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The clinical characteristics, treatment and prognosis differences between occipital brain tumors with venous flow obstruction and occipital brain tumors without venous flow obstruction

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Abstract

Objective To examine the clinical characteristics and prognosis of occipital tumors that mimic Pseudotumor cerebri (PTC) at presentation due to venous flow obstruction compared to occipital tumors that do not cause venous flow obstruction.

Methods The medical records of all patients who presented with increased intracranial pressure symptoms and occipital tumors were retrospectively reviewed. The control group included, an age matched group of patients with occipital tumor who presented due to homonymous visual disturbances, visual hallucinations or incidental homonymous visual field defect but without symptoms of increased intracranial pressure at presentation. Data regarding demographics, ocular presenting symptoms and signs, neurological sings, diagnosis, treatment and prognosis were collected.

Results At the end of follow up, None of the study group patients, with the exception of one who developed optic disc atrophy and visual deterioration, had visual complaints at the end of follow-up. In the control group, 3 patients had deterioration in the visual field at the end of follow up. Two patients, from the study group, died while in the control group, all patients were alive at the end of follow- up.

Conclusions Patients with occipital tumors may present with symptoms similar to PTC secondary to venous drainage obstruction. Therefore, it is important in patients with PTC symptoms and occipital tumor to preform Magnetic-Resonance-Venography or Computed-Tomography-Venography as well. Most of the patients needed surgical intervention in addition to medical treatment in order to preserve visual functions. Probably the early treatment to this group brought to good visual prognosis that was not different from the group without venous drainage obstruction. Therefore, early diagnosis and prompt multi-disciplinary treatment may lead to better results in cases of occipital tumors with venous drainage obstruction.

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Introduction

Central nervous system (CNS) tumors are rare, but cause significant morbidity and mortality in adults and children [1]. The most common primary CNS tumors in adults are meningiomas, pituitary tumors, and malignant gliomas [2]. However, most cases of CNS tumors in adults are metastasis [3]. Lung cancer is the most frequent source of brain metastasis in men and women [3].

Brain tumors can present with focal or generalized manifestations. It depends on the localization of the tumor and its nature i.e. single or multiple space occupying lesion (SOL) or injury of normal tissue caused by tumor infiltration [4]. SOL may also compress on some brain structures and cause obstruction of cerebrospinal fluid (CSF) flow which usually results in ventriculomegaly. SOL that compresses or invades the major dural sinuses may cause occlusion of the venous circulation followed by elevation of the intra cranial pressure (ICP) [5, 6].

Increased ICP may cause the following symptoms: headache, tinnitus, diplopia, nausea and vomiting [7]. Those non-localizing symptoms resemble the presentation of pseudotumor cerebri (PTC). Therefore, detailed imaging is needed for correct diagnosis [8, 9].

Occipital lobe tumors encompass numerous neoplastic processes such as: tumors of neuroepithelial tissue (mainly gliomas), vascular tumors, mesenchymal as well as metastasis [10, 11, 12]. As in other brain tumors, headaches and seizures are common symptoms of occipital tumors [13]. Clearly, occipital lobe tumor may cause visual disturbances as hallucinations, prosopagnosia and homonymous visual field defect [14, 15, 16].

There are reports about treatment of meningioma engaging major venous sinuses in the neurosurgical literature, mainly involving the sagittal sinus [16, 17, 18]. But there is no data regarding ocular symptoms and signs. Some reports focus on management challenges and surgical complications, while occipital tumors with venous flow obstruction are less reported [16, 17].

The purpose of this current study is to examine the clinical characteristics and prognosis of occipital tumors that mimic PTC at presentation due to venous flow obstruction compared to occipital tumors that do not cause venous flow obstruction.

Methods

Patients

The medical records of all consecutive patients who presented with increased intracranial pressure symptoms and occipital tumors that were treated in the ophthalmology neurology and neurosurgery departments at Sheba Medical Center from January 2008 to December 2018 were retrospectively reviewed (study group). We excluded, in the study group, patients that were diagnosed as having focal neurologic symptoms or seizures, hallucinations, homonymous visual field (VF) defects, obstructive hydrocephalus, meningitis, as well as patients with leptomeningeal carcinomatosis.

