·Clinical Research·

Analyses on the misdiagnoses of 25 patients with unilateral optic nerve sheath meningioma

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Abstract

• AIM: To investigate clinical features of optic nerve sheath meningioma (ONSM) that was misdiagnosed, and to find methods to reduce the misdiagnoses.

• METHODS: Retrospective series study. Twenty-five misdisgnosed patients with unilateral ONSM were collected from Jan. 2008 to Jan. 2015 and the clinical records reviewed.

• RESULTS: Patients were misdiagnosed with acute papillitis most frequently (n=17), immediately followed by optic atrophy (n=8), ischemic optic neuropathy (n=5), acute retrobulbar optic neuritis (n=5), optic disc vasculitis (n=3). For each patient, the minimum frequency of misdiagnoses was once and the maximum was 4 times. As for the lasting time of being misdiagnosed, the shortest was 1.5mo and the longest was 45mo. Twenty-one cases (84%) were once treated with glucocorticoids, and its side effects was found in seventeen patients. Twenty patients (80%) complained with varying degree of vision loss. When a definite diagnosis was made, sixteen cases (64%) showed slight exophthalmos and eighteen cases (72%) had the tubular ONSM.

• CONCLUSION: ONSM without loss obvious exophthalmos is easily misdiagnosed in clinic, and for most of these ONSMs are tubular.

• KEYWORDS: optic nerve sheath meningioma; misdiagnosis; clinical feature
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INTRODUCTION

Optic nerve sheath meningioma (ONSM) is a benign tumor originated from arachnoid cells of optic nerve sheath. It accounts for about 2% of orbital tumors and 1%-2% of meningiomas [1-3]. Exophthalmos, loss of vision sharpness, chronic edematous atrophy of optic disc and ciliary veins are ONSM's typical clinical features. In clinic, many patients experienced loss of vision first without obvious exophthalmos so they were often misdiagnosed as neuropapillitis[4], ischemic optic neuropathy[5] *etc* and were treated in wrong ways. In this study, we collected 25 cases with unilateral ONSM with the misdiagnosed history in early stage. We analyzed clinical features and reasons of misdiagnoses, which was conducive to increase the accuracy of early diagnosis of ONSM and reduced the misdiagnosis and mistreatment.

SUBJECTS AND METHODS

Subjects Twenty-five patients with single-side ONSM who were received by Department of Ophthalmology, Xiangya Hospital of Central South University were collected from January, 2008 to January, 2015. All patients had the misdiagnosed history when visiting doctors in other hospitals (23 cases) or in our hospital (2 cases). They were proved to be unilateral ONSM by orbit magnetic resonance imaging (MRI). Intracranial lesions were excluded from through brain MRI. All patients had no history of oculopathy such as optic nerve diseases, glaucoma, ocular fundus diseases and strabismus, or history of intracranial meningiomas, neurofibromatosis, hyperthyreosis, diabetes *etc*. Our research was approved by the Human and Animals Ethics Committee of Xiangya Hospital, Central South University and performed in accordance with the principles outlined in the Declaration of Helsinki (2008). Every patient comprehended and kept in line with our research.

Methods These indexes, such as gender, age, chief complaint, visual acuity, pupil, exophthalmos degree, optic disc and tumor morphology, were recorded. The best corrected visual acuity was taken; pupil examination included diameter and light response to determine whether there was the relative afferent pupillary defect (RAPD); visual field (only 12 cases with visual acuity >0.02); flash visual evoked potential (F-VEP); tumor shape means to record the shape of ONSM based on orbit MRI and its shapes included the tube, fusiform, cone and spherical[6-7].

Each patient should be asked in details about the medical history, and the misdiagnosed disease, misdiagnosis frequency, the time of right diagnosis, drug treatment

(especially glucocorticoid) should be recorded. Diagnosis times refers to the time gap between the onset of disease and correct diagnosis. Glucocorticoid application, including prednisone, dexamethasone, methylprednisolone, refers to its dosage, medication time, and side effects.

RESULTS

Clinical Features There was 4 male and 21 female patients; the oldest was 52 years old and the youngest was 16 years old while their average age was 38.92. Fourteen cases (56%) had ONSM in the left eye and 11 cases (44%) in the right eye. Twenty cases (80%) had the chief complaint of loss of vision acuity and 5 cases (20%) had other chief complaints including diplopia (2 cases), amaurosis (2 cases), asthenopia (1 case).

