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OCULAR MANIFESTATION ON FUNCTIONAL PITUITARY MACROADENOMA

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ABSTRACT

Background: Pituitary adenoma is a benign, slow-growing tumor originating from pituitary gland cells, and accounts for 10-15% of all intracranial neoplasms. Ocular manifestation occurs in 50-60% of pituitary macroadenoma patients.

Case Presentation: A 10-year-old female with chief complaint of partial blurred eyes since ± 1 month ago. Complaints are accompanied by occasional headache. From ophthalmology examination, a decrease in the vision of both eyes and right papil in red-pale color, confrontation test found that the patient's visual field is narrower than the examiner's and there was hypoesthesia in the right frontal and facial area. An MRI scan of the head with contrast showed a mass resembling a multi-lobulated mass with inhomogeneous strong amplification was seen in the sella-supra sellar region 27 mm x 13 mm which included the right cavernous sinus and right optic chiasma. DD/Macroadenoma; hypervascular period.

Discussion: History, ophthalmology examination, and ancillary tests established diagnosis of pituitary macroadenoma. As soon as diagnose was established, surgical intervention is the first choice for the patient. Pituitary adenoma complications arise in form of increased Intracranial Pressure, causing more complications such as respiratory failure and decreased consciousness. Increased ICP results in increased risk of mortality.

Conclusion: Surgical management is recommended to patients with pituitary macroadenoma, and is expected to remove the tumor mass and can restore hormonal secretions functionally. Delay in tumor removal increase the risk of morbidity and mortality in patients.

Keywords: Ocular manifestation, pituitary macroadenoma

BACKGROUND

Pituitary adenoma is a benign, slow-growing tumor originating from pituitary gland cells, and accounts for 10-15% of all intracranial neoplasms. This tumor is discovered incidentally in approximately 10% of patients undergoing brain imaging studies. This tumor is also the second most common histopathological tumor in patients aged 20-35 years based on the Central Brain Tumor Registry of the United States.[1,2]

Based on the size, pituitary adenomas can be divided into macroadenoma and microadenoma. Macroadenomas are pituitary adenomas larger than 10 mm while microadenomas are smaller than 10 mm. Pituitary macroadenoma is a rare case with a prevalence of 0.2%.[1-3]

In patients with pituitary macroadenoma, clinical manifestations related to endocrinological manifestations depend on the excess or deficiency of hormones produced due to the presence of the tumor. Disorders of hormonal balance in the body with various manifestations, such as changes in body size, menstrual disorders in women, as well as effects due to mass pressure on surrounding structures. Local pressure can cause headaches, visual field disturbances to blindness. If the mass extends to other structures such as the cavernous sinus, it can cause manifestations in the form of ophthalmoplegia, proptosis or other

disorders. This disorder is known as cavernous sinus syndrome.[4-6] Abnormalities of visual function in the form of visual disturbances that occur in pituitary adenomas with symptoms ranging from blurred vision with or without headache to total loss of vision. Visual field defects are found due to compression of the second cranial nerve structure (optical nerve). These clinical manifestations occur in 50-60% of pituitary macroadenoma patients. [5-8] The purpose of this case report is to report ocular manifestations of patients with intracranial tumors in the form of pituitary macroadenoma.

CASE PRESENTATION

A 10-year-old female came to an outpatient opthalmology clinic of Muhammad Hoesin Palembang Hospital on August 6, 2022 with chief complaints of partial blurred eyes since ± 1 month ago. Patient and her mother admited that since about 1 year ago, the patient complained the partial progressive blurred vision in both eyes, especially on the outer side, when looking at distance or near. There were complants of headache, ocassionally. Complaints of cloudy vision, seeing like in tunnel, or the view was like the closed curtains were denied. There was neither red eye, double vision, or droopy eyelid. Denied complaints of nausea and vomiting. The patient has not been taken for treatment.

Previously, the patient complained of increasingly blurred vision in both eyes, especially on the outer side, since two months ago. There are complaints of double vision, especially felt by the patient when he glances to the right side. The patient also complained that he had difficulty glancing in the right eye accompanied by complaints that the right eyelid felt drooping. Droopy eyelid happened all the time without improvement after patient taking rest.

The patient also complained of increasingly frequent and severe headaches and also complained of reduced sensation in the right facial area. The patient was taken by patients parents for treatment to an ophthalmologist and then referred to Mohammad Hoesin Hospital in Palembang.