The control group included, an age matched group of patients with occipital tumor who presented due to homonymous visual disturbances, visual hallucinations or incidental homonymous visual field defect but without symptoms of increased intracranial pressure at presentation.

Data collection

Data retrieved from the departmental database for the study and control group, included the patients' demographics and presenting symptoms, as well as the following findings at presentation and end of follow-up: neurological signs, visual acuity (VA), color vision (CV), relative afferent pupillary defect (RAPD), VF, papilledema, imaging studies, management, and ocular and systemic prognosis.

Method

Snellen VA was converted to log MAR value. Each participant underwent a VF test (Humphrey 24 – 2), and the mean deviation (MD) results and VF defects were recorded. Color vision was examined by the Hardy-Rand-Rittler (HRR) test and represented by the number of plates the patient recognized out of the 6 screening plates. Either the effected eye or the right eye of bilateral problem was included in the statistical analysis, and a separate analysis was performed for the left eye that showed no differences from the right eye.

The diagnosis of occipital tumor (OT) was confirmed by magnetic resonance imaging (MRI). The status of the venous sinus was determined by contrasted magnetic resonance venography (MRV) and contrasted computed tomography venography (CTV).

The study was approved by the local institutional review boards (IRB) of Sheba Medical Center which waived informed consent for this retrospective study and adhered to the Declaration of Helsinki.

Statistical analysis

Distributions of different categories parameters were measured. Since the group of patients was small, data were analyzed with non-parametric analysis tests in order to compare clinical characteristics at the end of follow-up with those at presentation. Student's t-test was performed to compare numeric differences, and Chi-square analyses were used to calculate proportional differences between the study group and the control group. The overall significance level was set as an alpha of 0.05. The statistical analysis was carried out with Microsoft Excel 16.1.1 (Microsoft Corporation, Redmond, WA,

Table 1 Neurological and ophthalmological symptoms at presentation

Clinical Symptoms	Study Group	Control group	*P*_Value
Headache	4 (66.67%)	3 (50%)	0.558
Transit visual obscurations	3 (50%)	1 (16.7%)	0.221
Blurred vision	3 (50%)	1 (16.7%)	0.221
Diplopia	1 (16.7%)	0 (0%)	0.296
Dizziness	1 (16.7%)	1 (16.7%)	1.000
hallucinations	0 (0%)	3 (50%)	0.213
Weakness head and leg	1 (16.7%)	0 (0%)	0.296

$- Known mild weakness of left arm and leg for the patient with right frontal anaplastic meningioma resection history

Table 2 Neurological and ophthalmological signs at presentation

Clinical Signs	Study Group	Control group	*P*_Value
VA for distance	0.17	0.00	0.029*
MD	-9.20	-16.88	0.541
CV	4.33	5	0.396
RAPD	3 (50%)	0 (0%)	0.046*
Disc edema	6 (100%)	1 (16.7%)	< 0.01*
OCT_RNFL	232.75	87	< 0.01*

VA- Visual Acuity, MD- Mean Deviation; CV- color vision; RAPD- Relative afferent pupillary defects. *- Statistically significant

USA) and SPSS software version 23.0 (SPSS, Inc., Chicago, IL, USA).

Results

Demographics and medical history

Eighty eight patients with increased intracranial symptoms were diagnosed during the study time period. Of them, 6 patients (3 males, 3 females) with an average age of 52 years (mean standard deviation 52 ± 14, range 27–67) were diagnosed with OT that causes venous outflow obstruction (study group). The control group included 6 patients (2 males, 4 females) average age of 52 years (mean standard deviation 52 ± 18, range 20–72).

Past medical history of the study group included: one had carcinoma of the breast, one had prostate cancer, and one was post-resection and radiotherapy for frontal anaplastic meningioma. The past medical history of the patients with meningiomas in the study group included one patient who received radiation because of tinea capitis during childhood, and one patient who sustained a cerebrovascular accident 16 years earlier. Past medical history of the control group included: asthma, hypertension, hyperlipidemia.

The mean (± SD) body mass index (BMI) of the study group was 26.45±5.57 while for the control group it was 26.96±0.70 (t-test, $p = 0.892$).

Presenting signs and symptoms

The mean duration of symptoms, for the study group, before diagnosis was 22±21.36 days (range 0–60) while for the control group 156.67±159.36 days (0-365) (t-test, $p = 0.047$). In the study group, only one patient had no symptoms and optic disc edema was found incidentally during a routine eye examination while in the control group all patients had a clinical presenting symptom.