Visual acuity was worse than 0.3 and RAPD was positive in all cases. There were 15 patients (60%) whose vision was lower than 0.05. Eyeballs in 16 cases slightly protruded forward (3 mm in 4 cases, 2 mm in 7 cases and 1 mm in 5 cases), when compared with its fellow eye. Optic disc in the diseased eyes showed atrophic changes at different levels, 3 cases only with lighter color and 19 cases with white color. There was opticociliary shunt vessels in 17 cases, and retinal vein dilation or even retinal hemorrhage in 6 cases. Change of visual field was as follow, 2 cases with defect sector, 3 cases with ring reduction, 2 cases with temporal visual island, 4 cases with irregular visual field defect and 1 case with half visual field defect. According to F-VEP results, the latency of P100 wave was prolonged (65.28±18.61ms) with the amplitude decreased (2.36 ±1.50 μV) in these cases. According to orbit CT and MRI images, tubular thickening of optic nerve was observed in 18 cases (diffuse expansion in 9 cases, anterior expansion in 4 cases and apical expansion in 5 cases); 4 cases had fusiform ONSM and 3 cases had conical ONSM. There was tram-tracking sign in 15 cases and calcification sign in 7 cases.

After making a correct diagnosis, 5 cases received stereotactic fractionated radiotherapy (SFRT), and other cases agreed to observe without treatment. During the observation, 6 cases received the craniotomy operation due to the intracranial extension, 1 case received the orbital exenteration because his eyeball was invaded by tumor, and 5 cases lost follow-up.

Misdiagnosis Condition As for the time period of misdiagnoses, the shortest was 1.5mo and the longest was 45mo, with the average time being 8.58mo. One case was misdiagnosed at least once and 4 times at most, with 1.72 times being the average level. Most cases were misdiagnosed as acute papillitis, 17 times in total, followed by optic atrophy with 8 times, ischemic optic neuropathy with 5 times, acute retrobulbar optic neuritis with 5 times, optic disc vasculitis with 3 times and visual fatigue with once.

Treatment with Glucocorticoid and Side Effects Twenty-one patients misdiagnosed as acute optic neuritis, ischemic optic neuropathy, or optic disc vasculitis were treated with glucocorticoid and its application methods included 500-1000 mg of methylprednisolone or 10 mg of dexamethasone for intravenous dripping, and oral administration of prednisone tablets *etc*. The shortest administration time was 7d and the longest one was more than 7mo. During glucocorticoid treatment , 17 patients showed side effects with different degrees, such as moon-face in 8 cases, buffalo hump in 4 cases, transient hyperglycemia in 10 cases, gastrointestinal discomfort in 5 cases, hiccup in 2 cases, erythema and acne in 5 cases, and severe osteonecrosis in 1 case.

Typical Cases This case is female, 42 years old, and visited the neuro-ophthalmology outpaitent on July 2013 with vision loss in the left eye for more than 9mo. Medical history: she was misdiagnosed as acute papillitis in October 2012, and was treated with a high dosage of glucocorticoids in local county hospital. Her vision got an improvement from 0.6 to 1.0 in left eye. In February 2013, her vision in the left eye suddenly decreased once again, and was accepted the same treatment. However, her vision became worse (left eye, hands moving/ 20 cm).

Ocular Examination Vision acuity: 1.5 (right) and no light perception (left). Corneas and lens of both eyes were transparent and RAPD positive in the left eye. No abnormity detected in the right fundus, and optic disc in the left eye was hoar edema, and opticociliary shunt vessels. Retinal vein dilation was detected and there was sporadic bleeding in the peripheral retina (Figure 1). As for exophthalmia, the right eye was 12 mm and the left eye was 14 mm.

Special Examination Orbital CT scan: optic nerve in the left eye enlarged in tubular, more obviously in the section close to orbit apex with enhancing signals, and no calcification ; craniocerebral and orbital MRI scan: optic nerve of the left eye enlarged in tubular with unclear rims, particularly obvious in the top of orbit with invasion to the left front corner of chiasma opticum, presenting the same T1 and the same T2 signals, obviously enhancing and dual track sign was positive (Figure 2). Diagnosis: ONSM in the left eye. She gave up to be treated. Intensive follow-ups and observations were performed. Reexamination in June 2014: tumor invaded to the cerebral space and she was transferred to the neurosurgery department for surgery.

DISCUSSION

ONSM is a very common optic nerve tumor following optic nerve glioma , accounted for 1/3 of all optic nerve primary tumors. ONSM was often found in adult women and 95% of all cases were single-eye disease. However, there are a few of ONSM primary growth in bilateral optic nerve [8-10]. Some

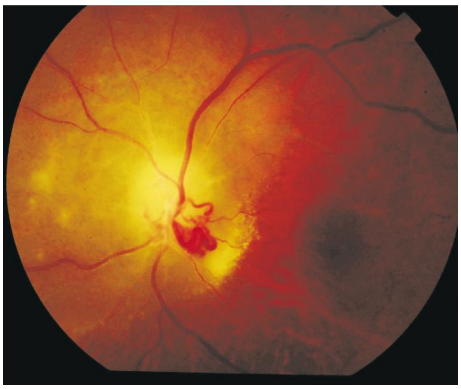

Figure 1 Fundus photograph in the left eye Optic disc was hoar edema, and opticociliary shunt vessels. There was grey edema and effusion around the optic disc.

