Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Abnormal Optic Nerves Signals in Orbital MRI: a Rare Sign in Idiopathic Intracranial Hypertension

Zhonghua Ma (ma_zhonghua@163.com)
Capital Medical University https://orcid.org/0000-0001-8209-4175
Hanqiu Jiang
Capital Medical University
Jiawei Wang
Capital Medical University

Research article

Keywords: Idiopathic intracranial hypertension, Optic nerves sheaths, Orbital MRI

Posted Date: July 18th, 2019

DOI: https://doi.org/10.21203/rs.2.11621/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Abstract

Background It is recognized that radiological examination is essential for the diagnosis of Idiopathic intracranial hypertension (IIH). The present study demonstrated a rare sign of IIH in optic nerves on MRI images. Methods Review the medical records and MRI images of 82 the patients with IIH referred to our neurology department from January 2017 to December 2018. Inclusion criteria were: 1) accorded with the IIH diagnostic criteria adapted from Friedman et al. [1], 2) abnormal optic nerve signal with enhancement on orbital MRI, 3) no better explanation for the optic nerve involvement. Results 12 patients are enrolled. The age of patients ranged from 16 to 55 years, median age 32.91±14.36 years, two patients were male and ten were female. The CSF opening pressures (OP) of all patients were all above 30 cmH2O. Enhancement of optic nerves sheaths (ONS) in retrobulbar segments were observed in all affected eyes showed on coronal orbital MRI gadolinium (Gd)-enhanced T1WI sequence. Conclusions Enhancement of ONS on MRI is a rare sign of IIH that clinicians should recognize in order to avoid misdiagnosis and mistreatment. Keywords: Idiopathic intracranial hypertension, Optic nerves sheaths, Orbital MRI

Background

Idiopathic intracranial hypertension (IIH), is frequently considered as a cause of headache, blurred vision and papilloedema with elevated intracranial pressure, normal CSF composition and normal neuroimaging results. Despite extensive clinical investigation and basic scientific research, the precise etiology of IIH is still a mystery. It is rare, but due to the risk of visual impairment, accurate diagnosis is essential. Evolution has been made in the recommendations for assessment, especially in the field of MRI imaging. The purpose of this passage is to demonstrate a rare sign of orbital MRI in the IIH and to avoid misdiagnosis.

Methods

We conducted a retrospective review of all the patients with presumed IIH referred to our neurology department from January 2017 to December 2018. All participants were re-identified respectively by two neuro-ophthalmological specialists before enrolled in our registry. Clinical data including diagnoses, clinical characteristics, laboratory findings, DSA and MRI images of these patients were reviewed. Age, gender, height and weight were recorded. In addition, their actual body weight were categorized into three types according the classification of overweight and obesity for Chinese adults as follows: 18.5≤BMI<24, normal; 24≤BMI□28, overweight; BMI≥28, obese. The inclusion criteria should be: 1) accorded with the IIH diagnostic criteria, adapted from Friedman et al [1], 2) abnormal optic nerve signal on coronal orbital MRI gadolinium (Gd) - enhanced T1WI sequence, 3) no better explanation for the optic nerve involvement. On the contrary, exclusion criteria are: 1) history of prior optic neuropathy, 2) presence of central nervous system (CNS) mass or other primary causes of increased intracranial pressure (ICP), 3) dense media opacity, 4) treatment with topiramate or acetazolamide for longer than 2 weeks before testing could be obtained, and 5) failure to fulfill the revised diagnostic criteria for IIH.

For all patients, best corrected visual acuity, funduscopic examination, and visual field tests were performed; Conventional blood routine test, biochemical test and coagulation examinations were measured; Serum aquaporin-4 antibody (anti AQP4-IgG), dsDNA antibody, ANA, ENA antibody, CRP, ANCA, and mt-DNA mutation testing were also arranged. Besides, Intracranial hypertension (elevated intracranial pressure ≥25cmH2O) was confirmed by open lumber puncture in the lateral decubitus position, and cerebral spinal fluid (CSF) analysis was obtained on all patients to exclude infection or inflammation events.

