NEUROOPHTHALMOLOGIC MANIFESTATIONS AMONG 195 PATIENTS WITH INTRACRANIAL TUMOR AT NATIONAL REFERRAL HOSPITAL

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ABSTRACT

Introduction & Objective: Intracranial tumor might show neuroophthalmological manifestations. Early detection and prompt treatment could alter the visual outcome. Ophthalmologists need to be aware of neuroophthalmological features commonly found among patients with intracranial tumor. This study revealed those signs and symptoms.

Methods: Study was done in tertiary referral hospital. Subjects were patients with intracranial tumor attending neuroophthalmology clinic between the specified period. It was a descriptive study using retrospective data of the patient’s initial visit to the clinic. Data was retrieved from the medical record archive and electronic health record.

Results: There were 195 patients, 67.7% of them were women, with average age 43.4 years old. Half the patients arrived within 6 months after eye related symptoms occurred and the referring physicians was equal between ophthalmologists and other specialties. The most frequent symptom and sign were blurred vision and optic nerve head abnormality (atrophy, edema). Hemianopia outnumbered other patterns of visual field disturbance, yet bilateral pattern was difficult to be evaluated as most patients had either one or both eyes blind.

Conclusion: Intracranial tumor was one of the diseases that could show ophthalmic signs and symptoms. Neuroophthalmological manifestations in those cases was related to the extraocular process and the relevant pathway affected by the tumor.

Keywords: Intracranial tumor, brain tumor, blindness, optic atrophy, hemianopia

INTRODUCTION

Intracranial tumor or brain tumor is an abnormal mass of tissue in which cells grow uncontrollably. It could be located in cerebrum, cerebellum, brain stem, pineal gland, pituitary gland, brain ventricle, and some parts of optic nerve. Intracranial tumor could be benign or malignant. Yet, benign intracranial tumor could disrupt the adjacent structures and their functions, causing significant morbidities.

Visual impairment is a common manifestation among patients with intracranial tumors. A meta-analysis studying patients with pituitary apoplexy due to pituitary adenomas concluded that before treatment, 37% suffered from visual acuity or visual field disturbance and 47% had
ocular motility disorders.\textsuperscript{2} Another study in patients with suprasellar tumors showed that the visual acuity of the worse eye were between 6/60 to no light perception in 80\% of the subjects.\textsuperscript{3}

In some cases, those visual acuity and visual field disturbance could be improved by prompt treatment, whether surgical or conservative.\textsuperscript{2,4,6} One of the factors affecting the prognosis of visual recovery was visual symptoms duration. Patients with complete visual recovery were operated within 3 months in average after the visual symptoms, whereas those with partial visual recovery were operated within 12 months in average after the symptoms.\textsuperscript{6}

Therefore, ophthalmologists play a crucial role in early detection and efficient management of intracranial tumor patients with neuroophthalmological manifestations. By recognizing the neuroophthalmological manifestations of intracranial tumors, we could improve the outcome of those patients.

METHODS

This descriptive study utilized the data of initial visit to neuroophthalmology clinic of a tertiary health center, Cipto Mangunkusumo Kirana Hospital. Data was retrieved from written and electronic health records. Data collection was done from March to November 2021. This study methods had obtained approval by institutional ethics committee.

The subjects were patients of neuroophthalmology clinic in 2019-2020 that had also been examined by Neurosurgery Department before or after the visit to neuroophthalmology clinic. Patients included were those who had been confirmed radiologically for having intracranial tumor. Later, those whose health record were incomplete or was uncooperative for ophthalmic examinations were excluded from the data collection.

The neuroophthalmological examinations which results were recorded included visual acuity test using Snellen chart, swinging light test, direct or indirect funduscopic examinations, static perimetry using Octopus or Humphrey, Pelli Robson contrast sensitivity test, and Farnsworth Munsell or Ishihara color vision test. For the classification of visual impairment, WHO grading based on visual acuity was used.\textsuperscript{7}

- Mild: Worse than 6/12 to 6/18
- Moderate: Worse than 6/18 to 6/60
- Severe: Worse than 6/60 to 3/60
- Blindness: Worse than 3/60
RESULTS

There were 195 patients included in the study. As many as 132 patients (67.7%) were female, while the other 63 patients (32.3%) were male. Age showed normal distribution (Figure 1) with average 43.4 years old.

