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Case Series

An ophthalmologic overview of pituitary adenoma

Shrinkhal[1], Arvind Kumar Suman[2]*, Suyash Singh[2], Shruti Gupta[3], Arijit Jotdar[4], Dhruv Kapoor[4]

[1]*Dept. of Ophthalmology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India*
[2]*Dept. of Neurosurgery, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India*
[3]*Dept. of Pathology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India*
[4]*Dept. of ENT, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India*

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ABSTRACT

Pituitary adenomas are the most common tumours of the sellar region. They generally have a slow but severe impact on vision due to compression of the optic nerves, optic chiasm and cavernous sinus. They can have varied presentation depending on the size, location and extension of the mass and its relation to the surrounding structures. This 8 case series reviews the clinical presentation, varied visual field defects, histopathological and neuroimaging findings and the management of the pituitary adenomas.

1. Introduction

Pituitary adenomas (PA) are most common tumor of the sellar region with an overall estimate incidence of 16.7%.[1] Most commonly, pituitary adenomas (PA) are slow growing tumors that do not invade into the surrounding tissues. However, 20 to 25% of PAs invade and infiltrate the surrounding structures including bone, cavernous sinuses and sphenoid sinus.[2] A study estimated the prevalence rates of pituitary adenomas to be 14.4% and 22.5%, in post mortem and radiologically respectively. This indicates that pituitary tumors are common in the general population. If you suspect that a patient has a nonfunctioning pituitary adenoma, the following steps are warranted: visual acuity testing, color plates, a cranial nerve examination, an assessment for a relative afferent pupillary defect, an evaluation of the optic discs' appearance, visual field testing, and OCT imaging. This article with eight case series, focuses on pathophysiology and different presentations of pituitary adenomas.

2. Case Series

Informed consent has been obtained from the patients still in follow-up for publication of the case reports and accompanying images.

2.1. Case 1

A 35 years old male presented with chief complaint of gradual onset headache and diminution of vision in both the eyes. After detailed ophthalmological examination and neuroimaging, he was diagnosed with Pituitary lesion compressing the optic chiasm, most probable diagnosis being Pituitary adenoma (Figure 1). He was managed surgically via transnasal trans-sphenoidal endoscopic excision of the tumor. A lesion measuring approximately 0.4*0.3*0.2 cm was sent for histopathological examination (HPE). Histopathological examination revealed tumor cells disposed in nests composed of largely monomorphic cells

* *Corresponding author*.
E-mail address: dr.arvindkumar.ns@gmail.com (A. K. Suman).

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with no viable tumor cells. The HPE concluded the mass to be pituitary adenoma with apoplexy.

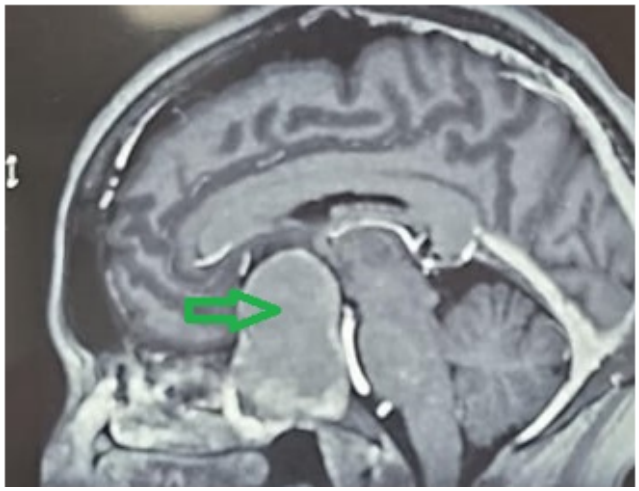

Figure 1: Green arrow: Contrast MRI brain saggital view showing sellar and supra-sellar homogenously enhancing lesion pushing the optic chaism and hypothalamus above

2.2. Case 2

A 50 years old male presented with chief complaint of gradual onset diminution of the vision in both the eyes (L>R) for 3-4 months. After detailed ophthalmological examination and neuroimaging, he was diagnosed with Pituitary lesion compressing the optic chiasm, most probable diagnosis being Pituitary adenoma. He was managed surgically via transnasal trans-sphenoidal endoscopic excision of the tumor (Figure 2). A lesion measuring approximately 1.0*0.8*0.6 cm was sent for histopathological examination (HPE). Histopathological examination (HPE) showed tumor composed of monomorphic cells arranged in sheets and clusters and at places forming pseudorosettes, alongwith interspersed numerous thin-walled vessels. The cells were round to polygonal with oval inconspicuous nucleoli and moderate amount of basophilic cytoplasm with some areas of bony spicules along with haemorrhage. The HPE concluded the mass to be pituitary adenoma.