The neurological and ophthalmological symptoms and signs at presentation for both groups are summarized in Tables 1 and 2.

In the study group, one patient had Freisen grade + 1, 3 Freisen grade + 2 and 2 patients had Freisen grade + 4 while in the control group 1 patient had Freisen grade + 1 (Fig. 1A-D).

Visual fields of the study group, at presentation, included: an enlarged blind spot for all patients, nasal or arcuate depression for three patients, generalized field constriction for one patient (Fig. 1A-D). None had a homonymous VF defect at presentation, with the exception of the patient with a history of cerebrovascular accident who had a small residual VF defect (Fig. 1A). In the control group, 4 patients had homonymous VF defect at presentation (chi_squ, $p = 0.041$) (Fig. 1B).

Diagnosis

All patients underwent MRI and MRV or CTV. In the study group, an occlusion of the venous drainage system was found in all patients while in the control group it was not found. Tumor-compressed venous drainage was observed in all study patients. Secondary thrombosis was detected in 3 patients, and meningioma appeared to infiltrate the venous system of one patient. The tumor in the study group was a meningioma in 4 patients with several locations (bilateral infra- and supratentorial patient # 1 right parasagittal patient #2, left parasagittal patient #3, left occipital anaplastic meningioma patient#6). The other 2 patients were diagnosed with occipital lobe metastasis whose primary sites were prostate (patient #5) and thyroid (patient #4). In the control group, 4 patients had meningioma in the occipital lobe, 1 patient had Glioblastoma multiforme (GBM)- CNS WHO grade 4 in the parieto-occipital lobe and one patient had Papillary Glioneuronal Tumor (PGNT) in the occipital lobe. The average volume of the tumor in the study group was 41,221 mm [3] while in the control group 31,264 mm [3] (t-test, $p = 0.624$). No empty Sella turcica were demonstrated in the study group while one patient had empty Sella turcica in the control group (chi_squ, $p = 0.296$). None of the patients, in both groups had flattening of the posterior optic globe.

Five of the study patients underwent lumbar puncture (the sixth refused), and the mean opening pressure was 297.5 mmH_2O (mean 297.5 ± 46.5, range 250–360). The cerebrospinal fluid composition was within normal limits except mild elevation of protein level 50 mg/dl(upper limit < 45 mg/dl.) in one meningioma patient.