![Figure 1. Age distribution.](image)

There were slightly more patients that were referred by other specialties to the clinic for routine neuroophthalmological examination (47.2%, n=92) after diagnosed with intraocular tumor than those referred by ophthalmologists for neuroophthalmological workup and differential diagnoses (41%, n=80). Some patients came with unknown referral (11.8%, n=23).

Blurred vision was the most frequent symptom (83.1%, n=162), followed by visual field disturbance (16.4%, n=32). Other complaints comprised visual symptoms such as diplopia (7.2%, n=14) and eye-related appearance problems such as proptosis (7.2%, n=14), ptosis (4.6%, n=9), or squinted eye (2.6%, n=5). Headache was also claimed by nearly one third (32.3%, n=63) of all patients, yet the detailed characteristic of the headache was not described. While onset ranges from 2 days to 16 years, half of the patients came within 6 months after ophthalmic symptoms (50.2%, n=98). The rest came later (35.4%, n=69), did not recognize the onset (7.2%, n=14), and were referred without ophthalmic symptoms (7.2%, n=14).

In majority of the patients (65.6%, n=128), the eyeball alignment was still normal. As many as 41 (21.0%) had strabismus and 16 (8.2%) had proptosis. The alignment of the rest 10 patients was not stated. Normal eyeball movements were also preserved in 335 eyes (85.9%). Normal, quiet eyelids were found in 361 eyes (92.5%). In eyes with abnormality of the eyelid, 14 had ptosis, 5 had lagophthalmos, 2 had ptosis and lagophthalmos. There was also 1 eye with involuntary tic, 1 eye with lid mass, and 2 had inflammation of the eyelids.
Eyes were classified into better, worse, or equal eye based on the visual acuity relative to the contralateral eye. Based on WHO grading of visual impairment, most of the better eyes had no visual impairment \( (n=95) \), whereas most of the worse eyes were blind \( (n=93) \) as in Figure 2. Blindness was also found in the better eyes of 31 subjects and in equal eyes of 10 subjects. Therefore, bilateral blindness happened in 41 subjects \( (21.0\%) \) and unilateral blindness in 72 subjects \( (36.9\%) \) of this study.

![Figure 2. Visual acuity of the patients.](image)

Pupillary light reflex was still intact in most patients. Relative afferent pupillary defect (RAPD) was positive in 90 worse eyes and 4 better eyes. Pupillary light reflex was absent in 13 worse eyes.

The optic nerve head (ONH) findings were normal ONH \( (167 \text{ eyes, } 42.8\%) \), atrophic ONH \( (163 \text{ eyes, } 41.7\%) \), edema ONH \( (41 \text{ eyes, } 10.5\%) \), and cup-to-disc ratio enlargement \( (18 \text{ eyes, } 4.6\%) \). The atrophic ONH included primary atrophic ONH \( (126 \text{ eyes, } 32.3\%) \), secondary atrophic ONH \( (21 \text{ eyes, } 5.4\%) \), and partial atrophic ONH \( (16 \text{ eyes, } 4.1\%) \).

Hemianopia \( (58 \text{ eyes, } 14.8\%) \) outnumbered other specific patterns of visual field disturbance, followed by generalized depression \( (50 \text{ eyes, } 12.8\%) \), unspecified visual field disturbance \( (40 \text{ eyes, } 10.2\%) \), quadrantanopia \( (10 \text{ eyes } 2.5\%) \), arcuate scotoma \( (1 \text{ eye, } 0.2\%) \), and blind spot enlargement \( (1 \text{ eye, } 0.2\%) \). There were also eyes with normal visual field \( (41 \text{ eyes, } 10.5\%) \) and eyes in which visual field was unable to be evaluated due to poor vision \( (117 \text{ eyes, } 30\%) \). The average mean deviation of the better eye was -13.0 decibel and of the worse eye was -16.1 decibel.

In many eyes, contrast sensitivity was unable to be evaluated due to visual acuity \( (142 \text{ eyes, } 36.4\%) \). In whom contrast was assessed, 62 eyes \( (15.9\%) \) had normal and 59 eyes \( (15.1\%) \) had impaired contrast sensitivity.
In 144 eyes (36.9%), visual acuity was inadequate for color vision test. Of other eyes tested, 93 eyes (23.8%) had normal color vision and 19 eyes (13.2%) had impaired color vision. Diplopia was found in 14 subjects (7.2%). However, it should be noted that in many other patients with poor vision, diplopia was unable to be evaluated.