All patients underwent contrast-enhanced brain and obital MRI, including T1WI, T2WI sequences with fat suppression. The axial, coronal and sagittal MR imging were performed on a Discovery MR750 3.0-T MR imaging system (GE Healthcare, Milwaukee, WI) with an 8-channel head coil. A standard dose (0.1 mmol/kg) intravenous gadolinium based contrast agent was administered at 2.0 cc/second. Criteria of abnormality of optic nerve should be: increased signal of ON/ONS on T2WI sequence, with/without enhancement on T1WI sequence after given contrast. Every MRI image was reinterpreted by a neuroradiologist masked to the affected side. Bilateral distension of the perioptic subarachnoid space (DPSS), and empty sella turcica were assessed on coronal T2WI; while venous sinus thrombosis, sinovenous narrowing related to PTC, or congenital narrowing of the venous sinuses were evaluated on MRV/DSA. Last but not least, each image was assessed independently on the clinical data.

There were ten patients who received uniform therapeutic regime of oral acetazolamide with weight management, while the other two received surgical procedures of lumbo-peritoneal shunt. A trained resident doctor kept an additional telephone follow-up of them and monitored treatment compliance.

The statistical analysis was performed using package of SPSS (version 22.0), Categorical variables were reported as number and percent and continuous variable was presented as mean and standard deviation.

Signed informed consents were obtained from all participants.

Patient and Public involvement.

There were no patient and other ordinary people involvement in any design, implementation and analysis of this research, nor were in any planned dissemination activities.

Results

In this study, a retrospective non-interventional clinical observation was conducted and 12 patients were enrolled. The age of patients ranged from 16 to 55 years, median age 32.91±14.36 years. 2 (16.7 %) patients were male and 10 (83.3%) were female. All patients were suffering from blurred vision, which ranged in duration from 2 weeks to 8 years. In addition, 5 (41.67 %) patients had transient visual obscurations (unilateral or bilateral darkening of the vision typically seconds), 4 (33.3%) patients suffered from headache, 2 (16.7%) patients had tinnitus and 1(7%) patient endured double vision. Vision loss was described as the only symptom in 4 patients' complains. Regarding the weight of patients in the observed group, 4 patients were of normal weight with body mass index (BMI) 24, 2 patients were overweight (24≤BMI28), and 6 patients were obese (BMI≥28) . (Table 1). Their neurological examinations were normal. The best corrected visual acuity of 6 eyes was below 0.1, 7 eyes between 0.1 and 0.5, and 11 eyes above 0.5. Funduscopic examination revealed papilledema in 22 eyes of eleven patients, and pale optic discs in 2 eyes of one patient. The intraocular pressures were all within normal limits. In the lateral decubitus position, the lumbar puncture with opening pressure (OP) measurement was completed, and the CSF-OPs of all patients were all above 30 cmH_2O (Table 1).,serial serum immunological antibody tests were all negative.

All imaging exams were performed before the lumbar puncture. Gadolinium (Gd) - enhanced of optic nerves sheaths (ONS) were observed in all affected eyes showed on coronal fat-depressed T1WI (Figure 1). Brain MRI with contrast showed empty sella/DPSS in 11/12 patients (Figure 2), scattered lacunar infarcts in 1/12 patient, and no meningeal enhancement in all patients. Unilateral or bilateral transverse venous sinus stenosis (TVSS) were found in 6/12 patients by MRV/DSA (Figure 3).

As regards therapeutic regimes, monotherapy was used by 10/12 patients receiving oral acetazolamide for an average of 7.4 months, while the other 2/12 patients received lumbo-peritoneal shunt. As a result, elevated ICP and vision function of all patients got relieved in different degrees.

Discussion

As rapid development in radiological imaging, clinicians are able to make a more reliable diagnosis of IIH, combined with clinical and laboratory findings. Some imaging findings defined in the past decades can contribute to support or exclude the diagnosis of IIH in clinically suspicious cases. Several studies have reported significant correlations of imaging findings, such as empty sella, increased tortuosity of optic nerve, DPSS and flattened posterior globe/sclera with the diagnosis of IIH[2-4]. All these findings, together with intraocular protrusion of optic nerve head, bilateral transverse sinus stenosis or stenosis of a dominant transverse sinus, were adopted by the latest IIH guideline [5].