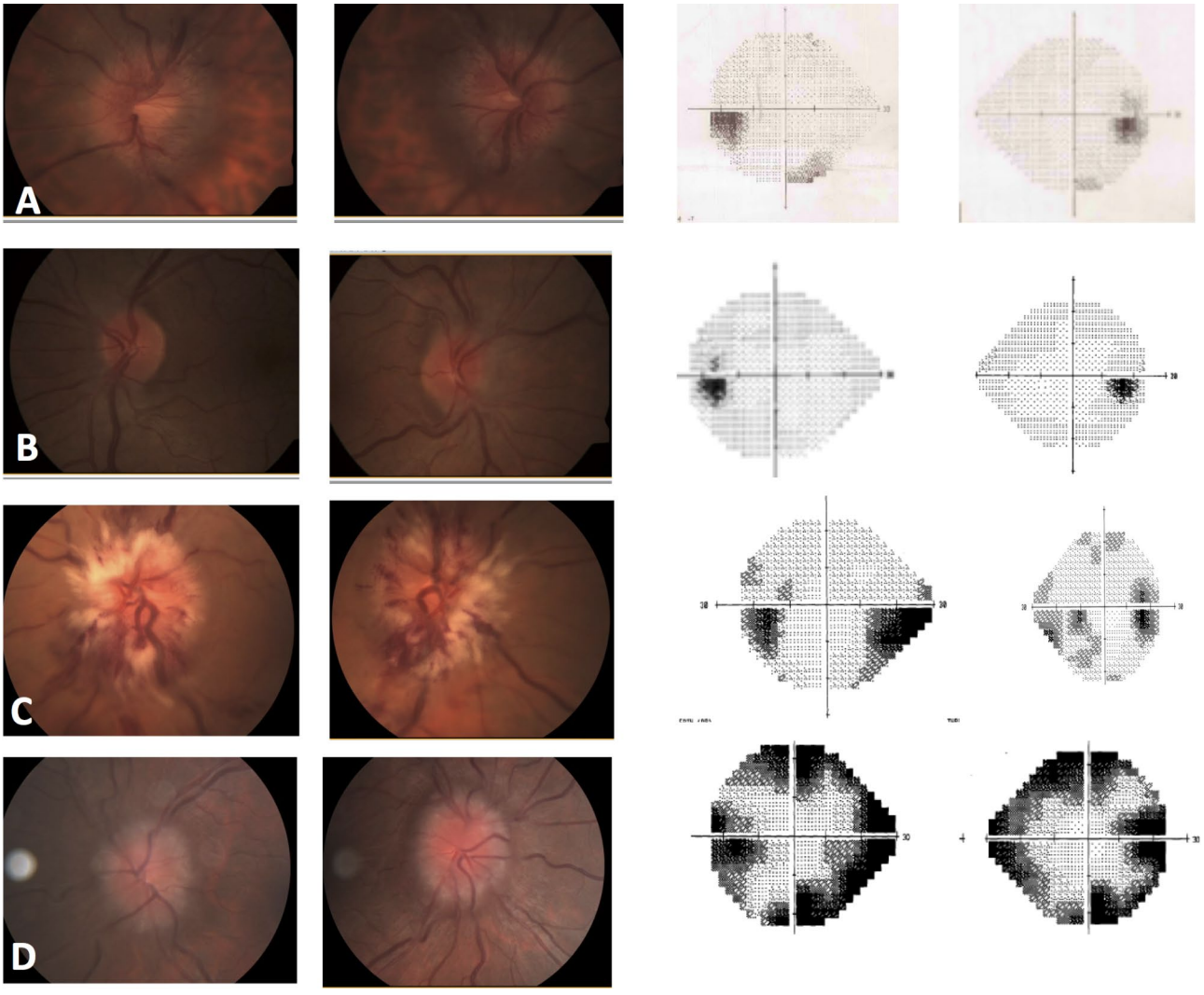

Fig. 1 Optic disc and visual fields. **A** Patient 3- OU: Freisen + 2; VF: Enlarged BS and residual old small homonymous from old stroke as 15 years prior. **B** Patient 4- OU: Freisen + 1; VF: Not significant VF disturbance (very mild enlarged BS). **C** Patient 5- OU: Freisen + 4; VF: Enlarged BS and nasal defect. **D** Patient 6- OU: Freisen + 2; VF: Enlarged BS and Constricted VF. Abbreviations: OU- both eyes; VF- Visual Fields; BS-Blind spot

Management and disease course

During the follow-up period of the study group, which lasted an average of 5.38 years (mean 5.38±4.73, range 1.3–14), all 6 patients (100%) were treated with acetazolamide and 5 patients (83.33%) were treated with dexamethasone. Three patients were also treated with enoxaparin for thrombosis. The surgical management for the acute elevated ICP, was discussion with the neurosurgery team. Five (83.33%) patients underwent insertion of a ventriculoperitoneal shunt because of visual function deterioration despite maximal tolerated medical treatment. Two patients (33.33%) were treated with continuous drainage of, and one patient (16.67%) underwent optic nerve fenestration due to visual function deterioration. Following those acute treatments, all 6 study group patients underwent radiosurgery for tumor treatment, while 3 also underwent partial resection followed by radiotherapy.

The follow- up period of the control group was 5.30 years (mean 5.30±3.37, range 0.8–10). During this period of time, all patients underwent resection of the tumor and 2 patients underwent radiosurgery.

At the end of follow-up, 2 patients, from the study group, died: one from anaplastic meningioma and one from GBM, and the remaining 4 patients from the study group, were stable. In the control group, all patients were alive at the end of follow- up but one patient developed epilepsy and deterioration in cognitive status.

Visual outcome

None of the study group patients, with the exception of one who developed optic disc atrophy and visual deterioration, had visual complaints at the end of follow-up.

