# GIANT PROLACTINOMA. A CASE REPORT

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## SUMMARY

**Aim:** Prolactinoma is a pituitary adenoma that secretes prolactin. Approximately 40% of all pituitary adenomas are prolactinomas. According to size, they are divided into micro, macro and giant prolactinomas. In women, prolactinomas cause irregularities of the menstrual cycle such as amenorrhea, galactorrhea, weight gain, in both sexes they cause sterility, hypogonadism, decreased libido and depression. In macroadenomas, symptoms due to the compression of the surrounding structures are also manifested, such as headache, vomiting, lower chiasmatic syndrome and ophthalmoplegia. Loss of the visual field due to compression of the optic chiasm is caused by a tumor larger than 10–15 mm with suprasellar spreading, which breaks through the diaphragma sellae. Giant prolactinomas are larger than 40 mm and make up 1–5% of all prolactinomas.
**Case report:** In this article I present the case of a 38-year-old woman from Ukraine with advanced chiasmatic syndrome caused by a giant prolactinoma. The tumor is infiltrating the left cavernous sinus, causing left-sided amaurosis and right-sided temporal hemianopsia.
**Conclusion:** Inferior chiasmatic syndrome is characterized by bitemporal hemianopsia, a deterioration of visual acuity, bilateral bow-tie descendent atrophy of the optic nerve disc, and hemianopic rigidity of the pupils. Macroprolactinomas occur more frequently in men than in women. The diagnosis is often delayed, probably because the symptoms of hyperprolactinemia are less obvious in men, while women tend to present earlier due to menstrual cycle irregularities. Prolactinomas usually have a good prognosis. Effective medical treatment with dopamine agonists is available. Knowledge of the prolactinoma symptoms could help the diagnosis of compressive lesions of the optic chiasm.
**Key words:** prolactinoma, pituitary gland, bitemporal hemianopsia, hyperprolactinemia

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## INTRODUCTION

Prolactinoma is a pituitary adenoma that secretes prolactin. Approximately 40% of all pituitary adenomas are prolactinomas, according to epidemiological studies their prevalence is 50/100 000 and the incidence is 3–5/100 000 of the population per year [1]. It is diagnosed more frequently in women than in men. In women, hyperprolactinemia causes amenorrhea, galactorrhea, sterility, weight gain, water retention and depression. Osteoporosis occurs as a consequence of the deficit of sex hormones. In men it is manifested in hypogonadism, decreased libido, impotence, sterility, hair loss, arterial hypotension, acromegaly, and in rare cases gynecomastia and galactorrhea. The symptoms in men are less pronounced, as a result of which the diagnosis of the condition is often delayed [1,2].

According to size, they are divided into microprolactinomas (up to 10 mm), macroprolactinomas (more than 10 mm) and in rare cases giant prolactinomas, with a size of over 40 mm. Microprolactinomas are diagnosed more commonly in women, and make up 60% of all prolactinomas. Thanks to their slow growth they have a good prognosis. Macroprolactinomas are diagnosed more commonly in men. In addition to manifestations of hyperprolactinemia, they are also accompanied by symptoms caused by the compression of the surrounding structures,

such as headache, vomiting, disorders of the visual field or manifestations caused by compression of the cranial nerves. Giant prolactinomas are rare and make up 1–5% of all prolactinomas. They are usually diagnosed within the age range of 20–50 years in men, and less commonly in post-menopausal women, with the reported ratio of men to women at 9:1. Although giant prolactinomas are generally benign, their local growth may be invasive, and potential manifestations include behavioral changes, dementia, hemiparesis, epilepsy or rhinorrhea [1–3].