In this report, we found that ONS were Gd-enhanced confirmed by orbital MRI in 12 patients with IIH, which has never been reported in Chinese population before. Only a few studies in Caucasian mentioned the similar sign. A report from Brodsky MC[3] in twenty patients with IIH, discovered that enhancement of the prelaminar optic nerve has observed in 50% of these patients. Another two research observed also marked enhancement of optic nerve heads in patients with IIH[2,4]. But significantly different from the previous studies, Gd-enhanced ONS found in the present observation located in the retrobulbar segment of ON.

The median age of these 12 patients was 32.91±14.36 years, females account for the majority (83.3%), with common symptoms of IIH such as blurred vision (100%), headache (33.3%), and transient visual obscurations (41.67 %), pulsatile tinnitus (16.7%), and double vision1(7%). According to the IIH guideline of 2018[5], only 6/12 patients in this cohort (patient 1, patients 6, patient 7, patient 9, patient11 and patient 12) are “typical IIH” who satisfy the following criterion: female, childbearing age, obese BMI with typical symptoms. While four of the six patients with “atypical IIH” experienced misdiagnosis and mistreatment in local hospitals, especially those with longer clinical courses. These IIH sufferers had been misdiagnosed as “optic neuritis”, “ischemic optic neuropathy” or other optic neuropathies, and received treatment of intravenous/oral methylprednisolone in different dosage after misdiagnosis. But no obvious alleviation has made on these symptoms, inversely, they aggravated gradually. Then, all the patients received complete examinations together with lumbar puncture after receiving admission from our department. A rare imaging sign of IIH, enhancement in optic nerves/ ONS on MRI scan, surprisingly appeared in front of radiological and neuro-ophthalmological clinicians. The first possible diagnosis was a certain kind of optic neuropathy according to the medical records. However, the markedly elevated CSF-OP and chronic courses of the patients are confusing. Moreover, imaging findings, such as empty sella, DPSS, unilateral or bilateral TVSS, indicated the possibility of increased ICP. Series of in-depth tests were arranged to clarify underlying causes for secondary intracranial hypertension and optic nerves injury, including infectious/immunological diseases, medications,

systemic disorders, obstruction to venous drainage, and so on. Finally, the diagnosis of IIH was confirmed. The lumbar puncture OP was one debatable area. It was reported that there seemed to be a “grey zone” of lumbar puncture OP between 25 cm and 30 cm H2O, people in “grey zone” might be normal for some individuals[6]. In this report, there are no such “grey zone” concerns, for CSF OPs of all patients were all above 30 cmH2O.

The etiology of IIH is still unknown, however, there has a strong connection between IIH and obesity. The pattern of fat distribution in patients with IIH may be relevant. The mechanical effects of excessive abdominal fat elevate intra-abdominal pressure, which increases intrathoracic pressure and, thereby, increases cerebral venous pressure, and, eventually leads to the intracranial hypertension[7]. Moreover, obesity is a chronic inflammatory condition, consequently, pathogenic inflammation may cause IIH [8-10]. But the hypothesis would not explain why only a proportion of all individuals with obesity develop IIH. Some researchers have shown a significantly increased level of the chemokine CCL2, IL-2 and IL-17 in CSF of patients with IIH , compared with controls[11, 12]. These investigations indicate that inflammatory factors are involved in the occurrence of IIH, although lack of compelling evidence. Immunomodulatory therapy therefore has not been listed as one of the main treatment strategies for the disease until now.

The principal pathogenic mechanisms of IIH has been in dispute, which makes it difficult to illuminate the abnormal singles of ONS detected in this report. Some scientists assumed that enhancement of the optic nerves is reflective of the same pathology leading to papilledema: increased pressure referred from the cranial fossa generates venous congestion, capillary leakage, and possible breakdown of the blood-retinal barrier[13]. It remains unclear that in which way and to what extent the CSF space is affected in response to increasing intracranial pressure. It has been assumed that what leads to increased transmission of CSF into the sheaths of optic nerves shall be ICP, which also impedes axoplasmic transport of synaptic vesicles, organelles, and molecules followed by optic nerve fiber swelling[14]. However, scientists have not found any correlation between increased ICP and the degree of hypophysis compression or the DPSS supporting this hypothesis. [15].