2.3. Case 3

A 36 years old male presented with chief complaint of blurring of the vision in both the eyes for 6-7 months associated with binocular diplopia. His presenting visual acuity was finger count at 3 meters in both the eyes. His visual field analysis demonstrated bitemporal hemianopia (Figure 3). After detailed ophthalmological examination and neuroimaging, he was diagnosed with Pituitary lesion compressing the optic chiasm, most probable diagnosis being non-secretory pituitary adenoma with bilateral optic

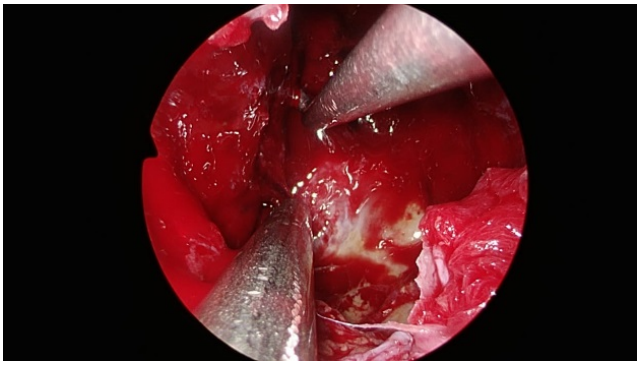

Figure 2: Colored picture of intra-operative transnasal trans-sphenoidal endoscopic excision of the tumor

atrophy (L>R). He was managed surgically via transnasal trans-sphenoidal endoscopic excision of the tumor.

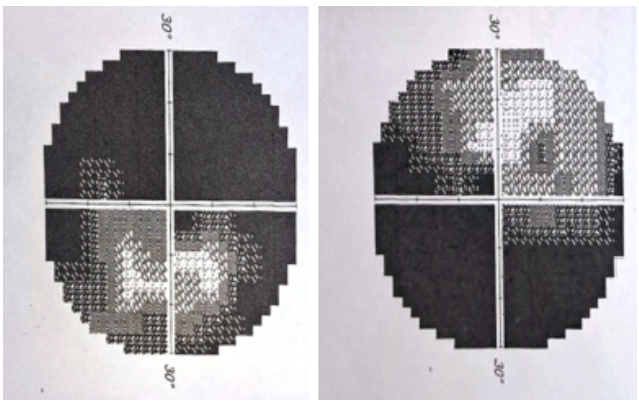

Figure 3: Visual field analysis demonstrating bi-temporal hemianopia

2.4. Case 4

A 45 years old female presented with chief complaint of loss of the vision in the right eye for 12 months back and dimunition of vision in the left eye for last 3 months associated with severe headache. Her presenting visual acuity was no perception of light in the right eye and 6/18 on Snellen's chart in the left eye. Her visual field analysis demonstrated Right eye anopia (PL negative) and left eye temporal hemianopia (Figure 4). After detailed ocular examination, she was diagnosed with bilateral optic disc pallor with right eye complete optic atrophy (Figure 5 green arrow). Neuroimaging revealed a sellar and suprasellar mass compressing the optic chiasm. She was managed surgically by endoscopic transnasal trans-sphenoidal excision of the tumor. Two containers with mass measuring 1*0.7*0.3 cm and 0.6*0.3*0.2 cm were sent for HPE. Her HPE revealed monomorphic tumor cells arranged in sheets, papillae and clusters. The tumor

cells showed numerous pseudorosettes like perivascular arrangement along with inter-sparsed thin-walled blood vessels. The tumor cells were round to oval , nuclei with coarse chromatin, inconspicuous nucleoli, moderate amount of eosinophilic to clear cytoplasm with surrounding areas showing haemorrhage and cholesterol clefts. Second container sample showed coagulative necrosis of the tumor with few viable areas having similar morphology. The final HPE concluded as pituitary adenoma with apoplexy.

