CASE REPORT

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SARCOIDOSIS OF THE ORBIT: A RARE CLINICAL CASE AND LITERATURE REVIEW

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Abstract. *Sarcoidosis is a systemic disease of still-unknown etiology in which characteristic granulomas develop in various parts of the body. Symptoms depend on the localization of the formations. The isolated orbital form, in which granulomas develop only in the orbit of the eye, is very rare and presents a challenge in terms of differential diagnosis. Treatment for the orbital form may include a conservative, surgical, or combined approach. The goal of surgical treatment is to completely remove the tumour formation, which achieves excellent results in many cases. The current article presents a clinical case of an isolated orbital form of sarcoidosis, in which surgical treatment was undertaken with complete removal of the granulomatous formation. In the postoperative follow-up, a complete reversal of the symptoms was observed without residual disturbances in vision or eye movements.*

Key words: *isolated sarcoidosis, orbital tumour, exophthalmos*

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INTRODUCTION

Sarcoidosis is a systemic disease with an unclear etiology and pathogenesis [1]. Some authors accept it as a non-caseous granulomatous inflammatory process. Other authors suspect an autoimmune condition with an unknown triggering mechanism [1]. Histologically, the sarcoidosis granulomas show a tuberculosis-like pattern. The granulomatous tissue is composed of epitheloid and giant multinucleated cells but lacks the indicative caseous tissue of tuberculosis [1]. The absence of Mycobacterium tuberculosis bacteria in the granulomatous formations also excludes tuberculosis as a differential diagnosis [1].

Sarcoidosis most often affects the lungs (over 90% of the cases), but the characteristic granulomas can develop in many other organs as well [2]. In some cases, granulomas can be disseminated in various organs at the same time. Frequently involved are the lymphatic system and the skin [2]. The central and peripheral nervous systems are affected in 5-15% of all patients [3]. Fairly common is the ocular form of sarcoidosis (more than 40% of cases), in which the eye is affected and which can lead to visual disturbances [2]. Cases in which granulomas are found only in the orbit and its adnexa are classified as isolated orbital sarcoidosis [4].

The symptoms can vary widely according to the location of the formations, which can compress anatomic structures or obstruct hollow organs [5].

The disease creates serious diagnostic and therapeutic difficulties, but the prognosis is usually favourable [5]. Treatment encompasses different approaches, including the administration of various medications in most instances and surgical methods in select cases [2].

The current article presents a case of orbital sarcoidosis, in which the granulomatous formation caused

large exophthalmos and seriously impaired ocular movements. The granuloma affected the orbital adnexa without involving the eyeball. After surgical treatment, a complete reversal of the symptoms occurred.

CASE PRESENTATION

The current clinical case concerns a 61-year-old female with known arterial hypertension and type 2 diabetes mellitus on peroral drug therapy and with optimal control of arterial blood pressure and blood glucose levels. The medications, regularly taken by the patient, were as follows (Table 1):

Table 1. Medications, taken regularly prior to the diagnosis of orbital sarcoidosis

Medication	Dosage	Dosage interval
Perindopril/amlodimipine indapamide	4 mg/ 5 mg/1.25 mg	1 tablet/ day in the morning
Amlodipine	5 mg	1 tablet/ day in the evening
Nebivolol	5 mg	1 tablet/ day in the morning
Saxagliptin/ metformin	2.5 mg/ 850 mg	2x1 tablets/ day

The initial symptoms of the patient were hard to define. A slowly progressing discomfort in the right orbit for about a year prior to the first examination was reported. A few months before the first clinical examination, the right eye was progressively protruding, and the patient experienced difficulties moving the eye bulb in the desired direction. The condition progressed slowly until complete loss of eye movement capabilities was developed. No visual acuity impairment was reported.

The patient was referred to an ophthalmologist, who found a large exophthalmos of the right eye with caudal-medial displacement of the eye bulb, complete immobilization of the right eye, ptosis of the right eyelid, and conjunctival ecchymosis. The visual acuity was slightly impaired for the right eye, while the intraocular pressure was normal bilaterally.

An MRI scan of the head was performed, which visualized a soft tissue formation in the right orbit adjacent to the lacrimal gland. The dimensions of the lesion were 35 mm axial and 22 mm cranio-caudal (Fig. 1). A chest X-ray (Fig. 2) excluded the presence of lung tumour lesions, while blood and urine laboratory results were within reference values. The patient was referred to a neurosurgeon.