Ocular manifestations of a pituitary tumor include disorder of color perception, defects in the visual field, descendent atrophy of the optic nerve, headache, motility disorder of the extraocular muscles, and in rare cases exophthalmos or Horner syndrome. Edema of the optic nerve disc (OND) is rare. Ophthalmoplegia results upon compression of the cranial nerves which pass through the cavernous sinus [4]. Inferior chiasmatic syndrome is caused by compression of the optic chiasm from the inferior side. It ensues upon compression of crossing fibers from the inferior nasal quadrants, which form the anterior Wilbrand's knee. In the early phases it is manifested as bitemporal superior quadrantanopia, with transition into bitemporal hemianopsia. Blind spots respect the vertical meridian. Inferior chiasmatic syndrome results in a typical image of atrophy of the OND in the shape of a bow-tie on optical coherence tomography (OCT) in the nasal and temporal quadrant. Fibers penetrate through the upper and lower edge of the papilla from the periphery of the temporal quadrants, and these are the last to be damaged in this compression [5]. Compressive blind spots of the visual field in the region of the chiasma are frequently asymmetrical. Upon examination of color perception, we may detect desaturation of colors across the vertical meridian. This finding is an early sign of compression of the chiasma. If atrophy of the optic nerve disc is present on OCT, the prognosis for recovery of visual functions is limited [4,5].

Prolactinomas usually have a good prognosis. Effective medicamentous therapy is available in the form of dopamine agonists, which bind to the D2 dopamine receptor and thereby reduce the production of prolactin, with the result that the tumor is reduced in size, compression of the chiasma is alleviated and visual functions are gradually corrected. Visual functions remain unchanged even after treatment in approximately ¼ of patients. The decisive factor in the prognosis is time. The shorter the duration of the visual defect, the better the restoration of the visual field following decompression. Cabergoline has fewer adverse effects in comparison with its predecessor, bromocriptine. In the case of failure of the drug or intolerance thereof, the neurosurgeon indicates selective transsphenoidal adenomectomy or alternatively radiotherapy. In both cases there is a risk of hypopituitarism, damage to the cranial nerves and the formation of secondary tumors. Malignant prolactinomas are extremely rare [5–8].

## CASE REPORT

In March 2022, a 38-year-old female patient, a refugee from Ukraine, was referred by a local ophthalmologist to the Department of Ophthalmology at the University Hospital in Trenčín with a diagnosis of suspected retrobulbar neuritis in the right eye. The patient was suffering from a deterioration of vision in the right eye persisting for 10 days. In the left eye she had been blind for approximately 10 years but did not know the reason, since she had not reported the condition to an ophthalmologist. The patient had no health documentation, and the recording of her medical history was impeded by the language barrier. The patient was not using any medications or being treated for any condition. She had been vaccinated twice against COVID19, with the last dose administered 5 months previously. Two weeks before being referred to the department she had been present during bombing and an explosion. She complained of frequent headaches. Twelve years previously, she had experienced a stressful incident when she was attacked by a schizophrenic individual, and at the time she suffered numerous knife wounds on her body. The patient did not report any other health complaints. Best corrected distance visual acuity in the right eye was 0.2. In the left eye, visual acuity was without light perception. The value of intraocular pressure was normal, in the right eye 13 and in the left eye 14 torr. She was not suffering from any pain in the eye, motility disorder or ophthalmoplegia. The anterior segment of the eye was quiet, in the right eye there was a relative afferent pupillary defect. On the ocular fundus a bordered OND was visible, which was pale with descendant atrophy, physiological excavation, the macula was smooth and the blood vessels were commensurate to the patient's age. OCT of the optic nerve detected the presence of bilateral critical reduction in the layer of the nerve fibers, with an average value of 57 in the right eye and 36 in the left eye (Fig. 1). A deeper analysis of the right eye revealed dominant atrophy in the temporal and nasal quadrant in comparison with the superior and inferior quadrant (T 29, N 29, S 83, I 87). This finding corresponds to bow-tie atrophy. Perimetry revealed an image of temporal hemianopsia in the right eye (Fig. 2). With regard to visual functions, complete anopsia was present in the left eye (Fig. 3). Basic laboratory screening did not demonstrate any deviations from the normal referential values. The patient also underwent neurological and internal consultation examinations, which detected a slight elevation of the hepatic parameters. On magnetic resonance imaging (MRI) of the brain, the radiologist described a solid cystic pituitary tumor in the shape of a walnut, with the size of 43x30 mm (Fig. 4, 5). The tumor manifested suprasellar spreading and was infiltrating the left cavernous sinus. The tumor was dislocating the optic chiasm. The pituitary stalk was thin, and was therefore not displayed on the scan. At a thorough recording of the patient's medical history with an interpreter, the patient reported a 20-year absence of menstruation (amenorrhea). With the aid of ultrasonography, a gynecologist determined atrophy of