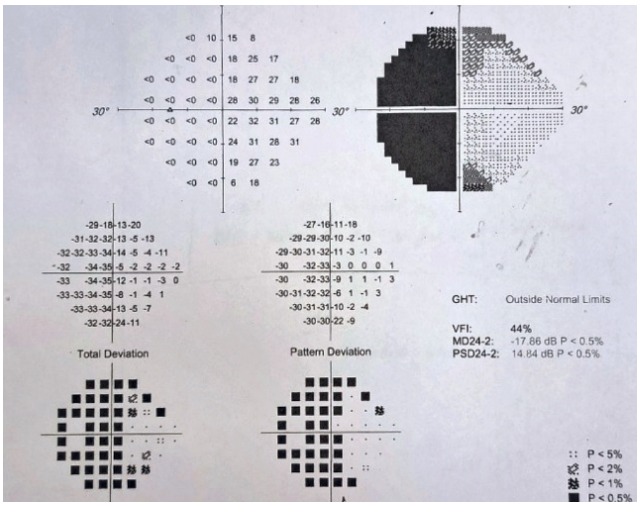

Figure 4: Visual field analysis demonstrating left eye temporal hemianopia

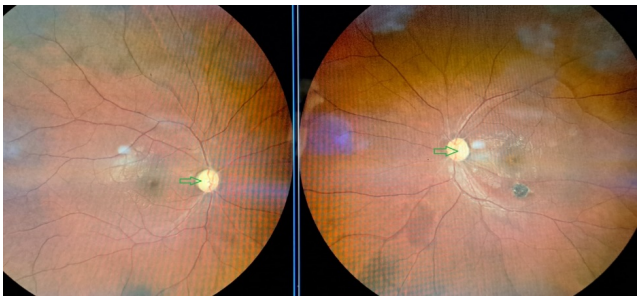

Figure 5: Colored photograph of fundus showing bilateral optic atrophy (green arrow)

2.5. *Case 5*

A 39 years old female presented with chief complaint of headache and blurring of the vision in the both the eyes since last 7 months. After detailed ophthalmological examination and neuroimaging, he was diagnosed with Pituitary lesion compressing the optic chiasm, most probable diagnosis being Pituitary macro-adenoma with bilateral optic atrophy. She was managed surgically via transnasal trans-sphenoidal endoscopic excision of the tumor. Her HPE demonstrated tumor cells arranged in pseudo-rosettes, peri-vascular pattern and solid sheets. The cells were uniform with stippled chromatin and indistinct cytoplasm (Figure 6).

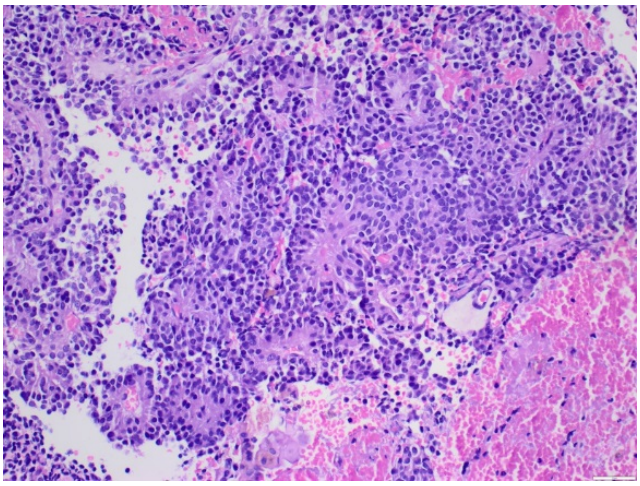

Figure 6: HPE demonstrating tumor cells arranged in pseudo-rosettes,peri-vascular pattern and solid sheets. The cells ware uniform with stippled chromatin and indistinct cytoplasm

2.6. *Case 6*

A 55 years old male presented with chief complaint of headache, blurring of the vision in the both the eyes and ptosis in the right eye since last 2 weeks. After detailed investigations, he was diagnosed with pituitary macro-adenoma with right eye cranial nerve three (CN III) palsy. He was managed surgically via transnasal trans-sphenoidal endoscopic excision of the tumor.