Most of the tumors were located at the sellar, parasellar, and suprasellar region (n=109). Other frequent locations were sphenoorbital region (n=9), frontal region (n=7), cerebellopontine angle (n=6), frontotemporal (n=5), pineal gland (n=4), and retrobulbar (n=3). Meningioma (24.1%, n=47) and pituitary adenoma (15.9%, n=31%) were the two histologic types frequently found among the operated subjects. In 85 subjects (43.6%), histologic examination was not done because there was no surgical management until the time of data collection.

**DISCUSSION**

The predominance of female gender in this study was parallel to 5 other similar studies. Endogenous sex hormones were suspected of being risk factors. Although its significance was still being debated, several studies still support it to be a risk factor. The average age was also similar to other studies by eye centers in developing world. It was different from what was said in textbook and a review by neurosurgery experts of a developed country that prevalence of intraocular tumor increases with age. This difference could be due to different geographical areas and health centers, where life expectancy and patient population differ.

A study from tertiary eye center found similar proportion between patients referred from neurosurgery unit and from general hospital. Another study, also from an eye clinic, found slightly more patients diagnosed with chiasmal lesion than patients came for differential diagnoses. Those results showed balanced proportions in detection and multidiscipline management.

Among all the eye-related symptoms, blurred vision profoundly outnumbered all other symptoms. There were also double vision and disturbed visual field complaints in lesser frequencies. However, since abnormality of visual field could happen without decreased central field visual acuity, the visual field should be assessed by objective measures to screen unrecognized visual field impairment. Another point to notice is that blurred vision is a general term. It is more commonly used by the patients rather than more specific or detailed experience of what they saw. Also, in this study many patients had serious visual impairment that made
them difficult to see any specific visual experience. Nevertheless, blurred vision being the main symptom is similar to the results of other studies on intracranial tumor.\textsuperscript{3,8,11,15,16}

Headache, in International Classification of Headache Disorders, related to intracranial tumor was described as heavy, worse in the morning, and triggered nausea and vomiting.\textsuperscript{20} However, clinical studies did not obtain those classic characteristics. American College of Radiology mentioned red flags that make a headache worth a radiologic investigation. Among those features were headache waking up the patient from sleep, new headache differs from any previous headache, or headache associated with neurological deficits such as blurred vision, diplopia, or papilledema.\textsuperscript{21}

In some patients with proptosis, tumor masses were 8 mm\textsuperscript{3} or larger. There were proptosis cases with smaller masses, yet the tumors were located nearby the orbits, or there had been hyperostosis of the orbital bones. Most patients with strabismus and those with impaired eyeball movements suffered from paresis of the cranial nerves innervating extraocular muscles due to compression along the ocular movement pathway, from the pons the nuclei center to the orbit. There were also cases of sensory strabismus due to poor vision.

Ptosis were mostly associated with compression of the third cranial nerve. They were also caused by dysfunction of the sympathetic nerve in Horner syndrome, and vascular problem unrelated to the tumor. Lagophthalmos were caused by compression to the seventh cranial nerve. Those compression were caused by the tumor mass, brain edema, or hydrocephalus.

Decreased visual acuity as the manifestation of neurogenic vision loss were more commonly due to optic neuropathy rather than chiasmal lesion or cortical blindness.\textsuperscript{22} Optic neuropathy in intracranial tumor might be caused by compression. Initially, the compression caused reversible damage: Disturbance of axoplasmic flow, conduction blockage, and demyelination. However, as it went chronic, axonal fibers degenerated and the irreversible optic atrophy occured.\textsuperscript{23} This is the reason why duration of illness is important in determining the visual recovery prognosis.

The occurrence of RAPD in 49.2\% patients was parallel to other studies in which the numbers were around 30-40\%\textsuperscript{3,8,10,15} RAPD occurred due to damage to visual pathway anterior to lateral geniculate nucleus, usually the retina or optic nerve as those were located anterior to optic chiasm.\textsuperscript{24} The RAPD in better eyes in this study happened because of the tumor’s location and size: Bilateral multiple tumors, intrasellar tumor, and tumor extending to contralateral optic nerve.

This study, as well as other similar studies, found that primary ONH atrophy outnumbered ONH edema and secondary ONH atrophy.\textsuperscript{8,10,15,16} The different mechanisms
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causing primary atrophy or edema of the ONH could explain it. Primary ONH atrophy formed after chronic disruption of axoplasmic flow. ONH edema formed after generalized intracranial compression, such as increased intracranial pressure due to ventricular obstruction. The tumor had to be sufficiently large or located in certain structures to give such effect, making ONH edema rarely found relative to primary ONH atrophy. Yet, chronic ONH edema could result as secondary ONH atrophy.

