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ORIGINAL ARTICLE

Idiopathic intracranial hypertension with optic nerve edema – treatment options, case report

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Abstract

Pseudotumor cerebri, benign intracranial hypertension or idiopathic intracranial hypertension are all terms used for a neurological syndrome consisting of increased intracranial pressure, headache and possible edema of the optic nerve head and decreased visual function. Normal findings in contrast agent computed tomography or magnetic resonance imaging of the head in physiological neurological findings, with the exception of paresis VI, indicate an increase in pressure of laboratory normal cerebrospinal fluid (CSF) of unknown cause. In this article we describe what idiopathic intracranial hypertension is, what manifestations can occur from an ophthalmological point of view and how to treat them.
Case report: The 47 years old female patient was sent for a consultation examination to the neurophthalmologic outpatient clinic of the Department of Ophthalmology, Comenius University, Bratislava. She reported about one and a half years of headache and impaired visual function. After repeated examinations in neurology, neurosurgery and ophthalmology outpatient clinic an edema of the optic nerve head was found. The patient was sent again for neurosurgical check-up. The lumboparietal drainage was performed. The patient continued to be monitored and received interdisciplinary treatment that resulted in the patient's central visual acuity decreasing slightly, but without loss of vision.

Abbreviations:

IIH	- Idiopatic intracranial hypertension
mm	- milimeter
CSF	- cerebrospinal fluid
VEP	- visually evoked potentials
OCT	- optical coherence tomography
ONH	- optic nerve head
RNFL	- Retinal nerve fiber layer
OU	- oculus uterque
OD	- oculi dexter
OS	- oculi sinister
S	- superior
T	- temporal
I	- inferior
N	- nasal

INTRODUCTION

Idiopathic intracranial hypertension (IIH) is a disease with increased intracranial pressure of unknown etiology, also called benign intracranial hypertension or pseudotumor cerebri. The most severe symptoms are chronic headache and impaired visual function due to compression of the optic nerve (Yri, Jensen 2012; Yri *et al.* 2014; Markey *et al.* 2016). The incidence of IIH is generally 1–3 per 100,000 population, but in young obese women aged 20–40 years the incidence

is up to 20 per 100,000 (Mollan *et al.* 2016; Andrews *et al.* 2014; Friesner *et al.* 2011; Raoof *et al.* 2011). More recent clinical evidence describes the involvement of hormones, androgens and glucocorticoids in the pathophysiology of IIH (Markey *et al.* 2016; Mulla *et al.* 2015; O'Reilly *et al.* 2019). Since many patients with IIH are obese, they may also have increased risk factors for cardiovascular disease. One study found that 56% of patients with IIH suffer from hypertension (Adderley *et al.* 2019; Jirásková *et al.* 2017). Humans produce about 500 ml of cerebrospinal fluid (CSF) per day, which fills the CSF spaces to a volume of 120–150 ml, indicating an average excretion rate of about 20 ml / h. Part of the cerebrospinal fluid is produced from the interstitial CSF by the ependymal lining of the ventricles and the pia mater, probably by hydrostatic forces, from the cerebral interstitial fluid. Most CSF, however, is produced by the choroidal plexus, an organ located in the ventricles that has a characteristic asymmetric distribution of fluid-carrying epithelial ion transporters. Elevated ICP is considered to be above 220 mm H2O measured by lumbar moisture puncture and above 250 mm H2O while sitting. The diagnostic criteria are summarized in Dandy's modified criteria for IIH:

- elevation of ICT over 250 mm H2O in a sitting position
- headache, edema of the optic nerve head
- neurological findings in the norm (except paresis n. VI)
- magnetic resonance imaging of the brain without signs of venous raft obstruction or without a tumor
- physiological composition of cerebrospinal fluid
- the patient is conscious and oriented
- benign clinical course in addition to visual impairment (Hlaváčová *et al.* 2009).