2.7. *Case 7*

A 60 years old male presented with chief complaint of headache, blurring of the vision in the both the eyes for last one month. His visual field analysis demonstrated bitemporal hemianopia. The MRI picture showed typical snowman appearance of the pituitary lesion (Figure 6). After detailed ophthalmological examination and neuroimaging, he was diagnosed with Pituitary lesion compressing the optic chiasm, most probable diagnosis being Pituitary macro-adenoma. He was managed surgically via transnasal trans-sphenoidal endoscopic excision of the tumor. A lesion measuring approximately 3.0*1.0*0.5 cm was sent for histopathological examination (HPE). Histopathological examination (HPE) showed features suggestive of pituitary adenoma (Figure 7).

2.8. *Case 8*

A 20 years old male presented with chief complaint of headache, blurring of the vision in the both the eyes for last one month. His visual field analysis demonstrated

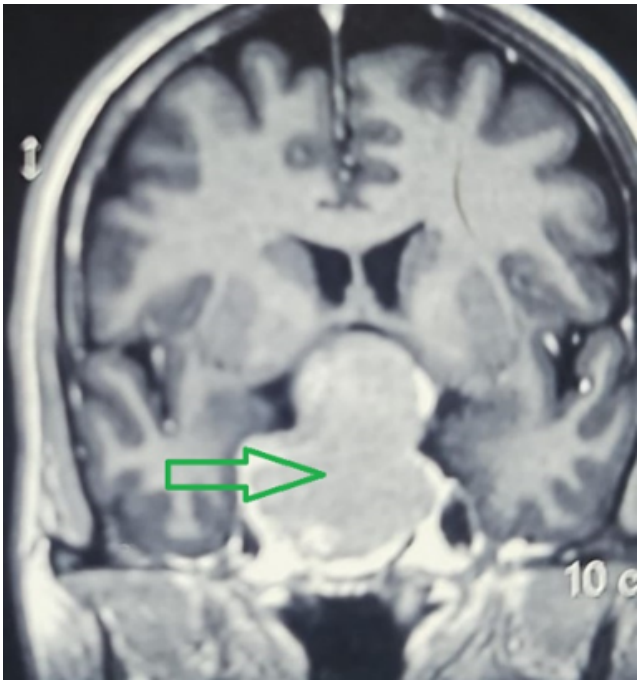

Figure 7: Green arrow: MRI coronal section picture showed typical snowman appearance of the pituitary lesion

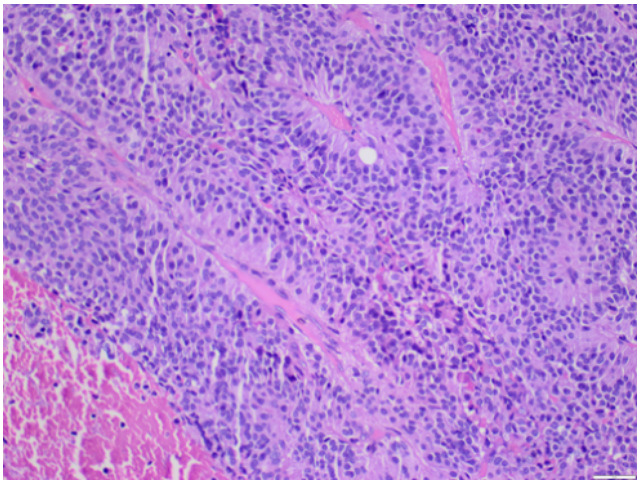

Figure 8: HPE demonstrating tumor cells arranged in pseudo-rosettes,peri-vascular pattern and solid sheets. The cells ware uniform with stippled chromatin and indistinct cytoplasm

bitemporal hemianopia. After detailed ophthalmological examination and neuroimaging, he was diagnosed with Pituitary lesion. He was managed surgically via transnasal trans-sphenoidal endoscopic excision of the tumor. His HPE demonstrated it to be pituitary adenoma.

3. Discussion and Short Review

3.1. Relevant anatomy

The size and shape of a normal pituitary gland shows dynamic changes during lifespan and is affected by the age and gender, however the average size of a pea is 2-8 millimetres in diameter and weighs about 0.5 g.[3] It is located within the sella turcica (also known as pituitary fossa) of the sphenoid bone at the base of the skull and is covered by a dural fold (diaphragma sellae). The pituitary gland is connected to the hypothalamus by the stalk. The optic chiasm lies about 10 mm above it. This implies that, any pituitary mass should be at least 10 mm in size (macroadenoma) to compress the chiasm. The cavernous sinus is present at the two sides of sella turcica in the middle cranial fossa. The cavernous sinus contain cranial nerves III, IV, VI, V1 (ophthalmic) and V2 (maxillary) and the internal carotid arteries are on either side of it.