Table 3 Neurological and ophthalmological signs at the end of follow up

Clinical Signs	Study Group	Control group	*P*_Value
VA for distance	0.03	0.018	0.283
VA for near	1.00	1.16	0.389
MD	-6.99	-10.08	0.541
CV	4.25	5.83	0.149
RAPD, Yes: No	1:0	0:6	0.296
Disc edema, Yes: No	0:6	0:6	1.00

VA- Visual Acuity, MD- Mean Deviation; CV- color vision; RAPD- Relative afferent pupillary defects

In the control group, 3 patients had deterioration in the visual field at the end of follow up. There were no significant differences at the end of follow up in the clinical signs between groups (Table 3).

A comparison between clinical signs at presentation vs. at the end of follow-up did not show significant differences in clinical characteristics at the study group. Atrophy of the disc at the end of follow-up was found in 1 of the 6 patients and no patient had disc edema.

Cases

We report 2 of the cases from the study group in detail to demonstrate their clinical course.

Case 1

This was a 47-year-old male who presented to the ophthalmology emergency room complaining of headache during the preceding 2 months and the onset of blurred vision during last few days. His past medical history was significant for having donated a kidney to his son 2 years prior. His visual functions at presentation were abnormal. The dilated fundus examination revealed optic disc edema (Fig. 2A), the MRI showed large bilateral infra and supra-tentorial meningiomas and the CTV demonstrated penetration of the meningioma to the confluent (Fig. 2B) and sagittal sinuses (Fig. 2C) but he refused to undergo LP. He was treated with acetazolamide and dexamethasone. Due to his damaged VF, VP shunting was recommended but he declined and left the hospital. Subsequently, he returned while sustaining deterioration of his vision and underwent an urgent VP shunt surgery and bilateral optic nerve sheath fenestration followed by radiotherapy for the meningioma. His vision continued to deteriorate to 20/400 in his right eye and hand movement in his left eye, despite all the above procedures to avoid optic atrophy and blindness.

Case 2

This was a 62-year-old female with recent diagnosis of breast carcinoma. She was referred to the ophthalmology emergency room due to bilateral optic disc edema found incidentally during a routine examination. The MRI showed a space-occupying lesion in the occipital lobe, and the MRV showed compression of the sigmoid and transverse venous sinuses (Fig. 3A-B). She was treated with prednisone and acetazolamide which led to improvement in the disc edema. The neurosurgical consultant recommended a follow-up MRI under the presumption that the tumor was a meningioma, while another neurosurgeon recommended resection. Finally, she decided to be treated medically. However, in the meantime, a thyroid nodule was diagnosed and so she underwent partial thyroidectomy that revealed follicular thyroid carcinoma. After 8 months since presentation to the ophthalmology service the size of the occipital lesion increased on follow-up MRI and resection was again recommended. She then underwent craniotomy and biopsy of the occipital SOL. The histopathological result was follicular thyroid carcinoma metastasis. Consequently, she underwent radiosurgery for the brain lesion and thyroidectomy 2 weeks later and then started radioactive iodine therapy. Four months after radiosurgery the optic disc edema worsened and the blind spot in the VF has increased. She underwent the insertion of a VP shunt which resulted in stabilization of the tumor size and resolution of the disc edema.

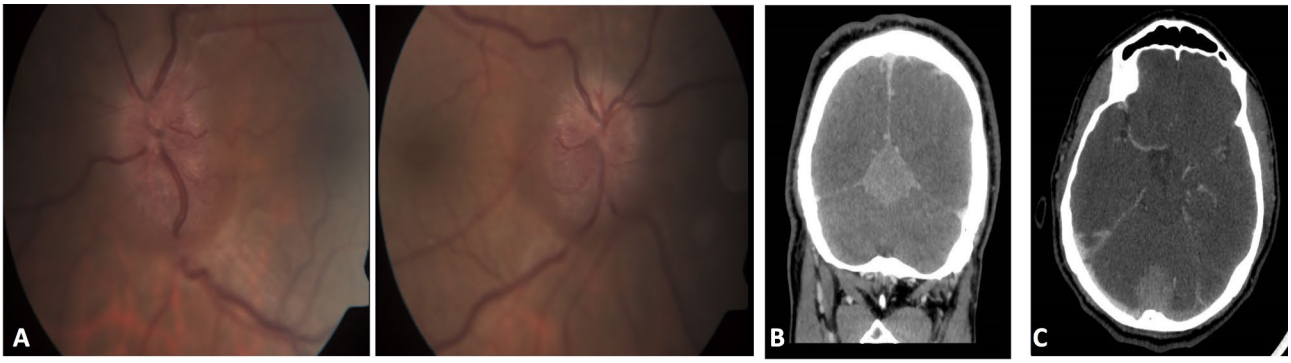

Fig. 2 Case number 1. Fundus examination: Bilateral optic discs edema **(A)**. CTV examination: meningioma penetration to the confluent sinus **(B)**. CTV examination: meningioma penetration to the sagittal sinus **(C)**