ONH atrophy might formed after 4-6 weeks of axoplasmic flow disruption. In this study, most patients came after that period and before 6 months. Therefore, the high frequency of ONH atrophy was explainable. However, other studies had not established any relationship between ONH pathologies and the duration of ophthalmic symptoms.

In other study, hemianopia was also the most frequent visual field pattern found among patients with intraocular tumor, followed by other nonspecific patterns. The nonspecific pattern was due to the variability of the tumor size, location, extent of the visual pathway damage, and visual acuity. In this study, many patients had poor visual acuity so that the visual field of one or both eyes were difficult to be assessed. In those with assessed bilateral visual field, the pattern frequently found was hemianopia bitemporal. This pattern occurred in patients with lesion at the optic chiasm. Other patterns such as hemianopia homonymous and quadrantanopia in this study were found in patients with post-chiasmal lesion.

Impairment of contrast sensitivity and color vision could occur in retinal or optic nerve damage. In retinal damage, the severity of those impairment would be parallel to the visual acuity. In optic nerve damage, the impairment of contrast sensitivity and color vision could be relatively worse than expected for certain visual acuity. In this study, contrast sensitivity and color vision tests were done for patients referred for routine neuroophthalmological examination. Higher number of patients with contrast and color vision impairment could be expected if all patients had the tests. Similar studies resulted in varying number, with the highest was 88.6% of 70 patients.

Diplopia was found in 3 patients with abnormality of eyeball position, eyeball movement, and paresis of nerve innervating extraocular muscles. The other patient had no such obvious cause, yet he had a tumor located at cerebellopontine angle (CPA) and had undergone stereotactic radiation. It was a similar condition to a report by Cosetti, that 4 patients post resection of CPA tumor or labyrinthectomy got vertical diplopia due to skew deviation, an acute vestibular deafferentiation.

The tumor location that were mainly around the sella turcica and followed by sphenoid bone and spheno-orbital region was relevant to neuroophthalmological manifestations. Those
structures were located in the visual afferent pathway before lateral geniculate nucleus. This result was similar to other studies.\textsuperscript{3,8-11,15,16}

The most prevalent histopathological feature of intracranial tumor, according to Central Brain Tumor Registry of The United States 2005-2009, were meningioma, glioma, and pituitary adenoma.\textsuperscript{13} The high frequencies of meningioma and pituitary adenoma in this study was parallel to that. The reason glioma not frequently found in our study was probably that main location of glioma was frontal lobe and cerebral cortex.\textsuperscript{28} Those location was quite separated from visual pathway and orbital region, compared to the main location of meningioma which included base of the skull and of pituitary adenoma.\textsuperscript{29}

It was the study on neuroophthalmological manifestations of intracranial tumor with the largest number of patients compared to other similar studies. The clinical features in this study were expected to be highly representative.

Located at an academic hospital, this study had the privilege to complete documentation of the clinical data, because residents were obliged to put the data completely on the medical records. It eased the data collection process of this study.

The use of electronic health records for the documentation of imaging and histopathological results as well as inpatient resumes was also an advantage for data collection. The data kept at electronic records was detailed and at the lower risk of being lost.

The first shortcoming of this study was difficulty to expose the main table of the data. It was due to the large number of patients as well as the clinical items collected. Diagram was therefore used to describe the data concisely.

Another limitation was that some written medical record archives were lost and therefore the related patients should be excluded from the study. The separated medical record units in the hospital obliged massive transportation of the archives that put the sheets at the risk of being damaged or lost. This problem is currently being managed by initiation of electronic health record use for outpatient clinic and inpatient ward.

CONCLUSION

Patients with intracranial tumor coming to neuroophthalmology unit were mostly female with age 43.4 years old in average. The main neuroophthalmological manifestations were ONH (atrophy, edema) and pupillary abnormalities, decreased visual acuity, and visual field impairment. In those whose visual fields could be examined, hemianopia was the most frequent pattern. In half of the patients, the visual impairment of the worse eye had reached blindness and visual field pattern could not be determined.
Many of the patients came within 1-6 months after eye-related symptoms began. The referring physicians were in equal proportions between ophthalmologists and other specialties.

The most frequent location of the intracraniat tumor among the patients were around the sella turcica. The most prevalent histopathology results of the tumors were meningioma, and pituitary adenoma in the second place.

REFERENCES