The patient did not have history of wearing glasses, trauma or allergy. A family history of the same disease was denied. Menarche was started at 9 years old with disturbance in the menstrual cycle.The history of breastmilk production and enlarged fingertips on the hands and feet were denied. Physical examination found the patient appeared to be moderately ill, compos mentis awareness, blood pressure 110/70 mmHg, heart rates 88x/minute, respiratory rates 18x/minute and afebrile.

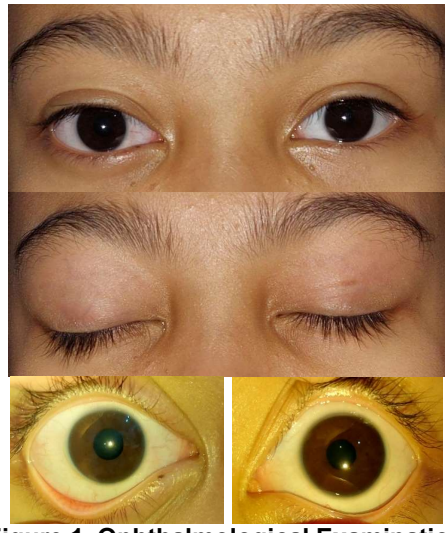

Figure 1. Ophthalmological Examination

Visual acuity was 6/6 in both eyes, and anterior segment within normal limit. there were ocular movement restriction in right eye, -4 in superotemporal, temporal, and inferotemporal direction, anda also -3 in superonasal direction, as well as - 1 in

nasal direction. MRD 1 in the right eye was slightly dropped with 4 mm and in left eye within normal limit. there was 5 mm diameter in pupil size in the right eye, with negative APD. Posterior segment in right eye showed that there was round, well demarcated optic nerve head, yet red-pale in color. Posterior segment of let eye showed that there was round, well demarcated optic nerve head, and hyperemic in color. Foveal reflect were within normal limit in both eye, and retina were within normal limit in both eye. Additional examination showed that Ishihara Test: discromatopsia ODS : (-), Contrast sensitivity test ODS : 2.25, Confrontation visual field testing ODS : the patient's visual field is narrower than the examiner's (in the superotemporal, inferotemporal and temporal directions). Facial Sensation Examination: Hypoesthesia in the right frontal and facial area (+)

History taking, physical examination, and ancillary testing established diagnosis of Right Cavernous Syndrome, Bitemporal Hemianopia, and Early Papillary Atrophy OD due to Susp. Functional Pituitary Adenoma. The differential diagnosis of Right Cavernous Syndrome, Bitemporal Hemianopia, and Early Papillary Atrophy OD due to Non-Functional Pituitary Adenoma and Right Cavernous Syndrome, Bitemporal Hemianopia, and Early Papillary Atrophy OD due to Craniopharyngioma. The patient hospitalized and prepared for laboratory examinations, fundus photograph and visual field tests. Patients were also consulted to the pediatric department. Prognosis patient quo ad vitam dubia, quo ad fungsionam dubia at malam and quo ad sanationam dubia ad malam.

Follow up on September 2, 2022 obtained visual acuity both eyes 6/7.5 PH 6/6, IOP of the right eye is 17.5 mmHg and left eye is 17.2 mmHg. The results of hematology laboratory examinations obtained hemoglobin levels of 11.7 g/ dl, RBC count 4.44 x $10^6/mm^3$, leukocytes 8.03 x $10^3/mm^3$, hematocrit 36%, platelets 311 x 10^3/ul. The results of clinical chemical examinations showed glucose levels at 94 mg/dL, ureum 15 mg/dL, creatinine 0.6 mg/dL, total cholesterol 177 mg/dL, HDL 24 mg/dL, 107 mg/dL, and triglyceride 336 mg/dL. The results of immuno-serology showed LH 0.14 IU/L, FSH <0.05 IU/L, progesterone 0.1 IU/L, prolactin 35.60 ng/ml, T3 1.38, T4 3.59, TSH 0.11 ng/mL. From laboratory examination showed dyslipidemia and hyperprolactinemia. Fundus photograph within normal limit. Humprey visual field test showed incongruous bitemporal hemianopsia in the both eyes. From Head and orbital MRI with Contrast there appears to be a mass resembling a multi-lobulated mass with inhomogeneous strong amplification seen in the sella-supra sellar region 27 mm x 13 mm which included the right cavernous sinus and right optic chiasma. Suggestiv of Macroadenoma or hypervascularized mass.