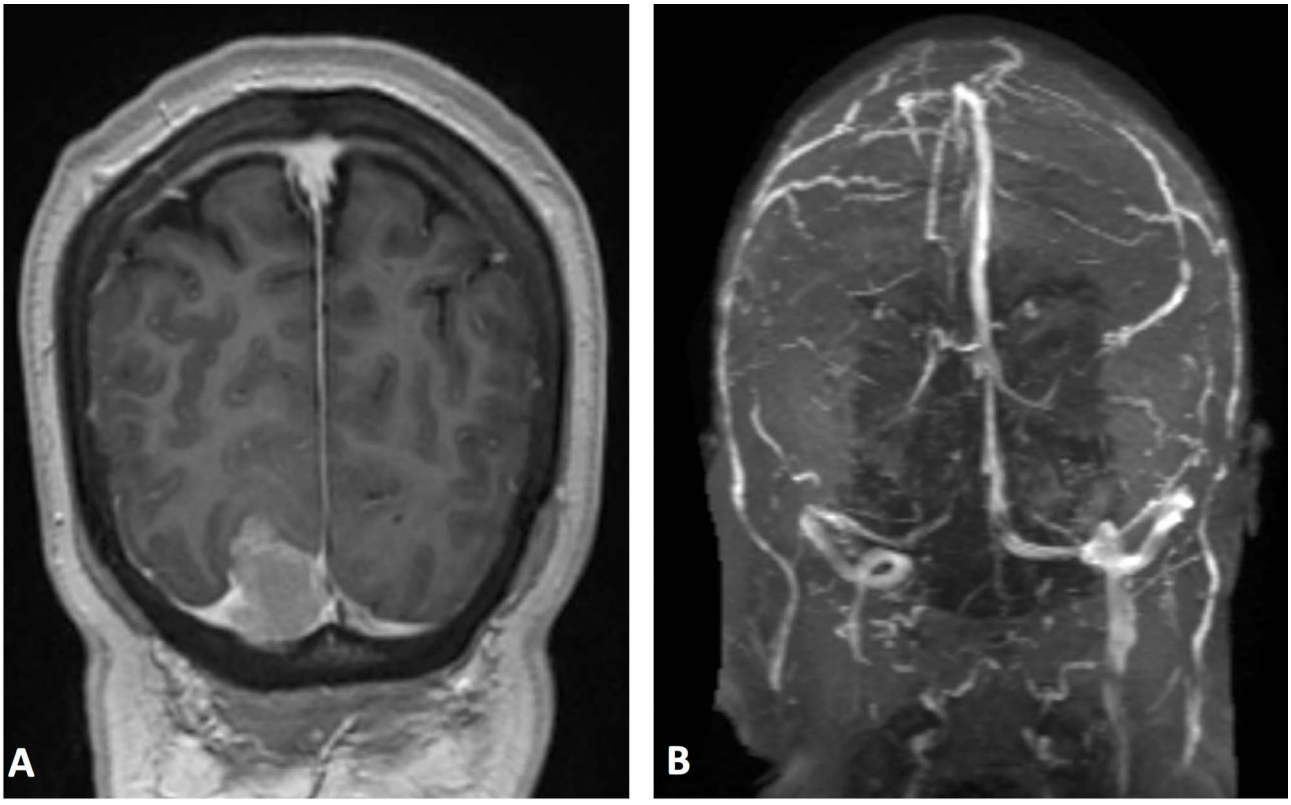

Fig. 3 Case number 2. MRI examination: space-occupying lesion in the occipital lobe **(A)**. MRV examination: compression of the sigmoid and transverse venous sinus **(B)**