In this group, only 6 of 12 patients are obese, and methylprednisolone treatments were proved ineffective in patients received glucocorticoid therapy. Combined with negative laboratory tests, neither of obesity nor inflammatory factors could be used to clarify the causes of IIH and abnormal signals of optic nerves. Significantly elevated ICP (>30cmH2O) is one of the characteristics of these patients. Moreover after receiving the treatments of lowering intracranial pressure, the visual functions and other symptoms of the patients has ameliorated., This suggests that intracranial hypertension plays a key role in the course of the disease. We tend to agree that increased pressure generates venous congestion and capillary leakage[13]. Possible Destruction of blood-brain barrier (BBB) around optic nerve aroused by elevated ICP, attributes to the abnormal signals of ONS. Regrettably, we failed to rearrange MRI scans for the patients in time when the symptoms became relieved, hence failed to observe whether the optic nerve signal disappears. In addition, whether inflammatory factors are involved in or not, still need to be further clarified through subsequent experiments.

Conclusions

The diagnosis of IIH cannot be made without neuroimaging examination, if there is an additional clinical or imaging indication to suggest a greater likelihood of IIH, we recommend coronal T2-weighted images of the orbits to assess ONS widening. But sometimes rare imaging signs discussed in this study may be ambiguous/confuse us. Clinicians should

understand and recognize the existence of rare signs, understand the clinical characteristics and pathogenesis of IIH, and ultimately achieve the goal of avoiding misdiagnosis and mistreatment.

Declarations

Acknowledgement Not Applicable

Funding Research fund of Development Program of Key Medical Discipline (Neuroimmunology)Capital Medical University affiliated Beijing Tongren Hospital(trzdyxzy201704). The funding body has not any role in the design of the study, collection, analysis, interpretation of data and in writing the manuscript.

Availability of data and materials The data set available from the corresponding author on reasonable request.

Authors'contributions JW contributed to the conception of the study. HJ designed the work. ZM contributed to the acquisition of the data. All authors contributed to the analysis and interpretation of data. ZM drafted the initial manuscript. JW, HJ revised the manuscript critically for important intellectual content. All authors have read the manuscript and gave their final approval of the version to be published.

Ethics approval and consent to participate Ethic Approval was obtained from the institutional ethical review boards of Beijing Tongren Hospital, Capital Medical University, Beijing, China. Written informed consents were obtained from the patients for participation.

Consent of publication Not Applicable

Competing interests The authors declare that they have no competing interests.

References

1.Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology 2013;81:1159–65.

2. Agid R, Farb RI, Willinsky RA, et al. Idiopathic intracranial hypertension: the validity of cross-sectional neuroimaging signs. Neuroradiology. 2006;48:521–27

3. Brodsky MC, Vaphiades M. Magnetic resonance imaging in pseudotumor cerebri. Ophthalmology 1998;105:1686 –93

4. Manfre´ L, Lagalla R, Mangiameli A, et al. Idiopathic intracranial hypertension: orbital MRI. Neuroradiology 1995;37:459 – 61

5. Mollan SP, Davies B, Silver NC, et al. Idiopathic intracranial hypertension: consensus guidelines on management. J Neurol Neurosurg Psychiatry. 2018 Oct;89(10):1088-100. doi: 10.1136/jnnp-2017-317440. Epub 2018 Jun 14.

6. Mollan SP, Hornby C, Mitchell J, et al. Evaluation and management of adult idiopathic intracranial hypertension. Pract Neurol. 2018 Dec;18(6):485-88. doi: 10.1136/practneurol-2018-002009. Epub 2018 Aug 28.