Figure 2. Fundus Photograph (September 2nd, 2022)

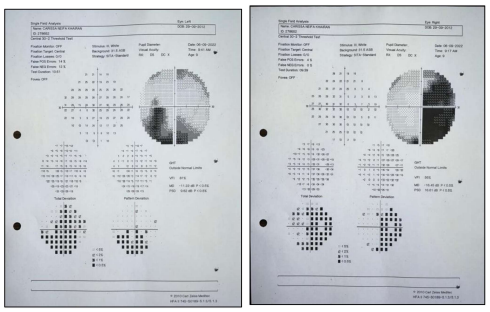

Figure 3. Humprey Field Analyzer showed inconguous bitemporal hemianopia

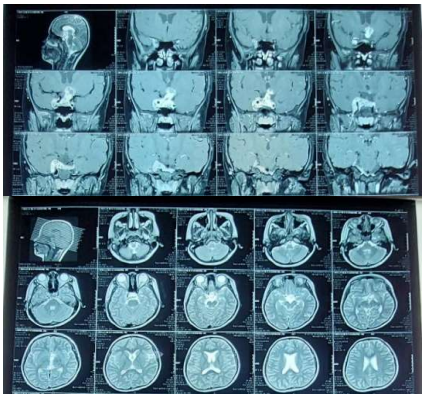

Figure 4. MRI Results of The Head with Contrast showed multiobulated mass in suprasellar region.

The patient's diagnosis was still the same and treated with Citicoline syrup 250 mg every 24 hours, and supplementation of Vitamin B1 100 mg, B6 20 mcg, B12 200 mcg, 1 tablet daily orally. Based on consultation with the pediatric department, patient was diagnosed as intracranial mass and ophthalmoplegia caused by nerve II, IV, VI paralysis in right eye and bitemporal hemianopia. The patient can be treated with Dexamethasone tablet 5mg / 8 jam PO, Estradiol tablet 0.7 mg/24 hours PO Thyroxine 50 mcg / 24 hours PO, and considering consultation of Neurosurgeon for Craniotomy. Patient was also consulted to neurosurgery department. Consult resulted with patient diagnosed with sellar tumor and planned to carry elective craniotomy. But in the following weeks patient did not come, and October 2022 family finally told that the patient has passed away.

DISCUSSION

Based on the results of the anamnesis, physical examination and ophthalmology performed on the patient, a clinical differential diagnosis was found in the form of: Right Cavernous Syndrome, Bitemporal Hemianopia, and Early Papillary Atrophy OD caused by susp. Functional Pituitary Adenoma, Right Cavernous Syndrome, Bitemporal Hemianopia, and Early Papillary Atrophy OD caused by susp. Non-Functional Pituitary Adenoma and Right Cavernous Syndrome, Bitemporal Hemianopia, and Early Papillary Atrophy OD caused by susp. Craniopharyngioma.[1-3]

In this patient, a differential diagnosis was made with Sinus Cavernous Syndrome, due to an ophthalmoplegia condition, where paresis was found in the function of NII, NIV, and NVI. The presence of a lesion or mass in the cavernous sinus area can cause pressure and result in functional paralysis of N. II, N. IV, and N.VI. In addition, the patient was also diagnosed with an optic chiasm lesion due to a bitemporal hemianopia defect in the patient. The presence of symptoms and signs such as pain in the head should be suspected of an increase in ICP which can be caused by the presence of intracranial SOL, which refers to the resulting clinical symptoms, in the form of a functional pituitary adenoma.[4-7]

The pituitary gland is located in the pituitary fossa, bounded anteriorly by the *tuberculum sellae* and posteriorly by the *dorsum sellae*. From the results of ophthalmological examination, a mass in the pituitary area can cause lesions in the optic chiasm, which in turn can manifest as visual field defects from the temporal side of both eyes,

decreased vision, atrophy of the papillae to blindness.[9-11]

The clinical manifestation of a pituitary adenoma in ophthalmology is a visual field defect caused by a lesion on the optic chiasm, namely bitemporal hemianopsia. Junctional scotoma can also occur in some cases of pituitary adenoma.[3,4] In this patient, laboratory tests were carried out and an increased prolactin value was found, which was 35.60 ng/ml (reference value 5.28 – 26.53 ng/ml). From these results, the possibility of a condition of over-secretion of the hormone prolactin, by the pituitary gland. The results of examination of levels of LH, FSH, TSHs showed normal levels. Based on the hormone that is produced, pituitary tumors consist of functional and non-functional. Functional pituitary adenomas are hormone-producing adenomas. Because the location of the tumor is in the posterior pituitary, hormones secreted by the anterior pituitary, such as TSH will be suppressed due to suppression by the posterior mass. In this patient, prolactin hypersecretion was found, and a decrease in TSHs levels of 0.11 (normal level 0.35-4.94 ng/mL).