Following an evaluation by a cardiologist and an endocrinologist, a surgical procedure in the neurosurgery department was conducted. By means of a limited fronto-orbito-zygomatic craniotomy, a tumour lesion in the right orbit was visualized using intraoperative ultrasound. The tumour formation, which partially engaged the dura mater, the lacrimal gland, the eyelid, and the lateral rectus muscle, was reached via orbitotomy. After a complete macroscopical removal of the tumour lesion, the dura mater was reconstructed. Finally, a cranioplasty with a 40/50 mm titanium mesh was performed.

Histologically, the removed lesion consisted of multiple non-caseating granulomas containing epitheloid cells. Among the granulomas, small lymphoid aggregates were found without the formation of lymph follicles. The data was consistent with the picture of orbital sarcoidosis (Fig. 3).

Postoperatively, a chest CT (Fig. 4) was conducted, which excluded dissemination of the granulomatous process in the lung. During follow-up one year after the operation, the visual acuity of the patient was normal for both eyes, and the additional symptoms were fully subsided: full reversal of the function of the oculomotor muscles and normal position and func-

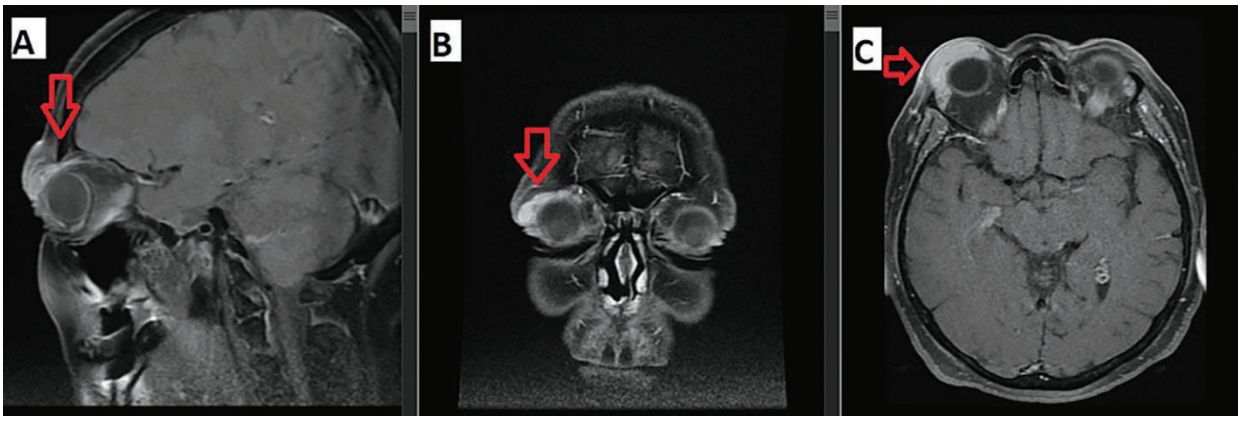

Fig. 1. Sagittal (A), coronal (B) and axial (C) MRI images of the tumour lesion in the right orbit

tion of the right eyelid were observed. An MRI scan confirmed the normal appearance of the orbits bilaterally, with postoperative changes in the right orbit and the normal position and appearance of the optic nerves and oculomotor muscles (Fig. 5).

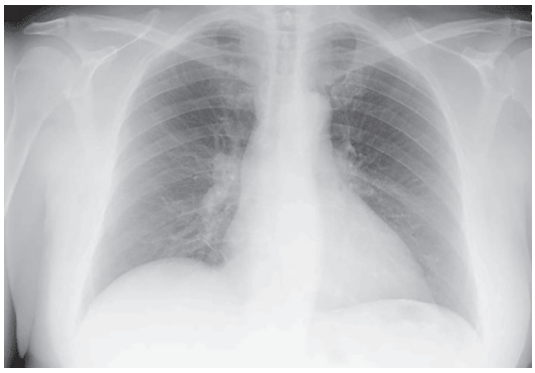

Fig. 2. Chest X-ray of the thorax in PA projection shows a normal appearance of the lungs with no focal changes or pleural effusions

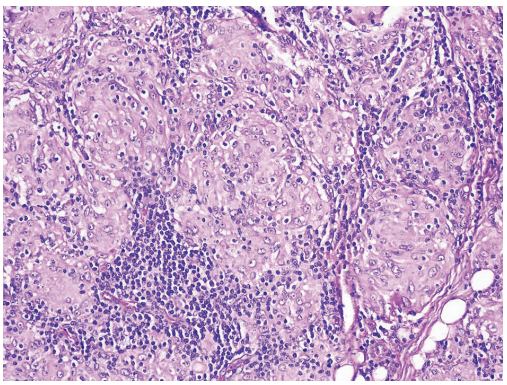

Fig. 3. Histological pattern of the granulomatous tissue in the removed tissue specimen