7. Sugerman HJ, DeMaria EJ, Felton WL III, et al. Increased intra-abdominal pressure and cardiac filling pressures in obesity-associated pseudotumor cerebri. Neurology. 1997;49:507–11.

8. Hotamisligil GS, Arner P, Caro JF, et al. Increased adipose tissue expression of tumor necrosis factor-alpha in human obesity and insulin resistance. J Clin Invest. 1995;95:2409–15.

9. Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science. 1993;259:87–91.

10. Sinclair AJ, Ball AK, Burdon MA, et al. Exploring the pathogenesis of IIH: an inflammatory perspective. J Neuroimmunol. 2008 Sep 15;201-202:212-20. doi: 10.1016/j.jneuroim.2008.06.029. Epub 2008 Aug 3

11. Dhungana S, Sharrack B, Woodroofe N. Cytokines and chemokines in idiopathic intracranial hypertension. Headache.2009;49:282–85.

12. Edwards LJ, Sharrack B, Ismail A, et al. Increased levels of interleukin 2 and 17 in the cerebrospinal fluid of patients with idiopathic intracranial hypertension. Am J Clin Exp Immunol. 2013;2:234–44.

13. Manfre L, Lagalla R, Mangiameli A, et al. Idiopathic intracranial hypertension: orbital MRI. Neuroradiology 1995;37:459-61

14. Acheson JF. Idiopathic intracranial hypertension and visual function. Br Med Bull 2006;79-80:233-44

15. Hoffmann J, Schmidt C, Kunte H, et al. Volumetric Assessment of Optic Nerve Sheath and Hypophysis in Idiopathic Intracranial Hypertension. AJNR Am J Neuroradiol. 2014Mar;35(3):513-8. doi:10.3174/ajnr. A3694. Epub 2013 Sep 12.

Tables

Table 1 Clinical information of patients

	Presenting complains	Medical History	BMI	Vision acuity (OD/OS)	CSF-OP (cm H_2O)	Fundus examination	Inflammation indicators in serum and CSF	Imaging (brain MRI DSA/CTA)	Abnormal signals of ONS on obital MRI
Patient 1 Female/34	Recurrent amaurosis fugaxfor 10 months	Healthy	30.38	1.0/1.0	>33	Bilateral papilledema	negative	Empty sella TVSS	Bilateral
Patient 2 Male/49	Headache, blured vision, amaurosis fugax for 18 months	Healthy	26.51	0.5/0.16	32	Bilateral papilledema	negative	Empty sella	Bilateral
Patient 3 Male/42	Blurred vision for 17 days	Healthy	22.84	1.2/1.2	>33	Bilateral papilledema	negative	Lacunar infarct TVSS	Right
Patient 4 Female/21	Blurred vision, amaurosis fugax for 8 years	Healthy	22.67	0.2/0.1	32	Bilateral papilledema	negative	Empty sella DPSS	Bilateral
Patient 5 Female/23	Hearing-loss and double vision for 2 months	Allergic dermatitis	18.91	1.2/1.2	30	Bilateral papilledema	negative	DPSS TVSS	Bilateral
Patient 6 Female/23	Blurred vision for 1 year	Healthy	28.58	0.3/0.5	31	Bilateral papilledema	negative	Empty sella	Bilateral
Patient 7 Female/55	Headache, blurred vision for 2 weeks	Hypertension Diabetes	34.52	FC/1.0	>33	Bilateral papilledema and hemorrhage	negative	Empty sella DPSS	Bilateral
Patient 8 Female/40	Blurred vision headache, double vision for 2 years	Healthy	25.64	0.01/0.02	30	Bilateral pale	negative	Empty sella DPSS	Bilateral
Patient 9 Female/53	Blurred vision for 11 months	Hypertension Thyroid cyst	30.82	LP/0.4	32	Bilateral papilledema	negative	Empty sella TVSS	Right
Patient 10 Female/16	Distorted/blurred vision, tinnitus for 2 weeks	Psoriasis	18.33	0.1/0.6	>33	Bilateral papilledema	negative	DPSS TVSS	Bilateral
Patient 11 Female/20	Blurred vision, amaurosis fugax for 1 month	Healthy	33.33	0.7/1.0	>33	Bilateral papilledema	negative	Empty sella DPSS	Bilateral
Patient 12 Female/19	Blurred vision, headache, amaurosis fugax for 1month	Healthy	31.20	1.2/0.05	>33	Bilateral papilledema	negative	DPSS	Bilateral

Note: RE right eye; LE left eye; FC finger count; HM hand moving; LP light perception; DPSS distension of the perioptic subarachnoid space; TVSS: transverse venous sinus stenosis.

