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OPIS PRZYPADKU
CASE REPORT

Diagnostic traps in orbital diseases – analysis and comparison of two cases

Pułapki diagnostyczne w chorobach oczodołu – analiza i porównanie dwóch przypadków

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ABSTRACT

Proptosis is a characteristic sign that might suggest the diagnosis of different diseases. Proptosis is characterised by the anterior displacement of the eye and its protrusion. The most commonly associated symptoms of proptosis are deteriorated vision, elevated intraocular pressure and inflammation of periocular tissues. The presented study describes two cases of patients with proptosis and periocular pain. In each case, the primary cause of proptosis was initially incorrectly diagnosed and required in-depth diagnostics.

In Patient A extrabulbar optic neuritis caused by Lyme disease was suspected and treated with steroids and antibiotics. Subsequently, Graves' disease was diagnosed and treated with anti-thymocyte globulin. Complete loss of vision was observed after one month of treatment. Radiotherapy and steroid therapy were introduced. Afterwards, the patient's vision was restored.

Patient B, who was treated for hypothyroidism, was admitted to the hospital with elevated intraocular pressure, double vision, a restricted visual field and proptosis. The primary diagnosis was Graves' ophthalmopathy (GO). However, after in-depth imaging and pathomorphological studies of a specimen taken from the orbit, B-cell lymphoma was diagnosed. After the introduction of correct treatment, significant improvement was noted.

Presented work indicates that in-depth diagnostics are crucial when it comes to the differential diagnosis of GO and a tumor of the orbital cavity.

KEY WORDS

Graves' disease, lymphoma, tumors, orbital disease

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STRESZCZENIE

Wytrzeszcz jest objawem charakterystycznym w różnych jednostkach chorobowych. To przemieszczenie gałki ocznej oraz jej wysunięcie do przodu. Pacjentom z wytrzeszczem najczęściej towarzyszą takie objawy, jak pogorszenie widzenia, wzrost ciśnienia śródgałkowego oraz zapalenie tkanek okołooczodołowych. W pracy opisano dwa przypadki pacjentów z objawami wytrzeszczu oraz bólu okołogałkowego, którego pierwotna przyczyna nie została właściwie rozpoznana i wymagała pogłębionej diagnostyki.

U pacjenta A wysunięto podejrzenie pozagałkowego zapalenia nerwu wzrokowego w przebiegu choroby z Lyme, leczonego glikokortykosteroidami i antybiotykami. Następnie rozpoznano chorobę Gravesa i zastosowano leczenie globuliną antytymocytarną. Po miesiącu terapii zaobserwowano całkowitą utratę wzroku. Wdrożono radioterapię i sterydoterapię, uzyskując powrót widzenia.

Pacjent B, leczony przewlekle na niedoczynność tarczycy, zgłosił się do szpitala z podwyższonym ciśnieniem śródgałkowym, dwojeniem, ograniczeniem pola widzenia oraz wytrzeszczem. Początkowo diagnostyka wskazywała na oftalmopatię Gravesa (*Graves' ophthalmopathy* – GO). Jednak po wykonaniu badań obrazowych oraz patomorfologicznych pobranego z oczodołu wycinka stwierdzono chłoniaka z drobnej komórki B. Po wprowadzeniu leczenia nastąpiła znaczna poprawa.

W pracy pokazano, jak ważna w przypadku rozpoznania różnicowego pomiędzy chorobami o etiologii zapalnej i nowotworowej jest pogłębiona diagnostyka.

KEY WORDS

choroba Gravesa, chłoniak, nowotwory, choroby oczodołu

INTRODUCTION

In ophthalmologic diseases like optic neuropathy, Graves' ophthalmopathy (GO) and orbital tumors, the symptoms might be very similar and unspecified. The most common are proptosis, periocular pain, visual disturbances, sight loss and eyelid swelling [1,2].

In this research paper the diagnostic processes and differential diagnosis of ocular diseases in patients that have more than one clinical cause are compared. Differential analysis of two patients that were hospitalized in an ophthalmology ward in Katowice was performed. Each case required in-depth diagnostics due to non-specific symptoms.