Furthermore, from the results of a follow-up radiological examination, namely MRI, it was found: The mass looks like a multi-lobulated mass. After contrast, an inhomogeneous strong enhancement was seen in the sella-supra sellar region 27 mm x 13 mm which included the right cavernous sinus and right optic chiasma. DD/Macroadenoma; hypervascular period. With a size that has reached >1cm, this condition can be classified as a macroadenoma, and judging from the clinical manifestations in the form of over-secretion of the hormone prolactin, it can be classified as a functional macroadenoma. A lesion in the right cavernous sinus was also confirmed based on the results of MRI where there was a multi-lobulated mass in the sella-suprasellar, which included the right cavernous sinus and the right optic chiasma. Based on the location of the optic chiasm which is about 10 mm above the pituitary gland, the presence of a macroadenoma can cause chiasm syndrome. On the results of the fundus photograph showed that patient had grade 2 papilledema on the papillae of the right eye and grade 1 on the left eye caused by increased intracranial pressure transmitted to the optic nerve sheath, which causes compression and impaired venous return to the disc. As is the case in this patient because a macroadenoma that extends above the sellar towards the optic chiasma will cause bitemporal hemianopsia, starting from the upper quadrant and extending to complete bitemporal hemianopsia but in this patient an incongruous bitemporal hemianopia occurs where the visual field of the right eye has a wider defect according to the location of the tumor dominant on the right side of the patient.[4-6]

Treatment for these patients required commitment from each of the disciplines involved, from ophthalmology, pediatrics, neurosurgery, and radiology considering that if not handled properly, the patient's prognosis can worsen. Surgical management is the first choice in most patients with pituitary macroadenoma accompanied by clinical signs of obvious local tumor mass effects such as chronic cephalalgia and decreased vision. Mostly, medical management is used as adjuvant therapy in pituitary adenomas that remain persistent after surgical treatment.[12-14]

In patients with macroadenoma without significant local effect of the tumor mass or the possibility of small surgical treatment (suprasellar mass), poor performance status, or who refuse surgery, somatostatin analogues and

dopamine agonists are the recommended second treatment options. Radiotherapy is only recommended as adjuvant therapy in patients with active disease activity even after surgery and medical administration.[9,15,16]

In this patient, there is a functional condition macroadenoma. Functional adenomas are those that secrete PRL, GH, TSH, or ACTH, which results in the clinical phenotype of amenorrhea-galactorrhea syndrome, acromegaly or gigantism, secondary hyperthyroidism, and Cushing's disease or Nelson's syndrome. Whereas nonfunctional adenomas that are not associated with a clinical hypersecretory state (gonadotrophic adenomas, null cell adenomas, oncocytomas, and various silent adenomas). The first choice for this patient was surgical intervention. The results of the consultation with the pediatric department due to the large size of the mass (> 1 cm) the patient was then advised to consult with the neurosurgery department. The results of the consultation of the neurosurgery department, the patient was advised to carry out Craniotomy Tumor Removal in an elective. However, the patient did not return for follow-up. The following month, the patient had passed away. Complications in the form of mortality in cases of pituitary adenoma tumors can be caused by an increase in ICP which causes further complications, such as respiratory failure and decreased consciousness.

CONCLUSION

A case of functional pituitary macroadenoma has been reported which is characterized by increased levels of the prolactine hormone. In this case, clinical manifestations were found in patients due to endocrine disorders. In addition, ocular manifestations were also found in the form of cavernous syndrome as well as right ocular ophthalmoplegia, with early atrophy of the right eye papillae, visual field defects in the form of incongruous bitemporal hemianopia which were evaluated from Humphrey Campimetry Examination. And the results of MRI scan found suggestive of a pituitary macroadenoma. Surgical removal of the mass is the first choice because the tumor mass is large and causes pressure on the optic chiasm so that it is very unlikely for medical treatment. Surgical management is recommended to patients and is expected to remove the tumor mass and can restore hormonal secretions functionally. Delay in tumor removal can be associated with the possibility of increasing morbidity and mortality in patients.

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