Most patients do not have a visual impairment or are not aware of minor visual deficits. Impaired visual function is not observed until the edema of the optic nerve head is high or the posterior pole is affected, such as in neurosensory ablation, macular lipid exudates or retinal hemorrhage. Perimetry is the most sensitive method for visual field testing. Most often we find an enlargement of the blind spot failures in the nasal part. Edema of the optic nerve head is important for diagnosis, but may not be symmetrical in both eyes. IIH can occur without edema of the optic disk if visual function should not be impaired (Talks *et al.* 1998; Friedman *et al.* 2013). Treatment Drug Treatment Acetazolamide. Acetazolamide, a carboanhydrase inhibitor, has been used for years to treat IIH, based on studies that have shown efficacy in improving optic edema and visual function, making acetazolamide the treatment of choice. Acetazolamide therapy can be initiated with a dose of 500 mg twice daily and increased by 250 mg weekly to a maximum dose of 4 g daily. When the edema of the optic disk disappears, a maintenance dose of less than 4 g per day is maintained. In a clinical study with acetazolamide, 47.7% of the participants experienced paresthesia, 30.2% had nausea and kidney stones were detected. Although acetazolamide statistically significantly improved the perimeter results, the degree of edema of the optic nerve head and improved quality of life, there was no significant difference in headache or improvement in visual acuity compared to the placebo group. Acetazolamide has also been found to reduce aquaporin-1 expression (Mollan *et al.* 2018; Wall *et al.* 2014; Libien *et al.* 2017; Hoffmann *et al.* 2018). Topiramate. Topiramate is a drug for the preventive treatment of migraine, which is a weak inhibitor of carbonic anhydrase and is commonly used to treat IIH. A small randomized clinical trial showed that doses of topiramate up to 150 mg daily were comparable to doses of acetazolamide up to 1500 mg daily. The degree of optic nerve head edema and the severity of headache also improved over time with topiramate

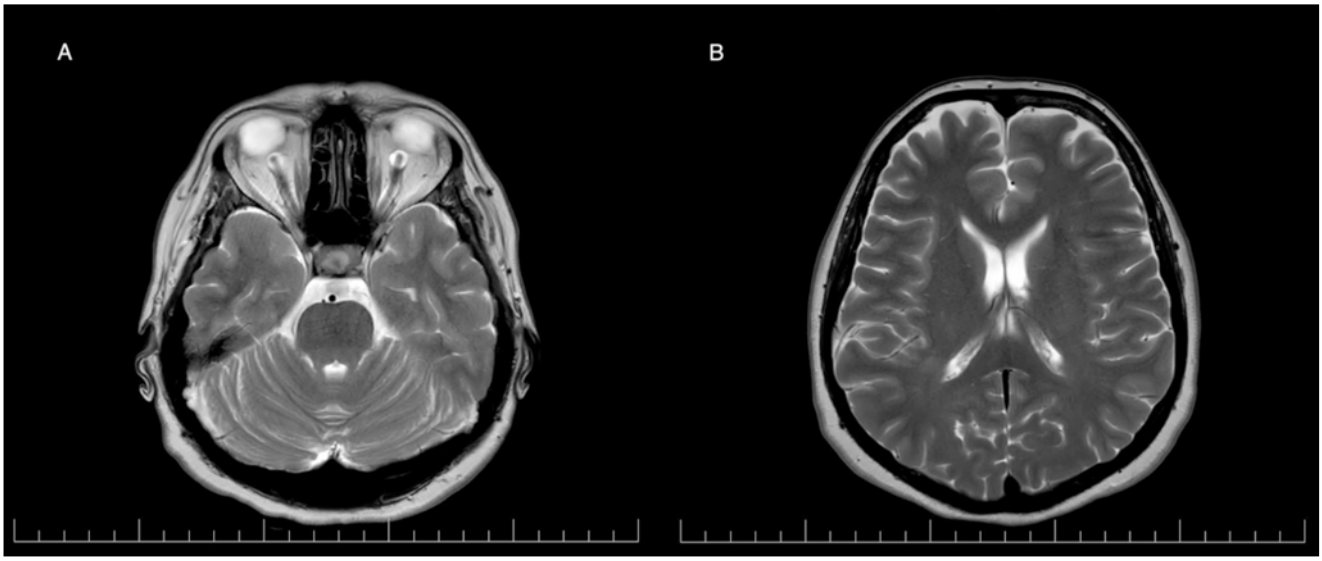

Fig. 1. Magnetic resonance of brain and orbit (A), magnetic resonance of brain (B) before neurosurgery.