CASE REPORTS

Case 1

Patient A, a 71-year-old, was diagnosed with Hashimoto disease. Six years earlier, his prostate gland was removed. In 2018 he reported binocular diplopia. In July Lyme disease was diagnosed, the patient was treated with doxycycline from September, but unfortunately he did not report any improvement. In January 2019 he was hospitalized in the infectious diseases ward and during examination neuroborreliosis was excluded. Magnetic resonance imaging (MRI) showed thickening of the upper and lower rectus muscles of the left eye. The patient took methylprednisolone orally from 32 mg, every 7 days reducing the dose by half, and ceftriaxone for 30 days. In March 2019 he was hospitalized again, borreliosis was confirmed; however, neuroborreliosis was excluded. The double vision persisted. Methylprednisolone was re-prescribed from 16 mg with a gradual dose reduction. In May 2019, he received ceftriaxone again. In July, he was suddenly admitted to the ophthalmology ward due to severe pain in the left eye and changes in colour saturation. Left optic neuritis was diagnosed. The patient was hospitalized and treated with methylprednisolone i.v. and methylprednisolone orally with little improvement. After in-depth diagnostics the patient was diagnosed with GO and was referred for endocrine therapy. Additionally, high intraocular pressure in the upward position of the eyes was found (23–31 mmHg) and anti-glaucomatous treatment was started (dorzolamide, timolol, brimonidine). The patient was qualified for the administration of anti-thymocyte globulin (ATG) and he received 2 doses. Despite the therapy, his eyesight was almost completely lost (best-corrected visual acuity – BCVA – 0.7 in the right eye and hand movements of the left eye). Methylprednisolone (total dose 6.0 i.v.) was prescribed for two weeks and continued orally with dose reduction. Radiation therapy of the retrobulbar region was performed. The patient regained vision acuity and the visual field improved (BCVA 1.0 in the right eye and 0.9 in the left eye). The ocular pain and double vision disappeared.

Case 2

Patient B, a 71-year-old, his medical history started with the diagnosis of hypothyroidism in 2015, which was managed with iodine treatment. In July 2018, protrusion of the patient's right eye, elevated intraocular pressure and diplopia were found. The diagnosis was right eye proptosis caused by Graves' disease. Because of progression of the complaints, the patient was admitted to the hospital in September 2018. MRI of the orbits showed neoplastic tissue in the superolateral part measuring 38/18 mm, modelling the lateral rectus muscle, superior rectus muscle, superior

oblique muscle and other orbital cavity structures. At the same height in the left orbital cavity there was a similar lesion measuring 16/9 mm, modelling the lateral rectus muscle and infiltrating the lacrimal gland. Non-specific inflammation of the orbits was recognized. The patient received medical recommendations which were methylprednisolone i.v. and then orally, and topically dexamethasone, dorzolamide, timolol and brimonidine. Two weeks later loteprednol etabonate was added and neurologic as well as laryngological consultations were recommended. In December 2018 the patient was admitted to the emergency ward due to right eye swelling. He admitted to not sticking to his treatment. The previously established medication was applied and 16 mg methylprednisolone was added. In January 2019, he was referred for a biopsy of the right orbit. A surgical biopsy was performed in the ophthalmology ward. Histopathological investigation revealed small B-cell lymphoma. After the diagnosis the patient began treatment in the Haematology ward. In October 2019 cataract surgery of the right eye was performed. For treatment dorzolamide, timolol and brimonidine were continued. BCVA of both eyes is now 1.0.

DISCUSSION

In various orbit diseases like inflammation of the orbit, B-cell lymphoma and GO, the clinical pictures might be similar. Pain, decreased vision and visual field loss but without swelling of the orbital tissues and proptosis are common in extrabulbar optic neuritis. Unfortunately, these diseases are very alike and difficult to differentiate without performing in-depth diagnostics.

Lyme disease (Lyme borreliosis) is caused by *Borrelia burgdorferi* that lives in animals (ticks) and can be transmitted to humans. Neuroborreliosis is a neurological manifestation of the disease that occurs several weeks after the transmission from the animal. It can affect every cranial nerve, even the optic nerve. The inflammation of cranial nerves II, III, IV or VI may cause diplopia and optic neuritis, leading to visual acuity or visual field loss, abnormal color saturation, in addition to periocular pain [3].