the uterus (hypogonadism). The next morning, we took a blood sample from the patient on an empty stomach in order to examine for pituitary hormones. The result of serum prolactin was 3082 µg/l (referential value 4.79–23.3 µg/l), and the value of serum macro-prolactin could not be evaluated. We were contacted by the laboratory due to the alarming results. On the basis of the examination, the endocrinologist presumed the presence of a giant prolactinoma. Therapy was commenced with the dopamine agonist cabergoline (Cabest® 0.5 mg tablet orally), with the dose progressively saturated to 4 tablets per week. This treatment brought about a significant reduction of the value of serum prolactin from the value of 3082 µg/l to 71.34 µg/l within the course of 21 days. Treatment with the dopamine agonist achieved a hormonal realignment and a partial remission of the tumor, but no correction of visual functions and the visual field was achieved. The patient was transferred to the Department of Neurology for a surgical solution, but for unknown reasons did not report for the operation, further planned ocular follow-up examinations and MRI of the brain.

## DISCUSSION

Pituitary adenomas are a heterogeneous group of tumors which constitute 10–15% of all intracranial

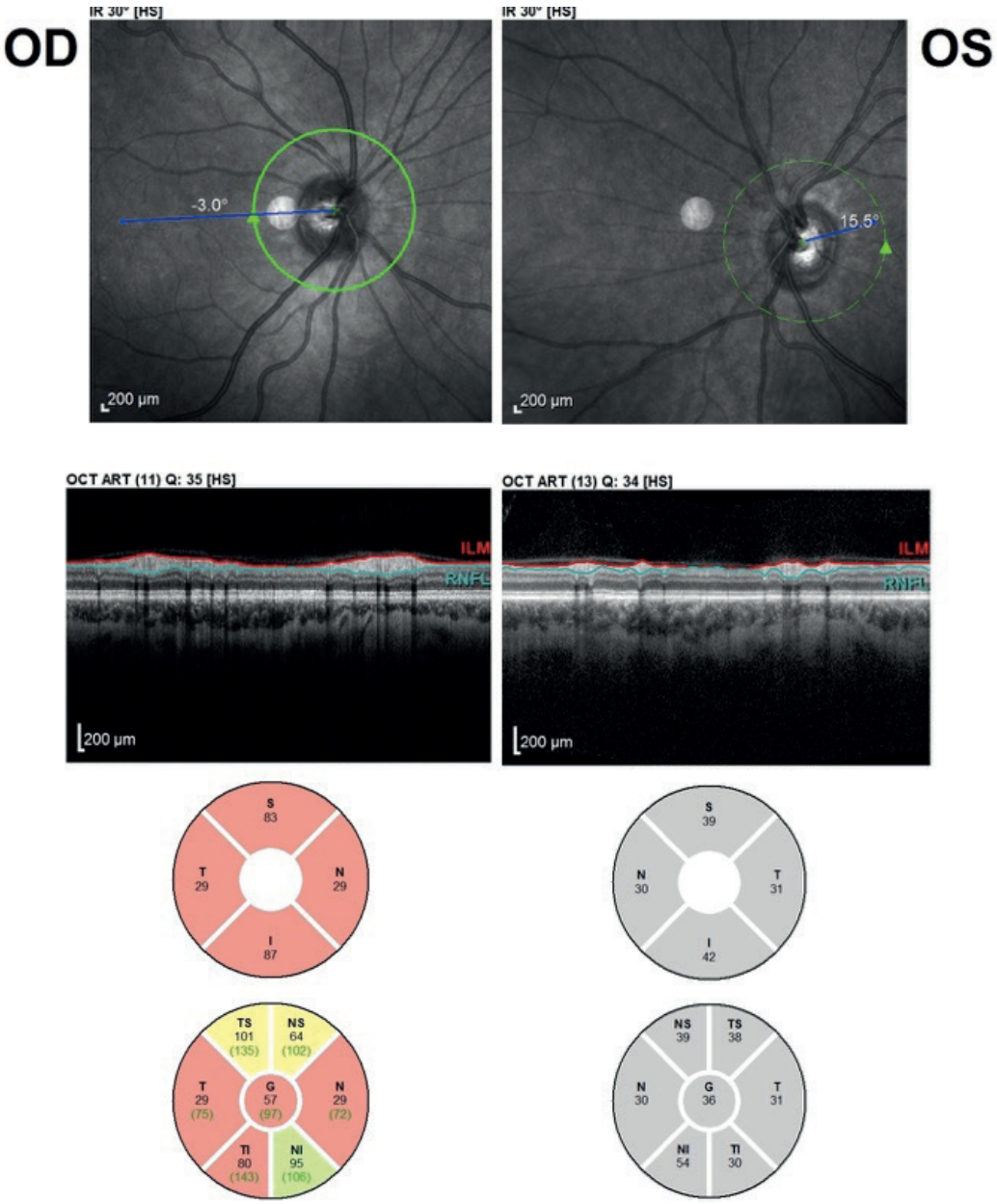


**Figure 1.** OCT of the optic nerve - critical reduction in the retinal nerve fiber layer bilaterally, average value of right eye 57 and left eye 36, on the right eye there is "bow-tie" atrophy in temporal and nasal quadrants, on the left eye there is advanced atrophy in all quadrants

