissue disorder. The clinical picture of this disease is not always typical, and due to various symptomatology its diagnosis may be a serious problem and therefore a wide differential diagnosis is necessary. It should always be remembered that many diseases may imitate GPA. Therefore diagnosis, especially in cases with an atypical clinical course (negative serology, atypical location of organ lesions), has to be carefully evaluated and verified if possible.

The authors declare no conflict of interest.

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