Figures

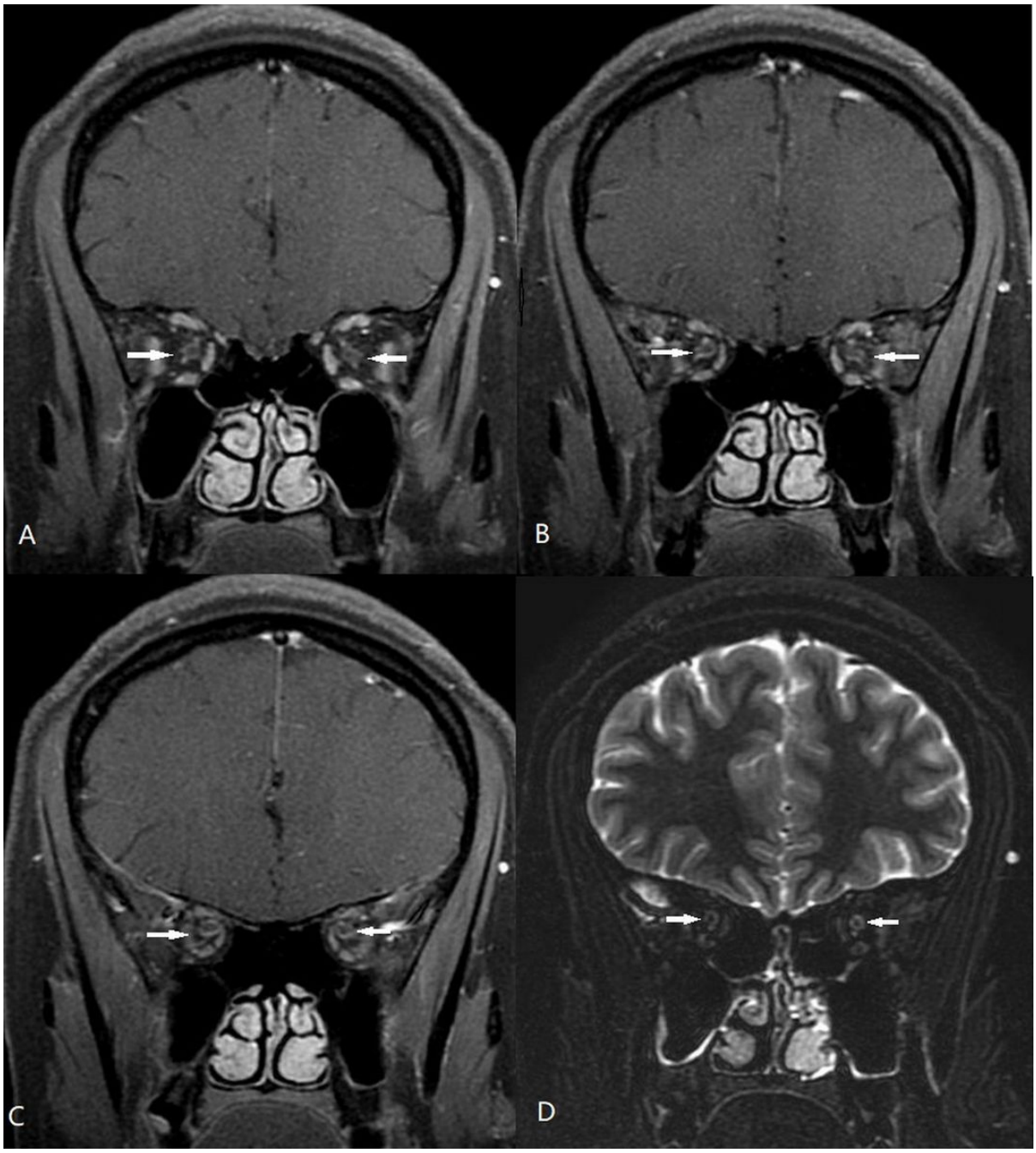