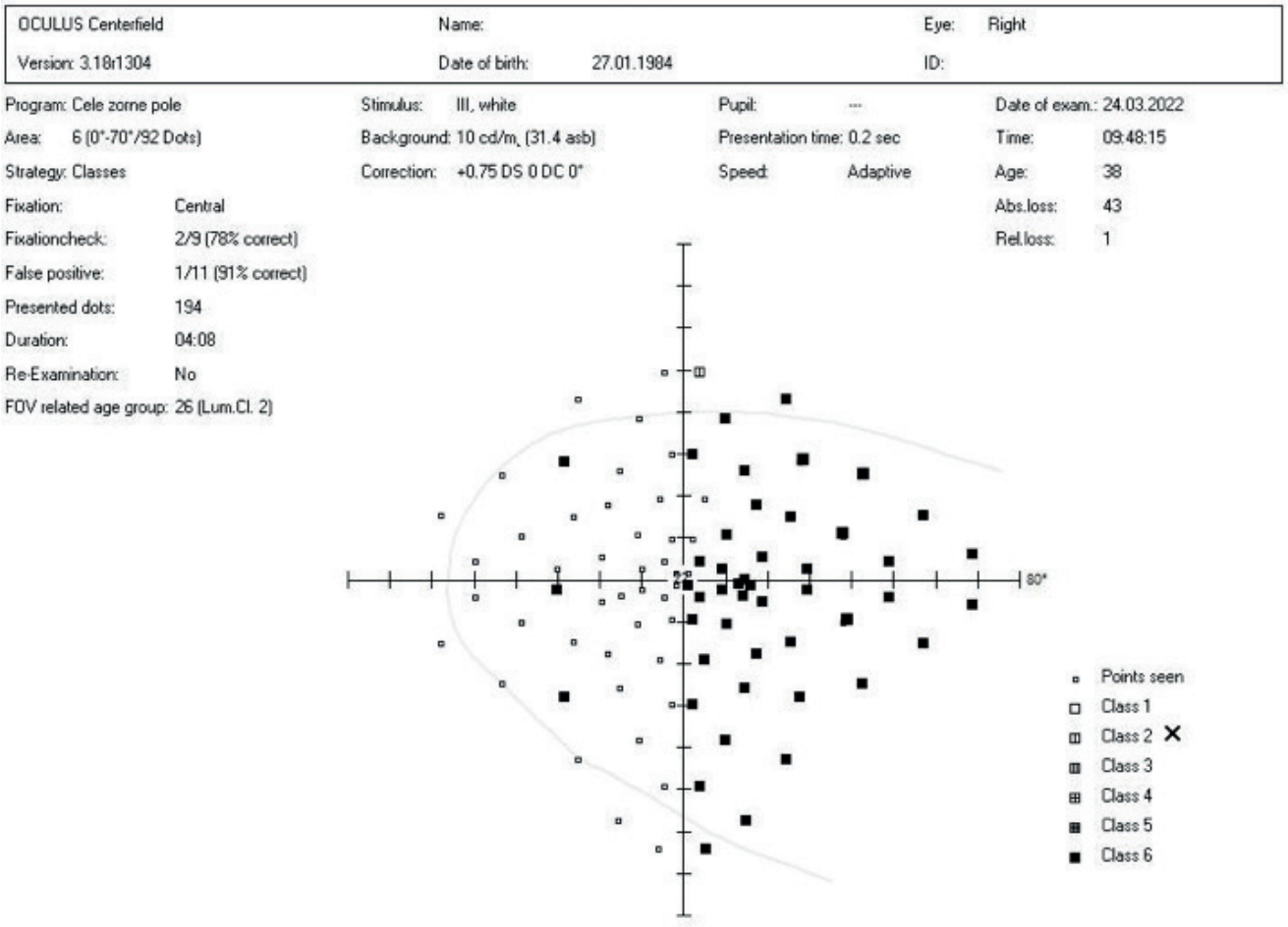


**Figure 2.** Visual field test with right eye temporal hemianopia

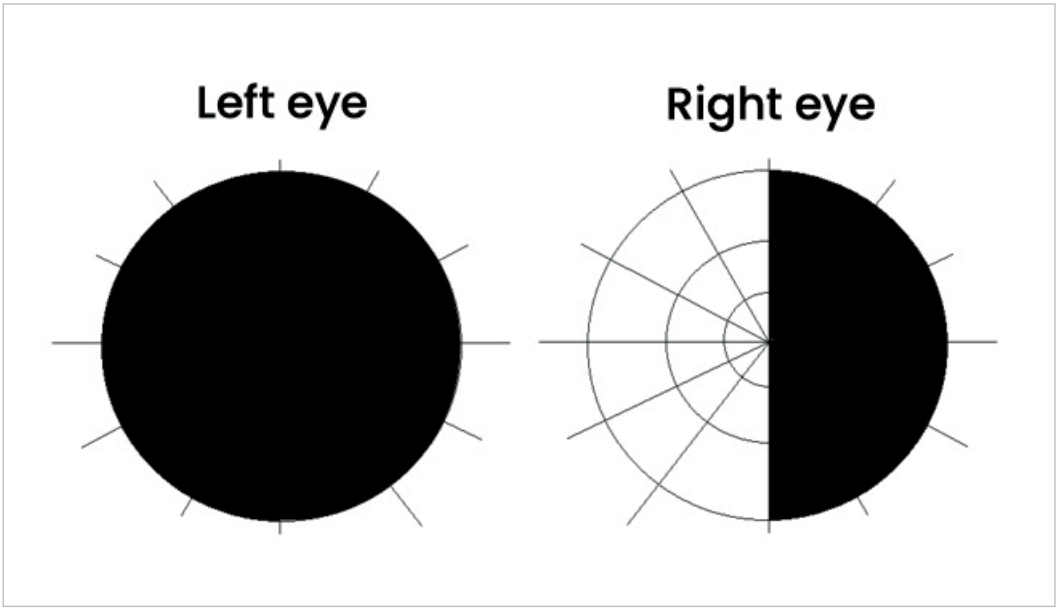


**Figure 3.** Model of visual field test - right eye hemianopia and left eye total anopia

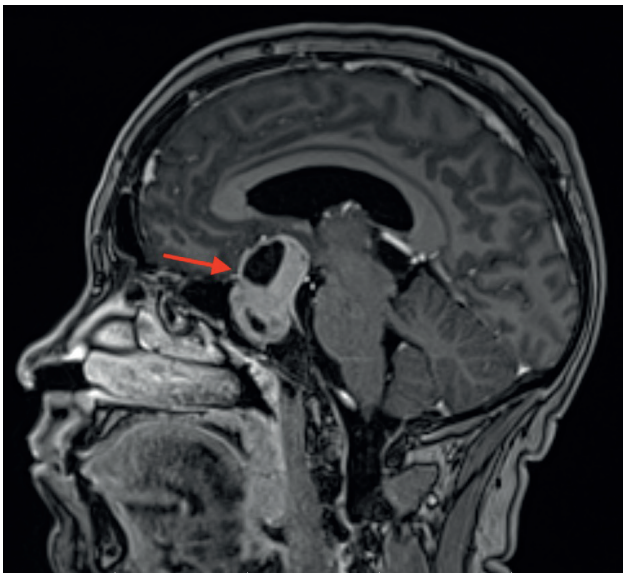

**Figure 4.** Brain MRI T1-weighted sagital scan reveal solid-cystic nut-shaped tumor of the pituitary gland, sized 43x30 mm, which originates from the sella and spreads suprasellarly

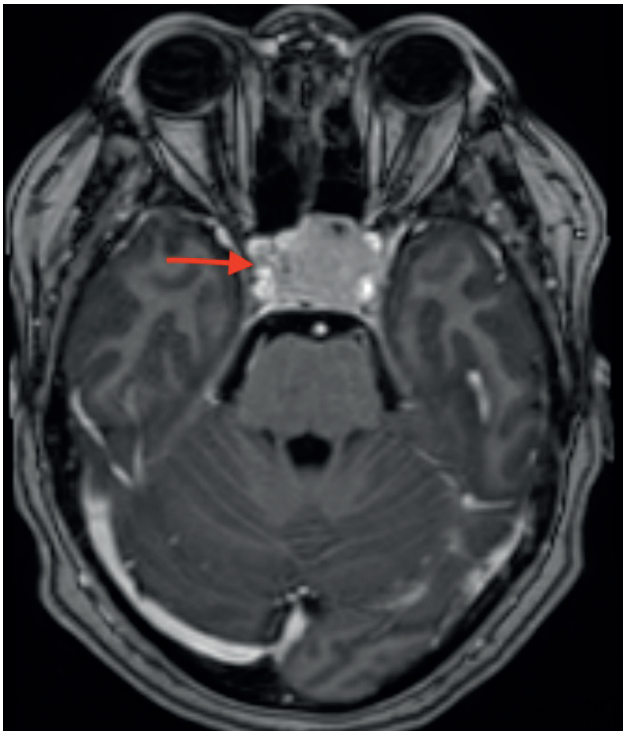

**Figure 5.** Brain MRI T1-weighted axial scan shows pituitary gland tumor with contrast enhancement

tumors, and in 40% of cases are made up of prolactinomas. The clinical manifestations are endocrine and neuroophthalmological. The first of these represent a combination of hyperprolactinemia and hypopituitarism, the second occur as a result of compression of the surrounding structures [1,7]. Inferior