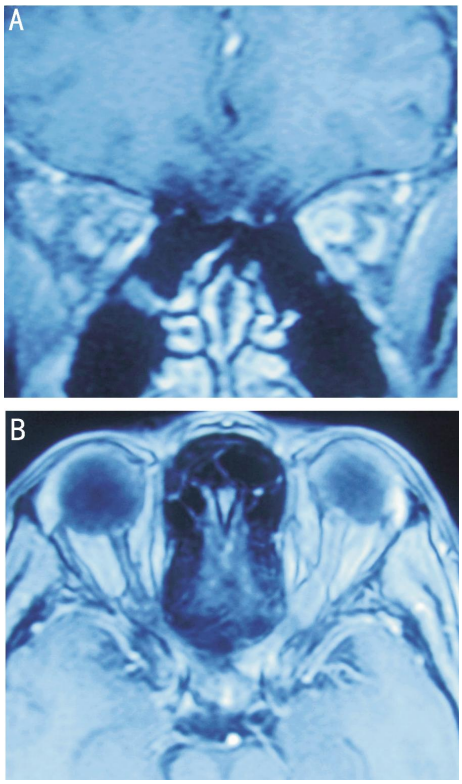

Figure 2 Orbit MRI Optic nerve in the left eye enlarged in tubular, particularly obvious in orbit apex with invasion to the left front corner of chiasma opticum, and the tram-tracking sign was positive. A: Coronal scan; B: Transverse scan.

of ONSM were primary diseases while some others were secondary[11-13].

Typical clinical features of ONSM were ocular proptosis, decreased vision, chronic disc edema atrophy and opticociliary shunt vessels. As for those patients with these typical clinical features, especially with ocular proptosis, the diagnosis could be easily drawn with orbit imaging scan and misdiagnosis seldom happens. Optic nerve biopsy is seldom necessary for ONSM diagnosis, because it may have the risk causing visual loss and tumor spread [14]. However, some patients visited doctors with the chief complaint of decreased vision with slight or no ocular proptosis. In these cases, doctors could easily neglect the manifestation of ocular proptosis and misdiagnose the patients with neuropapillitis, ischemic optic neuropathy *etc.* When optic disc became white colour in some cases, the patient might be misdiagnose optic atrophy and administered medication, such as blood vessel dilation and nerve protection, without looking for the cause of optic atrophy.

ONSM is a benign tumor, but usually causes severe damage to visual function. Some tumors can extend to the space in canales opticus and intracranial space; its natural development is mainly choronic and progressive vision loss, seldom cause death or metastasis. At present, the major target to treat ONSM is to preserve vision function, control tumor growth and decrease death rate [15-17]. In clinic, as for those patients without or with slight vision decrease, intensive follow-ups and observations can be performed; tumor growth in young patients may be faster, so the gap of follow-ups of children and young people should be shortened [18-19]. Incision of ONSM will definitely cause the complete loss of visual function, or even extraocular myoparalysis, ptosis *etc.* and the post-operative relapse rate is high, generally over 50%. So, operations will be done only when tumors invade to the intracranial space [20-21]. In recent years, SFRT has already become an effective way to treat ONSM. SFRT can stabilize or even improve the visual function in early and progressing stage, and can also be used for the severe cases that lost their vision or even with intracranial invasion. After radiotherapy, long-term prognosis of patients was better than that of patients who were not interfered; the visual acuity and field were improved in many patients after radiotherapy[22-23]. So, the earlier correct diagnosis is very important to control tumor progression. However, after radiation therapy, its toxicity, such as radiation optic neuropathy *etc*, may be taken place[24-25].

So, these details are described and taken seriously as follows.

Decreased Vision of the Chief Complaint In our study, there were 20 cases with vision loss as the chief complaint. Because ONSM is an orbital tumor that closely allied to optic nerve, many patients went to see doctors with chief complaint of decreased vision other than ocular proptosis. These ONSM patients often showed no ocular proptosis or at slight level in early stage, in order that this sign was often neglected in clinic. So, doctors should pay attention to examine the ocular proptosis before diagnosing acute optic neuritis and ischemic optic neuropathy. Optic atrophy should never be a final diagnosis and its cause should be detected to avoid misdiagnosis and mistherapy.

The Features of Fundus Changes Fundus signs are decided by location and extension way of ONSM. Compression and invasion at the retrobular segment of optic nerve can cause edema of optic disc or even grey edema with few bleeding and effusion. When tumor invaded into orbital apex, optic disc seldom showed edema, and its atropy usually

with clear rim. Generally, the tubular ONSM had a more serious influence on optic nerve than other shapes, and caused edema and atrophy more easily.