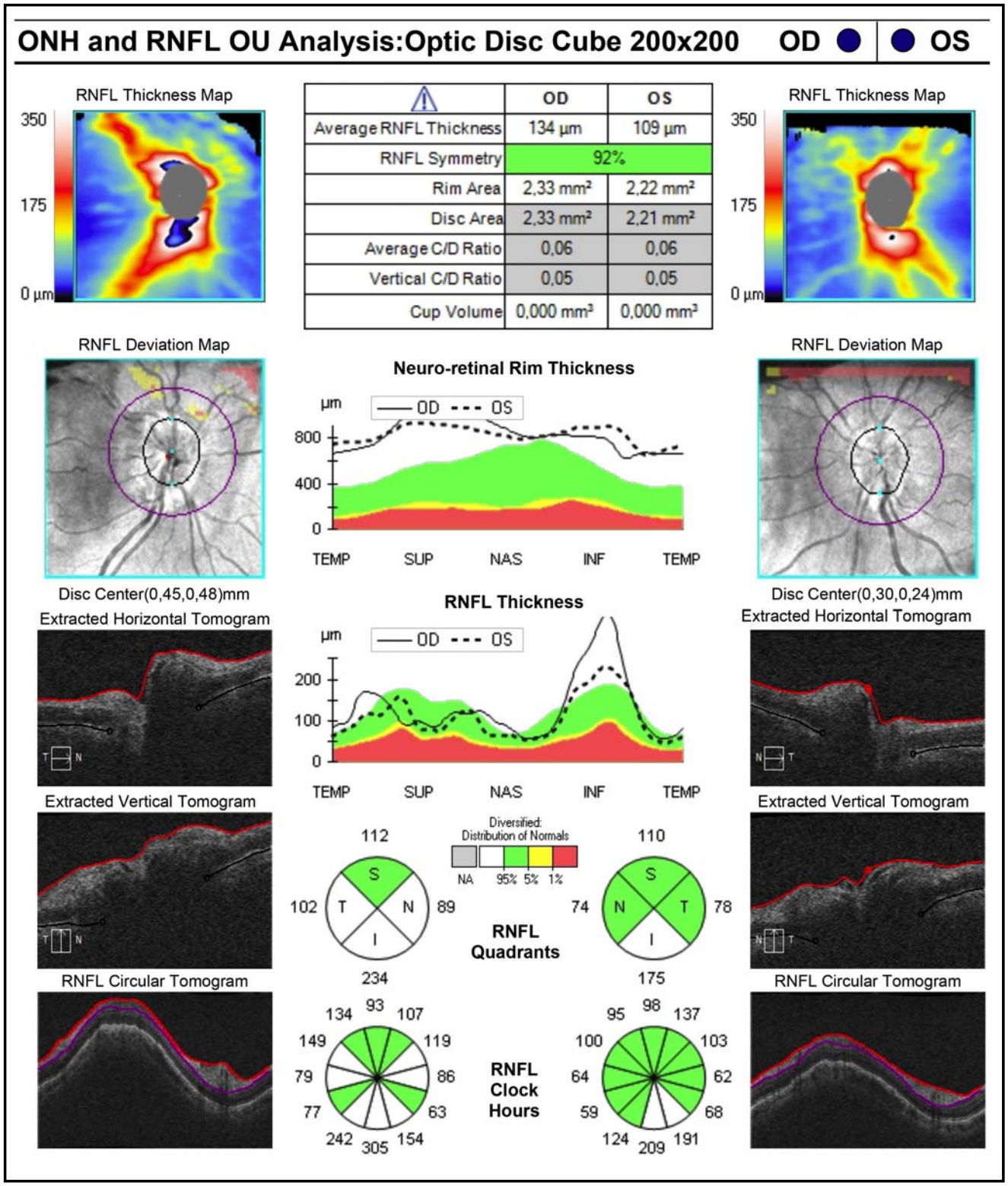

Fig. 2. Optical coherence tomography of optic nerve head of both eyes before surgery.