Discussion

In this case series occipital tumors mimicking PTC secondary to venous drainage obstruction is described and compared to those without venous drainage obstruction. Patients with occipital tumors mimicking PTC had shorter time from symptoms to diagnosis compared to those without venous drainage obstruction. This may be attributed to the fact that those patients presented with decreased visual acuity compared to those with occipital tumors without venous drainage obstruction. In the study group all patients had disc edema, half of them had RAPD and the OCT RNFL thickness was higher compared to the control group. Because of the high index of suspicion, all patients underwent MRV or CTV which supported the diagnosis in the study group and excluded the diagnosis of drainage obstruction in the control group. All patients, in the study group, were treated medically and surgically for the increased ICP which threatened their vision and at the end of follow-up 5 out of 6 patients had improvement in visual function and one who presented late ended with legal blindness. In the control group, all patients were treated surgically and at the end of follow-up there were no differences in clinical ophthalmic characteristics between groups.

Recently, Hartmann et al. published a multi-center series of 16 patients with meningioma that involve compression of the dural venous sinuses resulting in intracranial hypertension [19]. Their series is the largest published so far [19]. However, there are few single case reports of increased ICP secondary to occipital metastasis [20, 21]. In one case report, a child with transverse-sigmoid sinus junction compression caused by a small temporal bone osteoblastoma is described [20]. In another case a 61 years old male with transverse venous sinus obstruction causing a syndrome resembling pseudotumor cerebri is reported. In MRI a small, extra-axial mass near the torcula was seen. It was initially diagnosed as meningioma but following lesion biopsy it was diagnosed as prostate adenocarcinoma metastasis [21]. Sarrami [et] al, recently discuss the multiple modalities for imaging IIH, their limitations, and their contributions to the management of IIH [22]. Therefore, to the best of our knowledge, our current study comprises the first series that describe different tumors in the occipital lobe that presented as PTC due to venous drainage obstruction and compare them to those without venous drainage obstruction. Moreover, in this series we also present the ophthalmic characteristics and prognosis.

The occipital lobe is a pyramid-like structure with three surfaces (medial, lateral, and basal) and three borders (superomedial, inferolateral, and inferomedial) [23]. The lobe is located in a critical spot in relation to the venous

sinus drainage, next to superior sagittal sinus, transverse sinus, sigmoid sinus, occipital sinus and next to the sinus confluence [23]. It was reported that impairment in venous drainage next to occipital lobe may cause visual impairment [24]. Few reports of occipital pathology cases including venous infarcts, arterial occipital infarcts after trauma and craniosynostosis describe visual disturbances and decline of visual acuity and visual field defects [25, 26, 27]. Keiper et al. reported about 5 patients with brain tumors that underwent suboccipital craniotomy or trans labyrinthine craniotomy for resection of a tumor. Subsequently, they developed headache, visual obscuration, and papilledema as a result of ICP. They underwent MRV and in all patients, the transverse sinus on the treated side was thrombosed [8]. In this case series we described 6 adult patients with meningioma or metastasis in the occipital lobe that presented with clinical picture mimicking PTC without any typical manifestation of occipital pathology. Those tumors created a mass effect on the venous sinuses which led to increase of ICP and caused complaints typical of PTC. When we compared those tumors to occipital tumors that do not affect venous sinuses, we found that the time from symptom to diagnosis is shorter when there is involvement of the venous sinuses. This is probably, because the visual acuity was lower in the group with venous sinuses involvement compared to those without. In accordance, patients with venous sinuses involvement have signs of increased ICP like disc edema, RAPD positive and increased OCT RNFL. However, no differences were found in neurological symptoms between the groups.

In our series 33% of the patients had symptoms of blurry vision which is not very typical for PTC [28]. Moreover, PTC is more common in females and in patients with high BMI. However, in this current study, 50% of the patients were males and the BMI was slightly higher than normal. Those findings may suggest that it is not the typical PTC and further evolution is needed.

The etiology of the presentation was demonstrated by venous imaging with MRV and CTV and differ between those with or without venous sinuses involvement. Therefore, it is important in cases that present with PTC symptoms such as headache, visual disturbances and papilledema, to have vascular detailed imaging. Imaging can detect three mechanisms causing venous drainage obstruction: Compression, infiltration and secondary thrombosis. In this case series compression was noted in all patients with venous sinuses involvement, in addition to compression secondary thrombosis which was noted in 3 patients (#3,5,6) and infiltration in one patient (#1).