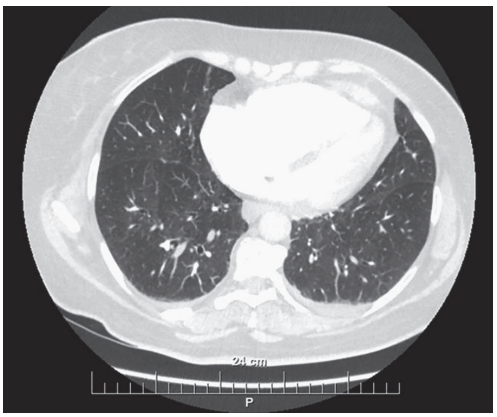

Fig. 4. Chest CT image with contrast, showing normal appearance of lung bases and heart, and which excluded lung dissemination of sarcoidosis

DISCUSSION

Sarcoidosis is a systemic granulomatous inflammatory disease that has no clinical or laboratory pathognomonic features. That makes the establishment of the diagnosis more difficult [5].

The aetiological causes of the disease are still unclear. There is a genetic predisposition, so some still-unknown genetic factors must play a role. Environmental factors also contribute to the development of the condition [1]. Research shows that the pathogenesis of sarcoidosis involves non-specifically activated T lymphocytes, which suggests that various immune system processes can also be responsible [2].

In the isolated orbital form of sarcoidosis, the soft tissues of the orbit, the lacrimal gland, the optic nerve, and the oculomotor muscles can be affected [4].

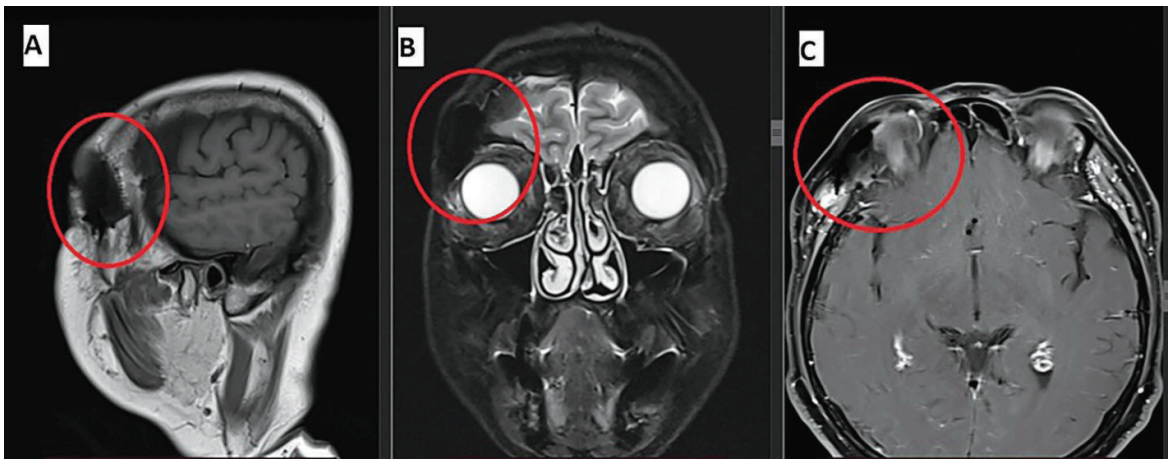

Fig. 5. Postoperative sagittal (A), coronal (B) and axial (C) MRI images of the head; the postoperative changes, where the extirpated lesion was once located, are shown with red circle

However, only a single instance has been observed in which bone destruction of the orbital walls was found [6].

The actual incidence of the isolated orbital form of the disease varies according to different authors. In most reports, it accounts for less than 10% of all sarcoidosis cases. Some authors observed sarcoidosis of the orbit and its adnexa in 8% of patients with confirmed sarcoidosis [7], while others determined its frequency at approximately 28% [8]. The most often affected orbital structure was the lacrimal gland [7]. Isolated orbital involvement is therefore uncommon, and it presents a challenge in terms of differential diagnosis, treatment, and follow-up [9].