or acetazolamide, and weight loss was comparable with each treatment. In a clinical study with acetazolamide, 50% of the participants had a history of migraine and 68% had headaches. Although the weight loss associated with topiramate and its correlation with IIH symptoms has not been studied, it is thought that this may be another mechanism for reducing intracranial pressure and headache. There is no evidence-based treatment regimen with topiramate. In practice, it is usually well tolerated. It starts with a dose of 25 mg once daily and titrates up to 100 mg twice daily (Celebisoy *et al.* 2007; Friedman *et al.* 2017). Furosemide is a diuretic that also inhibits carbonic anhydrase. Only few data are available on the furosemide under investigation. In a small series

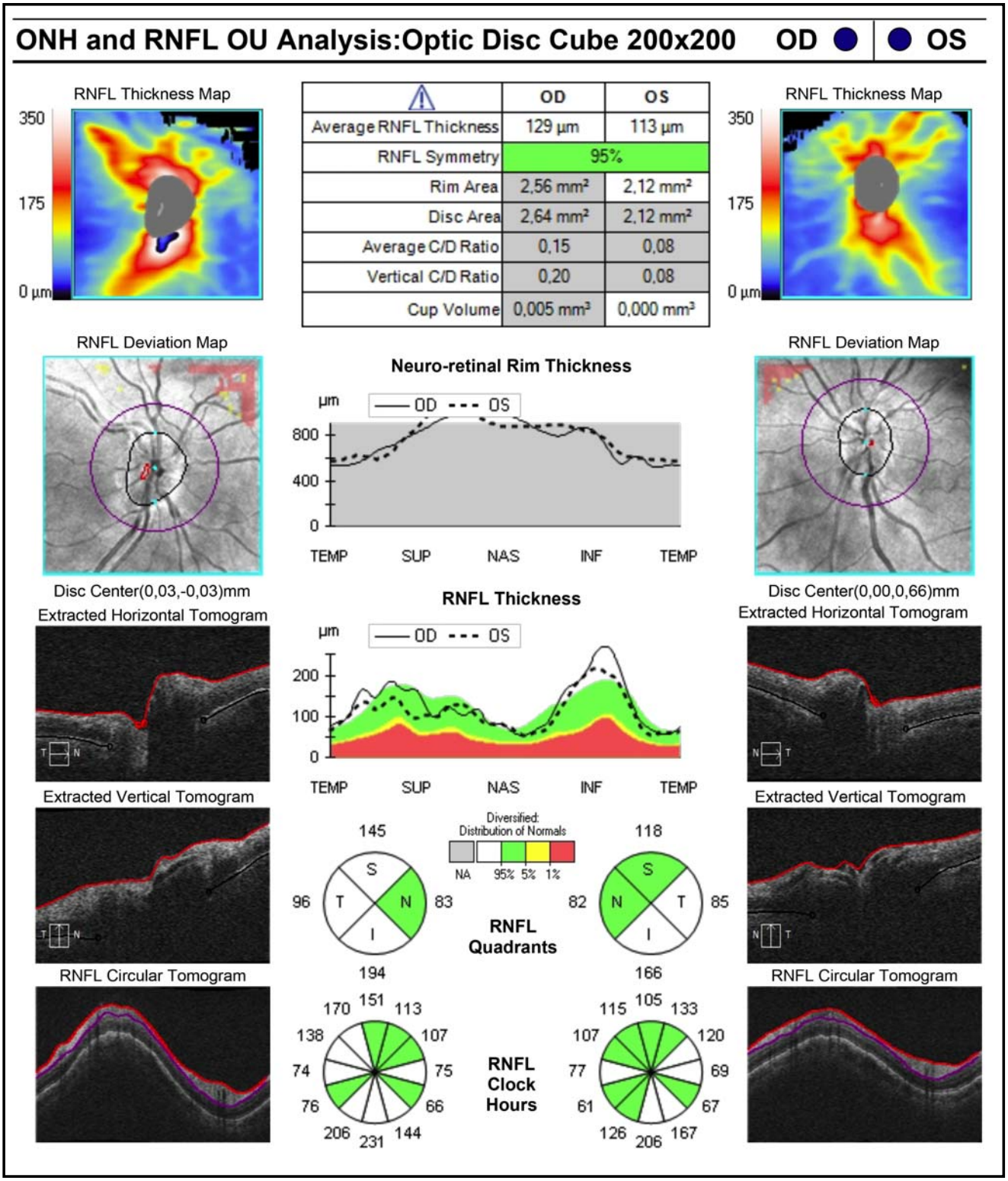

Fig. 3. Optical coherence tomography of optic nerve head of both eyes after surgery.