B-cell lymphoma is a malignant lymphoid tumor that grows from a type B lymphocyte. One of its types is extranodal marginal zone lymphoma (ENMZL) that grows from ocular adnexa. The main causes are genetic abnormalities and immunological disorders [4]. Orbital manifestation of the lymphoid tumor is similar to inflammation. An early biopsy may lead to early diagnosis and treatment. If it is possible, it should be done prior to non-specific conservative anti-inflammatory treatment [5].

GO is an ophthalmological manifestation of Graves' disease, which is an autoimmunological disorder of the thyroid. Genetics and environmental factors may lead to GO. Thyrotropin (TSH) receptors are targeted by the antibodies (TSHR-Ab) produced by B lymphocytes, which causes hyperthyroidism. TSH receptors are also present on the fibroblasts and adipocytes of orbital tissues. An immunological reaction leads to the production of proinflammatory cytokines and glycosaminoglycans (GAG). All these factors lead to edema, proptosis and the inflammatory infiltration of orbital tissues [6]. Extraocular muscle inflammation causes a restriction of ocular movements and IOP elevation. The most serious complication of the process is compressive optic neuropathy, which may cause transient or even permanent visual loss in 3% to 7% of cases. All these processes finally cause the fibrosis of orbital tissue [1,7].

The patients who were described above were admitted to the ophthalmology ward with proptosis, but its origins were different (Table I). Patient A was treated for neuroborreliosis and optic neuritis with antibiotics, but without recovery. GO was diagnosed when optic neuropathy did not improve.

Patient B was hospitalized because of the suspicion of GO. However, MRI examination showed neoplastic tissues in the area of right and left orbital cavities. After biopsy and further examination B-cell lymphoma was diagnosed.

Table I. Comparison of patients' age, symptoms, and diagnoses
Tabela I. Zestawienie wieku, objawów oraz diagnoz pacjentów

Characteristics	Patient A	Patient B
Age when diagnosed	71	70
Proptosis	+	+
Visual acuity loss	+	–
High IOP	+	+
Hypothyroidism	+	+
Primary diagnosis	Borreliosis/extrabulbar optic neuritis	Graves' ophthalmopathy
Final diagnosis	Graves' ophthalmopathy	B-cell lymphoma
Time to diagnosis (months)	18	10

To apply a treatment that is really effective, a correct diagnosis must be made. We aim to discuss conditions that present similar symptoms, though the treatment is radically different (Figure 1).

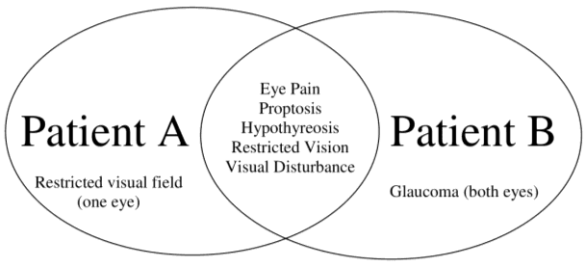

Fig. 1. Presentation of common symptoms for patients. Patient A and B – eye pain, proptosis, hypothyreosis, restricted vision and visual disturbances.

Ryc. 1. Prezentacja typowych objawów występujących u pacjentów. Pacjenci A oraz B – ból oka, wytrzeszcz, hypotyreoza, ograniczenie pola widzenia, zaburzenia widzenia.

Useful diagnostic tools that help physicians to distinguish between different eye diseases are computed tomography (CT) and MRI. These methods help to evaluate muscle swelling, the compression of optic nerves or additionally include or exclude GO as the cause, as well as orbital tumor [6,8]. When a tumor is suspected, surgical biopsy and histological examination of the tissues should be done by a pathomorphologist. In that way, extranodal marginal zone B-cell lymphoma can be confirmed [9].

CONCLUSIONS

Lesions in the area of the orbit are often difficult to diagnose and require in-depth diagnostics that include radiological and pathomorphological examination. Pain, proptosis and visual disturbances are common features for different diagnoses of inflammation and neoplastic proliferation as well.

Patient consent

All the patients gave informed consent to participate in the study.

Declaration of conflicting interests

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