chiasmatic syndrome is the most common form of compression of the chiasm. When a tumor breaks through the diaphragma sellae and continues to grow, it begins to compress the chiasm from below, where crossing fibers from the nasal quadrants of the retina are located, resulting in retrograde degeneration of axons and partial OND in a bow-tie shape. The deterioration of visual acuity and the defects on the periphery take place gradually, and as a result, in the initial stages of the disease, they may go unnoticed by the patient [5]. Frisen et al. determined that elevation of the chiasm by 6 mm is linked in 50% of cases with defects in the visual field, and upon an elevation of the chiasm by a further 5 mm the incidence of defects is 90%. Compression of the chiasm by a pituitary adenoma from below typically causes an image of bitemporal hemianopsia, but very often compression of the chiasm is asymmetrical [9].

Studies on macroadenomas describe variable defects in the visual field, e.g. unilateral superotemporal quadrantanopsia, bitemporal hemianopsia, superior bitemporal quadrantanopsia, homonymous hemianopsia, temporal hemianopsia in one eye and superotemporal quadrantanopsia in the other eye [10]. Hemianopsia is caused by a tumor with a size of at least 10–15 mm (macroprolactinoma) with suprasellar spreading above the diaphragma sellae. Macroprolactinomas are more common in men than in women, and the diagnosis is frequently delayed, probably because the symptoms of hyperprolactinemia are less pronounced in men, whereas women tend to present earlier due to irregularities of the menstrual cycle. They may manifest themselves in neurological complications upon spreading to the surrounding structures such as the chiasma, third brain ventricle, cavernous sinus, temporal lobe or sphenoid sinus [7].