of pediatric cases, there was a rapid improvement in intracranial pressure when people with IIH were treated with acetazolamide in combination with furosemide. Although there is no evidence of furosemide alone in the treatment of IIH, furosemide and other diuretics can be used in people who cannot tolerate acetazolamide or in combination therapy (Schoeman 1994; Friedman 2019). Octreotide, a somatostatin analog, has been shown to reduce intracranial pressure and improve headache. In a small group of patients in whom several drugs and surgical procedures failed, octreotide eliminated headache as a symptom of IIH. This case series did not include optic edema, loss of visual func-

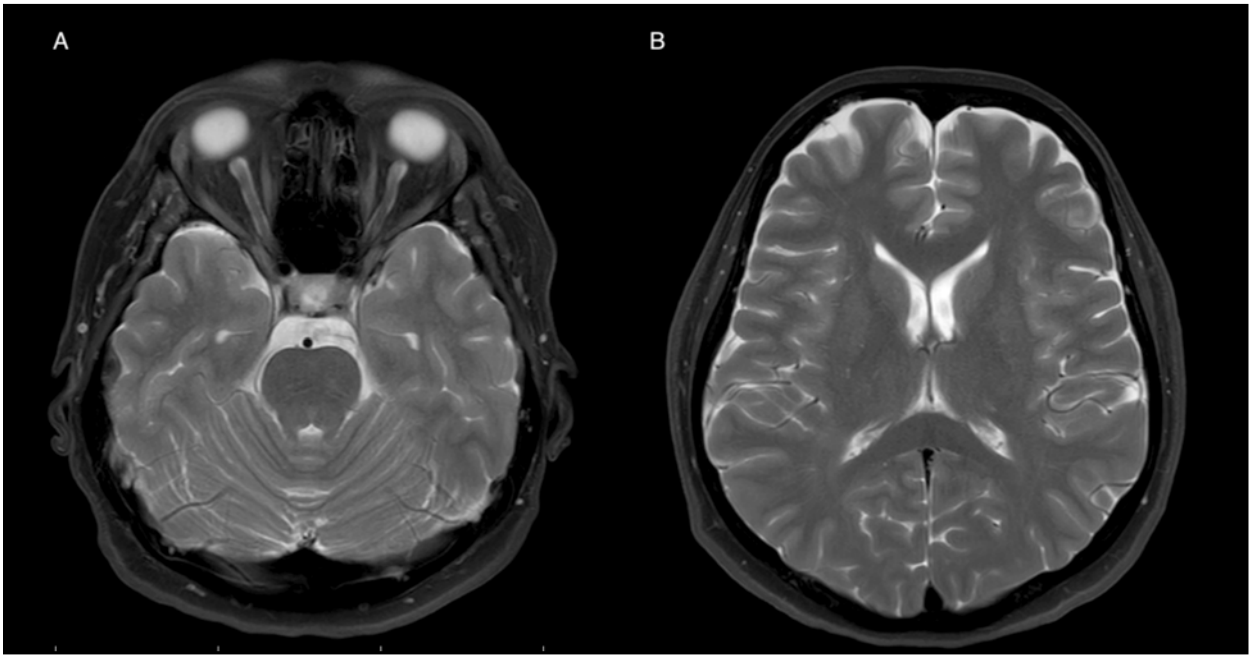

Fig. 4. Magnetic resonance of brain and orbit (A), magnetic resonance of brain (B) after neurosurgery.

tion or measurement of intracranial pressure as major parameters (Friedman 2019; House *et al.* 2016).