All patients in the study group were treated both medically and surgically (VP shunt, optic nerve sheath fenestration, radiosurgery and partial resection) in order to decrease ICP, to treat the causing tumor and to preserve vision. In the control group, the patients were treated surgically. As demonstrated in our group of patients the treatment must be tailored case-by-case according to the patients' clinical manifestation, visual functions status and the type of tumor. However, in case of venous drainage system involvement, the treatment should be given as soon as possible because it can be a vision-threatening status as diagnosed in one patient in this study. He arrived late with low VA that did not improve despite medical and surgical treatment.

The systemic prognosis is according to the tumor type and stage in both groups. In our case series most of the patients, in both groups, were stable, which may be related to the fact that most of the cases were meningiomas and not metastasis or GBM (and only one case of anaplastic meningioma).

Regarding the visual function prognosis, in this case series only one patient in the study group developed optic discs atrophy that caused decrease in vision functions while 3 patients in the control group had deterioration in the visual field at the end of follow- up. This may be due to the fact that the diagnosis was later in the control group. However, there were no significant differences at the end of follow- up in the clinical signs between groups. Therefore, it seems that early and appropriate treatment should be administered in order to preserve visual function in both groups.

In comparison to Idiopathic intracranial hypertension (IIH) patients, it was found that there are some demographic and clinical characteristics that differentiate between the two pathologies: First, occipital tumors that mimic PTC occur in older age. Second, occipital tumors that mimic PTC are more common in men than IIH. Moreover, it is less common that patients with occipital tumors will present with transient visual obscurations. Those clinical and demographic characteristics may raise the suspicion of physicians that the pathology is not IIH but another disease like occipital tumor that causes venous drainage obstruction.

Increased ICP as a result of venous outflow obstruction due to occipital lesion is rare and its management is challenging since, as previously cited, surgery may worsen the venous circulation and aggravate the situation [27]. Further larger studies are required in order to describe the clinical aspects of this pathology and to examine the best treatment for increased ICP due to venous outflow obstruction resulting from occipital lesion.

The limitations of our study are mainly its retrospective nature and the small number of patients which raises the possibility of referral bias as our center is a tertiary center and neurosurgery center.

In conclusion, we describe a case series of patients with occipital tumors with a presentation mimicking PTC secondary to venous drainage obstruction compared to

those without venous drainage obstruction. We found ophthalmic signs and symptoms similar to PTC in the group with venous drainage obstruction that caused an earlier diagnosis compared to those without venous drainage obstruction. The diagnosis of obstruction of the venous drainage system was done by MRV or CTV. Therefore, it is important in cases with PTC symptoms and signs, with tumors shown in MRI, to perform MRV or CTV as well. The patients with venous drainage obstruction were treated medically and surgically immediately after diagnosis in order to decrease the ICP. Probably the early treatment to this group brought to good visual prognosis that was not different from the group without venous drainage obstruction. Therefore, early diagnosis and prompt multi-disciplinary treatment may lead to better results in cases of occipital tumors with venous drainage obstruction.

Abbreviations

PTC	Pseudotumor cerebri
CSF	Cerebrospinal-Fluid
CNS	Central nervous system
SOL	Space occupying lesion
ICP	Intra cranial pressure
VF	Visual field
VA	Visual acuity
CV	Color vision
RAPD	Relative afferent pupillary defect
MD	Mean deviation
HRR	Hardy-Rand-Rittler
OT	Occipital tumor
MRI	Magnetic resonance imaging
MRV	Magnetic resonance venography
CTV	Computed tomography venography
IRB	Institutional review boards
BMI	Body mass index
GBM	Glioblastoma multiforme
PGNT	Papillary Glioneuronal Tumor
IIH	Idiopathic intracranial hypertension

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Author contributions
OZ: Protocol/project development, Data management, Data analysis, Manuscript writing and editing. MB: Data collection, Data analysis. RHB: Protocol/project development, Data management, Data analysis, Manuscript writing and editing The manuscript has not been published elsewhere, and was not submitted simultaneously for publication elsewhere.

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Data availability
The data that support the findings of this study are available on request from the corresponding author and agreement of the IRB.

Declarations

Ethics approval and consent to participate
The study was approved by the local institutional review boards (IRB) of Sheba Medical Center which waived informed consent for this retrospective study.

Consent for publication
Yes.

Competing interests
None.

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