The granulomatous lesions of orbital sarcoidosis can imitate the symptoms of a number of other pathological conditions [9]. Failure to establish a correct diagnosis can have serious negative outcomes [9]. A characteristic of orbital sarcoidosis is the discreet onset of the symptoms. There is an initial latent phase, in which there are no symptoms, and the course of the disease is usually slow and painless. Acute onset is extremely rare. Clinical manifestations may include increased lacrimation, orbital pain, eye movement impairment, and visual disturbances like diplopia and even blindness in extreme cases [9]. When the lacrimal gland is involved, proptosis and diplopia are usually observed [10]. Most often, patients are in good general condition with eyelid swelling and a palpable orbital painless mass [7, 9]. When the granulomatous process is located in the back of the orbital cone, vision loss can occur because of the greater spatial confinement in the area and the potential compression of the optic nerve [6].

Usually, the diagnosis is established by means of the method of exclusion [11]. The so-called orbital pseudotumor, lymphoma lesions, secondary cancer metastases, endocrine ophthalmopathy, vasculitis, some drug and bisphosphonate intoxications, and thalassemia should be considered as a differential diagnosis [2, 12].

The diagnostic process is based on CT and MRI studies, which complement each other [13]. CT scans are better at showing bone structures. In some cases, they provide easier differentiation of orbital fat tissue, areas of inflammatory changes, periorbital sinuses, and the oculomotor muscles. Bilateral hilar lymphadenopathy on radiographs or CT images is suggestive of sarcoidosis [4]. A lung CT is mandatory in order to rule out alternative lung pathologies. It can also determine the extent of the disease [7, 14]. A PET/CT scan provides information about the eventual whole-body dissemination of the disease [5]. It can also be of great value in monitoring the efficacy of the treatment.

MRI imaging facilitates a clearer visualization of the orbital cone, the superior orbital fissure, and the cavernous sinus. It also helps in better differentiating the soft tissue structures of the orbit. In T2W1 sequences, the area of granulomatous inflammation is marked by a less dense signal, while a denser signal is more typical for processes like metastases or lymphoproliferative diseases [15, 16].

In 60-90 % of sarcoidosis cases, the epithelial cells surrounding the granulomas secrete angiotensin-converting enzyme (ACE), which can be quantitatively detected and can contribute to establishing the diagnosis [17]. ACE has reference values below 50 U/l. The increased levels of ACE in the cerebrospinal fluid or the blood serum can be suggestive of sarcoidosis [17]. However, this biomarker is not specific and can also be increased in cases of hyperthyroidism, diabetes mellitus, joint inflammation, and other conditions. The results of the tuberculin tests and the functional liver tests are not essential for the differential diagnosis. Histological examination is crucial for confirming the diagnosis [5]. It is the only definitive diagnostic method. Biopsy material can be obtained from an aspiration punctate or from fragments of surgically resected lesions.

Treatment options are various and depend on the location of sarcoidosis granulomas and the level of functional organ damage caused by the lesions. The most commonly used treatment strategy is systemic therapy: the administration of corticosteroids or cytostatic drugs. The preferred initial regimen is oral corticosteroids, with a starting dose of 1 mg of prednisone equivalent per kilogram of body weight and then progressively reducing the dose over a period of three months [18, 19]. In order to avoid the systemic side effects of corticosteroids, some authors prefer local application by means of periorbital injection [7, 19]. This approach can also be implemented when corticosteroid intolerance is observed.

Methotrexate and other cytotoxic agents, such as azathioprine and cyclophosphamide, are considered when corticosteroids do not achieve satisfying results. Other authors use infliximab (an anti-tumour-necrotizing factor alpha monoclonal antibody) or other monoclonal antibodies [18]. Antimalarial drugs such as hydroxychloroquine can also sometimes be used with varying efficacy [18]. Some authors prefer different combinations of the aforementioned drugs [18].

Surgery may be an alternative or complementary to drug administration in select cases of orbital sarcoidosis. Surgical methods provide the singular defini-

tive biopsy-obtaining technique and solve all problems related to differential diagnosis. Moreover, surgical removal of solitary and well-defined lesions, if achievable, can produce good results when looking for prompt symptom relief. It must be noted, however, that surgery should be reserved only for cases in which conservative therapy is not effective in symptom control.

CONCLUSIONS

Isolated sarcoidosis of the orbit and its adnexa is a relatively rare condition, creating diagnostic and therapeutic difficulties. Clinical manifestations are diverse, and imaging and laboratory features are not specific. Corticosteroids are usually applied, especially in the early stages of the disease, with variable therapeutic efficacy. Operative treatment can achieve good results in symptom relief and guarantee the establishment of the diagnosis by means of histological examination. Surgery, therefore, might provide an additional treatment option complementing systemic drug therapy in select cases.

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