Changes on OCT are present earlier than changes on perimetry. This is confirmed on the basis of a study of patients with microprolactinomas of up to 7 mm without changes in the visual field. These patients had a significant reduction of the neuroretina on OCT in comparison with a healthy control group [11]. Upon examination of the ocular fundus it is necessary to distinguish the type of OND atrophy correctly, differentiating between ascendant, descendant, postneuritic or glaucomatous atrophy of the OND, together with correlation of the other ocular finding, intraocular pressure and image on perimetry. An example is the error made in the case of a 68-year-old man with a positive family medical history of glaucoma and excavation of the OND of 0.8. The patient was diagnosed with normotensive glaucoma due to the normal values of intraocular pressure and excavation on the OND. Upon a detailed examination, a giant prolactinoma was determined [12]. Ahmed demonstrated that as many as 6.5% patients with a diagnosis of normotensive glaucoma in his cohort had clinically relevant compression of the visual pathway [13].

Dopamine from the pituitary gland is the main regulator inhibiting the secretion of prolactin. Medicamentous therapy using dopamine agonists is the tre-

atment of first choice for prolactinomas of all sizes. The size of the dose and titration depends on the size of the tumor. Adverse effects of this treatment have been described, such as nausea, fatigue, loss of appetite, behavioral disorders, and disorders of the heart valves. If the adenoma is of large dimensions and is locally invasive it undermines the cranial base, and reduction of the tumor by this treatment may cause rhinorrhea [14]. In rare cases, herniation of the optic chasm has been described upon treatment with cabergoline, since upon remission of the tumor herniation of the chiasm into the empty sella turcica occurred, thus leading to a progression of visual defects [15]. The effect of cabergoline on the volume of the tumor is excellent even in low doses. Cabergoline functions in 85% of patients. A prolactinoma is resistant if no improvement takes place at a dose of 2 mg of cabergoline per week [16]. An analysis of 12 patients with a macro and giant prolactinoma with defects in the visual field confirmed a reduction of the tumor by an average of 43.6 ±4.5% after 3 months of treatment. After approximately 3 weeks of treatment, complete (83%) and partial (17%) regression of defects in the visual field was achieved [17]. By contrast, some studies have determined a slight worsening of defects in the visual field upon long-term treatment with cabergoline. These delayed defects occur after therapy lasting 2–5 years, and the presumed reason is direct toxicity of dopamine agonists on the nerve fibers. In the majority of cases the defects improved after reduction of the dose [18].

## CONCLUSION

The most common manifestations of microprolactinoma include galactorrhea, amenorrhea, gynecomastia, weight gain, sterility, hypogonadism, decreased libido and depression. Determining the general symptoms of prolactinoma and targeted examination thereof when recording the patient's medical history makes diagnosis easier upon suspicion of a compressive lesion of the optic chiasm. In the case of macroadenomas there are also accompanying symptoms caused by compression of the surrounding structures, such as headache, vomiting, inferior chiasmatic syndrome, ophthalmoplegia and hypopituitarism. Perimetry should be performed on every patient with an inexplicable unilateral visual defect. Inferior chiasmatic syndrome is characterized by bitemporal hemianopsia, deterioration of central visual acuity, bilateral bow-tie descendent atrophy of the optic nerve disc, and hemianopic rigidity of the pupils. Asymmetrical blind spots on perimetry are very common. Giant prolactinomas are generally benign, but may be aggressive due to local invasive growth, by which they impair the surrounding structures. These tumors respond well to medicamentous therapy using dopamine agonists, which may lead to a correction of the laboratory parameters, reduction of the tumor, and in certain cases also to an improvement of visual functions. If the response is insufficient, medicamentous therapy is combined with surgical therapy or radiotherapy. Treatment requires an interdisciplinary approach of a neurosurgeon, endocrinologist and ophthalmologist.

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