SURGICAL TREATMENT

In most patients IIH can be controlled by weight loss and medications that reduce cerebrospinal fluid (CSF) production, such as acetazolamide. Surgical intervention in the form of decompression of the optic nerve sheaths and introduction of a lumbo parietal (LP) shunt is usually reserved for patients with progressive visual impairment and failure of conservative procedures (Wakerley 2020). External ventricular drainage is implanted by inserting a drainage through the shaped hole in the lateral part of the large fontanel and provides the possibility of continuous CSF drainage and regular check-ups. The height adjustment of the drainage system prevents pre-drainage or under-drainage of the ventricles (Rizvi, Wood 2010; Kazan *et al.* 2005). A ventriculo-subgaleal shunt is rare. Its advantage is the constant drainage and the reduced need for punctures with CSF drainage. The intraventricular part of the shunt is usually implanted through the fontanel, possibly through a hole in the bone, and the distal part is placed in a preformed subgalacral pocket. The aim is to take advantage of the absorption capacity of the perioperatively created space under the galley. The shunt has a temporary function to achieve sufficient weight and correct CSF parameters before the actual implantation of the definitive ventriculoperitoneal shunt

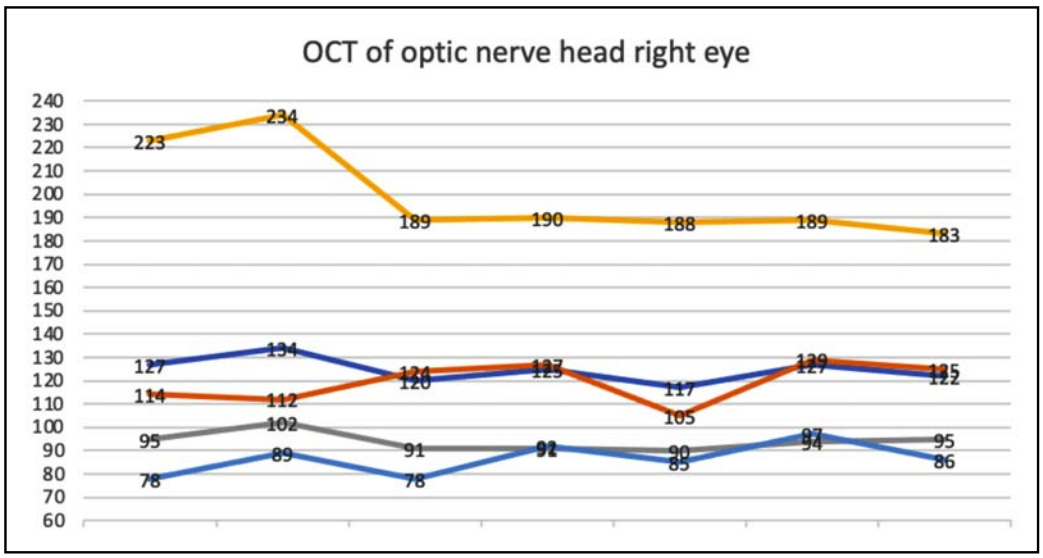

Fig. 5. Optical coherence tomography of optic nerve head of right eye during the follow-up.

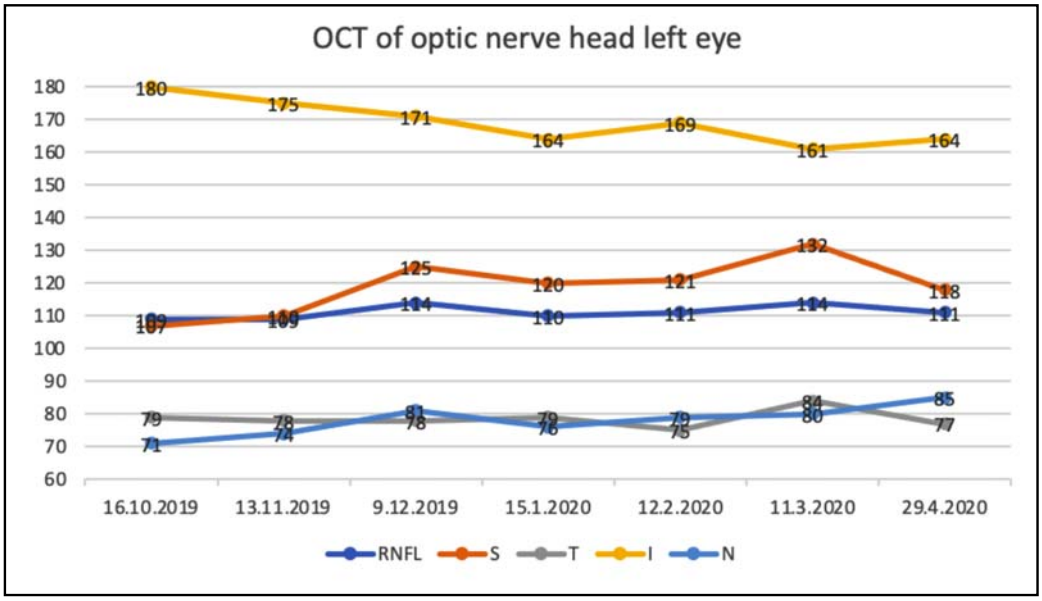

Fig. 6. Optical coherence tomography of optic nerve head of left eye during the follow-up.