Opticociliary shunt vessels, related with tumor compression on optic nerve, is an important fundus sign of ONSM, causing the blood backflow from retinal central vein into choroidal venous system around optic disc. In our study, opticociliary shunt vessels were found in 17 cases. With the disease developing, patients without opticociliary shunt vessels could gradually emerge in later stage. Except for ONSM, opticociliary shunt vessels can be found in these diseases causing optic nerve compression, such as optic nerve glioma, chronic optic disc edema, craniopharyngeal duct tumor, sarcoidosis and central retinal vein obstruction. The clinical significance is that, if a middle-aged woman shows this sign with progressing loss of vision in a single eye, grey edema or atrophy of optic disc, regardless of ocular proptosis, doctors should take the possibility of ONSM into consideration and complete orbit imaging scan in time. Posterior retinochoroidal folds are caused by the compression on eyeball posterior segment, and will appear when ONSM is close to eyeball or tumor is so big. In clinic, if doctors are visited by patients with this folds, they must consider the possibility of postocular occupying lesion.

Importance of Orbit Imaging Scan as Detecting the Cause of Vision Decrease Generally speaking, when doctors received patients with vision loss not caused by factors in eyeball, they will consider craniocerebral imaging scan to detect the cerebral diseases. However, most doctors will not do orbit imaging examinations, which easily caused the misdiagnoses of optic nerve tumors, orbital apex tumor, infiltrating optic neuropathy, and made it difficult to obtain the direct evidence of inflammatory changes, such as optic nerve demyelination. When treating these cases, it is better for doctors who prescribed craniocerebral and orbital imaging scan. ONSM patients can often be diagnosed based on clinical features and orbital imaging scan (CT and MRI).

Orbit CT has significant value for the diagnosis of optic nerve tumor, especially calcification. Thin layer CT scan can display ONSM well, but not show the invasion to canales opticus or intracranial space [26]. CT image of ONSM include the enlargement of optic nerve in tubular or fusiform; when tumor is relatively big, its shape become the cone, massive high density image. Luo *et al* [27] reported that about 23.81% of ONSM patients had calcification, presenting in dots, patchy or circular shape. Tumor image is enhanced while optic nerve is not in enhancing scan, presenting the typical tram-tracking sign. The tram-tracking sign and calcification are typical CT features in ONSM. However, tram-tracking sign is not the unique feature of ONSM and is also seen in other diseases, such as optic nerve inflammatory pseudotumor, inflammation around optic nerve *etc*.

MRI's advantage is a good imaing of soft tissue, which is very important in detecting and evaluating ONSM. ONSM is similar with intracranial meningiomas, having relatively special MRI signals. MRI shows optic nerve enlarges in tube or fusiform shap, or also in the shape of eccentric or spherical lump; tumor has the same signals with brain tissue in T1 weighted imaging and T2 weighted imaging and the tumor calcification has low signal. After enhancing scan, the tram-tracking sign was found in many cases. As small ONSM is not easily found in the non-enhancing MRI, doctors should consider orbital MRI scan and enhancing scan together when considering the diagnosis of optic nerve tumors. Using fat suppression technique in enhancing scan can get better imaging, and enhancing MRI fat suppression is the best method to show meningioma, especially tumor invasion to the intracranial space or the canales opticus. So, we should take it as the routine examination before and after ONSM surgery to detect intracranial invasion early[26]. Horizontal and coronal positions of enhancing MRI have good imaging results while sagittal position's imaging is not quite good due to the scan angle problem. When MRI detects that tumor has invaded orbital apex, no matter optic nerve is enlarging in tube shape, or orbital apex is filled with massive tumor, doctors should consider the condition of tumor invading to the intracranial space.

From the morphous perspective, tubular ONSM was most common in our cases, accounted for about 72%. It caused most severe damage to the optic nerve function, presenting vision decrease in early stage and patients often visited doctors with this reason. In this stage, patients often had no ocular proptosis and were easily misdiagnosed as neuritis optica, ischemic optic neuropathy *etc*. The glucocorticoid treatment was used in these patients, and its side effects were taken place sometimes. Among these cases, one patient was treated with glucocorticoid for 7mo which caused osteonecrosis of both sides, leading to permanent disability.

In conclusion, clinical doctors should further understand and master the clinical features of ONSM, especially pay attention to ONSM with no obvious ocular proptosis, commonly in adult females, chronic and progressive vision loss, unique disc edema and atrophy, opticociliary shunt vessels and mild monocular proptosis. For patients with unknown cause vision loss or optic nerve atrophy, doctors should pay attention to orbital imaging scan in time, in order to diagnose correctly as early as possible and avoid misdiagnoses and mistherapy.

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