Figure 1

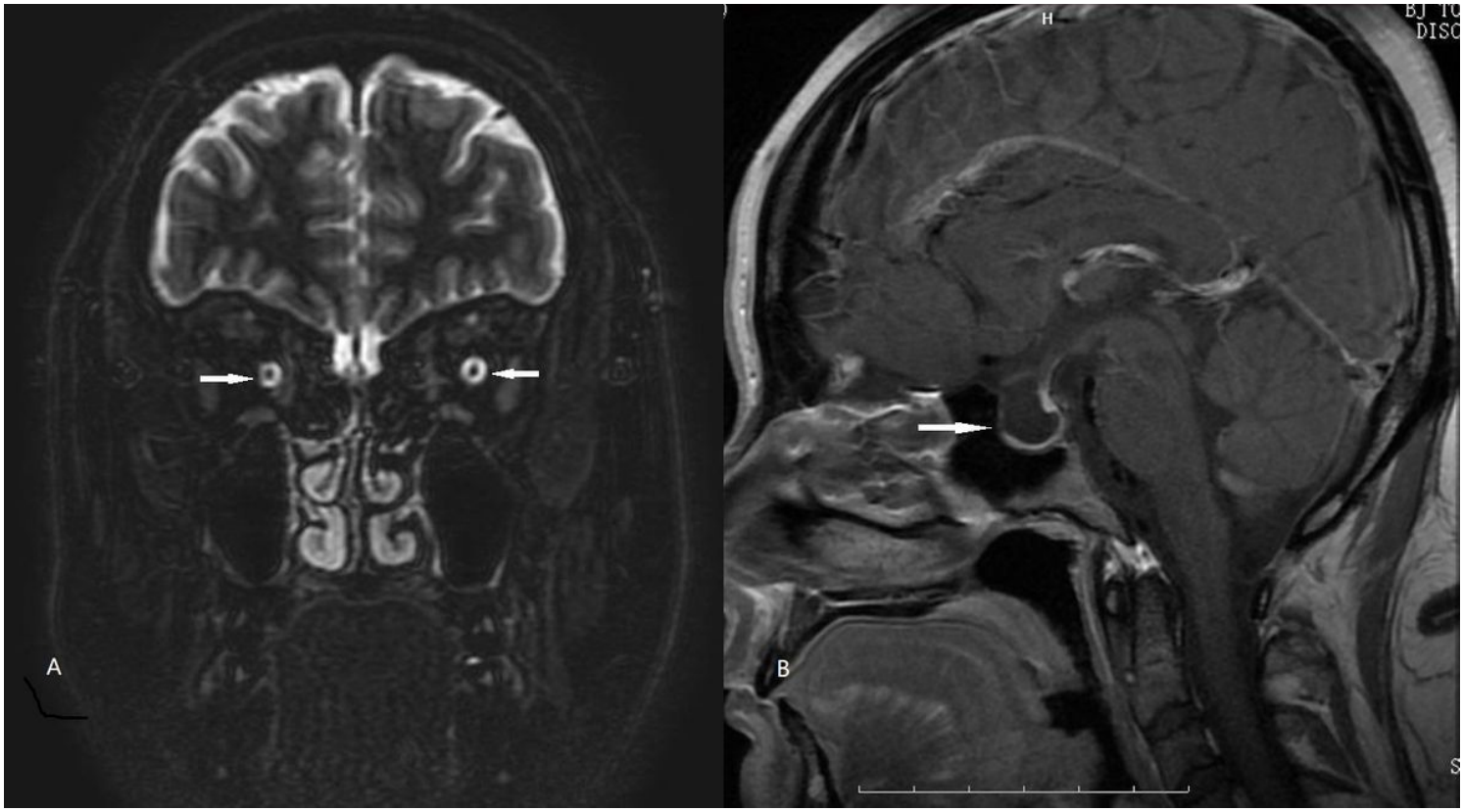


Figure 2