(Mazzola *et al.* 2014). The most commonly used shunt type is the ventriculoperitoneal (VP) shunt with CSF drainage into the peritoneal cavity. Significantly less common is the ventriculoatrial shunt with drainage into the right atrium of the heart and other drainage systems (e.g. ventriculolopleural shunt). The standard shunt consists of a proximal and distal catheter and a valve. The catheters are usually made of silicone. During the shunt an anti-siphon unit can be connected to prevent pre-drainage of the chambers, sometimes it is part of the valve. Lumboperitoneal drainage is used as an alternative method of ventriculoperitoneal drainage in patients who are not obstructed. The advantages of the disposable drainage LP are: extracranial capacity, low risk of obstruction, the possibility of spinal anesthesia in adults and there is no risk of slit ventricle syndrome.

CASE REPORT

Patient 47years old visited our neuro-ophthalmological outpatient clinic on 16 October 2019. She was previously examined by a neurologist and a neurosurgeon. She complained of headaches that lasted a year and a half. On August 8, 2019 she underwent magnetic resonance imaging with the result of the appearance of small non-specific focal hyperintensity frontal right up to 2 mm, the first chronic microvascular etiology. There is no intracranial extension. There is a venous anomaly in development – venous angioma frontal left. No pathological infiltration in either orbit or perichiazmatically was present. In the sheath of both optic nerves there is a perineal liquorrominence up to a thickness of 2 mm, differential diagnosis intracranial hypertension on magnetic resonance (Figure 1). On September 23, 2019 the patient underwent an examination of the visually evoked potentials (VEP). On the right side a pathological finding of a VEP pattern reversal with signs of slight conduction disorders in the right visual tract was detected. In our first examination the patient had visual functions in the right eye with a correction of +1.5 Dsph = 20/25, in the left eye with a correction of +2.5 Dsph = 20/25 in the distance, while in 2012 she had a pars plana vitrectomy in the left eye due to epiretinal membrane. The intraocular pressure was 17 Torr in the right eye and 18 Torr in the left eye. In the anterior segment of the eye without pathological changes bilaterally, direct and indirect pupillary reactions without obstruction are direct and indirect. On the right side the edema of the optic nerve head, otherwise fundus, without pathological findings. On the left side edema of the optic nerve head, in the area of the macula changes after pars plana vitrectomy in the sense of an irregular retinal surface. On optical coherence tomography (OCT) she had a partial edema bilaterally (Figure 2 and 3). The perimeter was bilateral without loss of vision in the visual field both before and after surgery. Acetazolamide 3x1 tbl per os was used. After one month of taking acetazolamide, the patient reported limb twitching, which is why furosemide was administered orally at a dose of 1 tbl. On 9 January 2020, the patient underwent bilateral drainage in the neurosurgical department of the lumbar parietal due to a decrease in central visual acuity in both eyes, headache and partial edema of the optic nerve head. The lumbar puncture was also performed perioperatively. The postoperative condition was without complications. Subsequently, the patient was regularly monitored once a month in the neurophthalmological outpatient department of the Department of Ophtalmology, Comenius University and University hospital Bratislava. She was regularly monitored ophthalmoscopically as well as at OCT (Figure 5 and 6). Magnetic resonance

after surgery was made (Figure 4). Gradually the edema of the optic nerve head decreased. See graphs 1 and 2. We gradually adjusted the patient's furosedmid dose to 1 tablet three times a week. This medication is still used in the patient. The visual acuity for the right eye with +1.5 Dsph correction is 20/20, for the left eye with +2.5 Dsph 20/20 correction with distance correction.