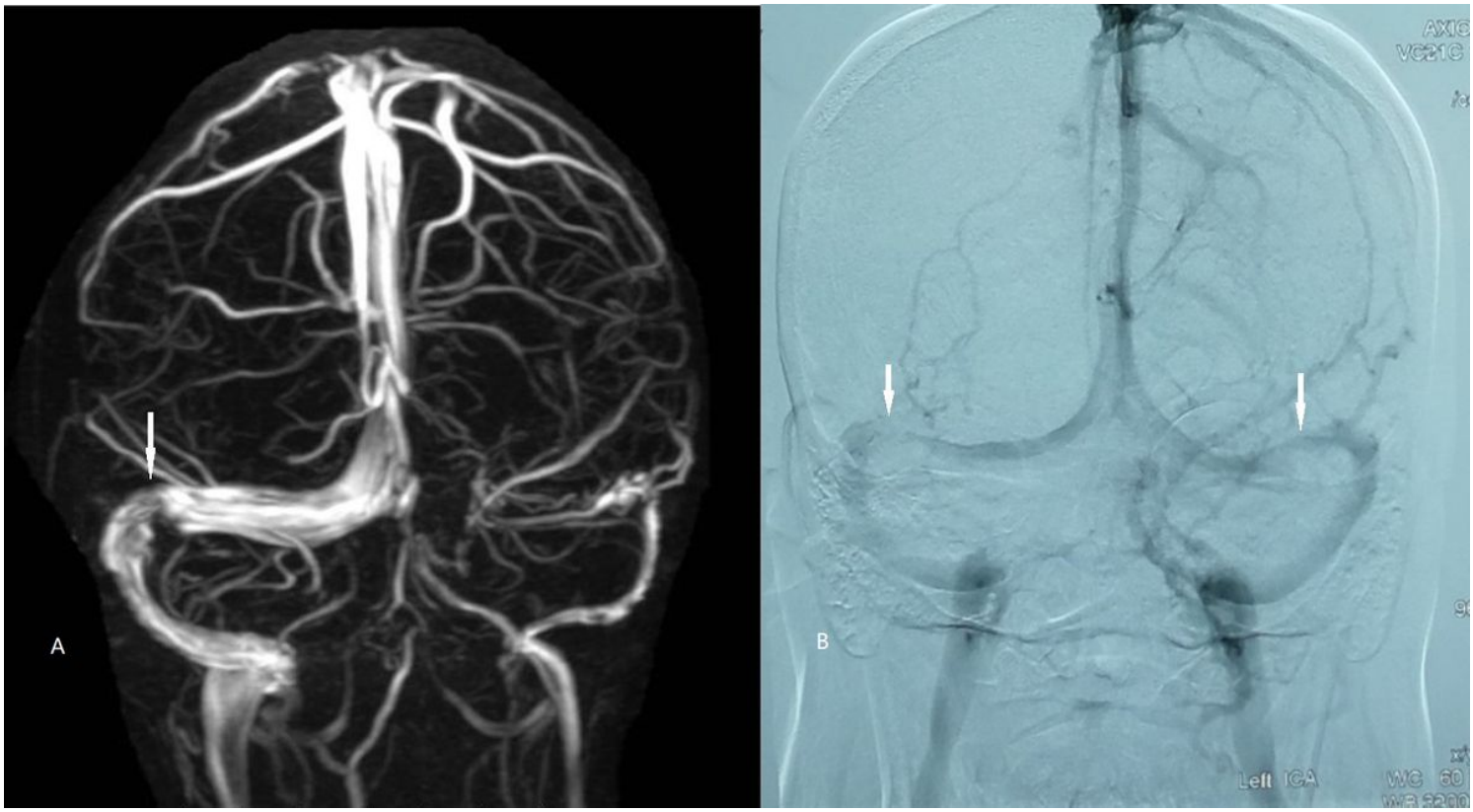


Figure 3