DISCUSSION

In our patient, there was an improvement in visual function after the operation, a reduction in edema of the optic nerve head bilaterally, but the furosemide treatment is still continuing. Subjectively, the patient reported a reduction in the intensity of the headache and an improvement in visual function. Obesity is associated with IIH, and people with IIH who have a body mass index (BMI) of more than 40 kg/m2 have a higher risk of vision loss, so weight loss is crucial in the treatment of IIH. A loss of 6% of total body weight is associated with remission of optic nerve head edema. In a clinical study in which all participants started with low sodium, weight loss with a loss of 6% of total body weight after 6 months was twice as high as that treated with acetazolamide, although both groups lost weight (Wall *et al.* 2014; Friedman 2019; Wall *et al.* 2014). Our patient had a BMI of 36.8 at baseline and was instructed to lose weight, which reduced her BMI to 33.5. The differential diagnosis of edema of the optic nerve head is challenging and requires a series of examinations by an experienced ophthalmologist. We distinguish between several other causes of optic disk edema, such as intrabulbar optic neuritis, central retinal vein occlusion, compression optic neuropathy, retrobubular optic neuritis, diabetic papilitis and ischemic optic neuropathy. Another option to be considered is pseudoedema of the optic nerve head. This may be due to congenital dysplasia, optic nerve head drusen or an immersed optic disk (Dhoot 2019). Since our patient had bilateral edema of the optic nerve head, it worsened central visual acuity, headache, local and clinical condition. After comparing the patient with the MRI examination, the VEP examination and repeated ophthalmological, neurological and neurosurgical examinations, we concluded that the patient suffered from idiopathic intrcranial hypertension. Surgery should be considered in persons at immediate risk of loss of visual function and suffering from a severe systemic disease. A systematic evaluation of the effectiveness of surgery in IIH has been evaluated on the basis of a number of cases and reports, which showed that fenestration of the optic nerve sheath resulted in improved visual field in about two-thirds of cases. Edema of the optic disk improved in 95% of cases. Similarly, ventriculoparietal (VP) and lumpoparietal (LP) shunts improved visual field in 71% and 71% of cases, respectively. In 69% of cases and optic disk edema improved in 91% and 90% of cases, respectively. Improvement in headache occurred in 41% of cases treated with optic sheath windowing compared to 96% and 93% of cases treated with LP and VP shunts (Friedman 2019; Kalyvas *et al.* 2017; Arca 2020). Several studies have shown that LP shunts, when functional, can effectively relieve headache and improve or stabilize visual symptoms in patients with IIH. Studies have shown that patients with IIH who have undergone the LP shunt have shown improvements in both visual function and visual field. Improvements in headache symptoms have also been reported after the LP shunt (El-Saadany *et al.* 2012; Binder *et al.* 2004 Abubaker *et al.* 2011). Since our patients had undergone progenesis surgery in the past due to altered anatomical conditions, the neurosurgeons decided to use the LP shunt. Our patient's central visual acuity improved after the operation and the headaches almost subsided. IIH causes a loss of visual field and impaired visual function. In her study, Wall conducted a retrospective study with 12 patients using a perimeter. In seven of the 12 patients the visual field loss seemed to be permanent. The visual field defects were those known to be associated with lesions of the optic nerve. The most common were an enlargement of the Mariott's point (all 12 cases), a narrowing of the isopters (nine cases) and a loss on the nasal side of the visual field (seven cases), especially in the inferonasal quadrant. Four patients had reduced visual acuity (Wall *et al.* 1983). In our patient, however, the deteriorated perimeter result could not be detected either before or after surgery.

CONCLUSION

Idiopathic intracranial hypertension is a disease that mainly affects women, but to a lesser extent also men. If suspected, an early ophthalmic examination is important to reveal this serious diagnosis. In particular, regular monitoring of central visual acuity and examination of the ocular background, as was in our patient, is necessary. In our patient we performed interdisciplinary examinations and diagnostics with a slight decrease in the patient's central visual acuity, and thus she did not lose her sight.

CONFLICT OF INTEREST

The authors hereby declare that the origin of the topic of the professional article and its publication is not in conflict with interests, is not supported by any pharmaceutical company and has not been assigned to another journal or printed elsewhere, except for congressional abstracts and recommended procedures.

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