3.2. Physiology

The pituitary gland secretes nine hormones that are responsible for the body homeostasis. The anterior lobe of the pituitary gland secretes seven hormones: growth hormone (GH), thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), beta-endorphin, follicle stimulating hormone (FSH), leutenising hormone (LH) and prolactin (PL). The posterior pituitary secretes two hormones: vasopressin and oxytocin.

3.3. Pathophysiology

Pituitary gland is situated in a bony cup like depression, known as sella-turcica. The tumours extend usually upwards due to the restriction of the bony sella laterally. This stretches the overlying diaphragma sellae initially, irritating its pain-sensitive nerves and often producing the headaches. As the tumour continues to grow, it engulfs the infundibulum and eventually press on the inferior aspect of the optic chiasm and producing the different types of visual field defects. The visual field loss are often variable and asymmetric due to the variable anatomy of the chiasm in relation to the growing tumor[4–7]. The retinal ganglion cells eventually die due to compression of the axons of the retinal ganglion cells, resulting in retrograde degeneration, and finally leading to optic atrophy. Hormonal changes occur as the tumour disrupts the normal function of the gland.

3.4. Hormonal basis of tumor

Community-based cross-sectional studies report a prevalence rate of 77 to 94 cases per 100,000 persons[8,9]. The clinical presentation of the tumor will depend on what type of the cell is affected. Somatotrophs adenoma account for nearly 5-15 % of the pituitary tumours and causes gigantism in pre-puberty and acromegaly in

adults. Prolactinomas account for about 25% of these tumors and lead to amenorrhoea and galactorrhoea in women and decreased libido and impotence in men. Corticotroph adenomas account for 15% of these tumors and are associated with Cushing syndrome. Other tumors are gonadotroph adenoma, thyrotroph adenomas, plurihormonal adenomas etc.

3.5. Clinical features

3.5.1. Signs and symptoms

The secretory tumors present usually early with systemic hormonal imbalance features. The non-secretory tumors present with visual complaints first due to mass effect. Secretory symptomatic pituitary adenomas produce systemic clinical features according to the cell affected. The key clinical ocular signs and symptoms of a pituitary adenoma include: bitemporal hemianopia, reduced visual acuity, headaches, photophobia, abnormal colour vision (red-green defect), poor stereopsis, optic atrophy and ocular palsies[10,11]. The clinical features of raised intra-cranial tension also manifest due to formation of non-communicating hydrocephalus by the enlarging tumor.

3.5.2. Visual acuity

Reduced visual acuity is often a main reason people with pituitary adenomas present for an eye examination (42 to 88 per cent)[12].People with bitemporal hemianopia have difficulty reading patterns in the temporal field.

3.5.3. Visual field defects (VFD)

As the tumour enlarges it pushes up on the chiasm and stretches it upward. Nearly 10 mm of the lesion is required to compress the chiasm as the infundibulum is around 10mm. HFA is the gold standard in perimetry.

Junctional scotoma with bi-temporal hemianopia is the most common VFD encountered due to compression of the central chiasm where nasal fibres of both the eyes decussate. The VFD is darker superotemporally than infero-temporally in contrast to mass effect by Craniopharyngioma where it compresses from above and leads to infero-temporal VFD extending later on to bi-temporal hemianopia. Sometimes only the nasal or temporal fibres of one eye get compressed, leading to unilateral hemianopia. This is known as Junctioonal scotoma of Traquair. There can be selective optic nerve or optic tract involvement, depending on the position of chiasm i.e. prefixed or post-fixed. If the position of optic chiasm is anterior to the pituitary gland, it is referred to as a prefixed chiasm. In this condition, a pituitary adenoma is more likely to compress the posterior chiasm and optic tracts to produce a macular bitemporal hemianopia or homonymous visual field defect. Conversely, postfixed chiasms may produce patterns of visual field loss related to the optic nerve or a junctional scotoma due to compression at the confluence of the optic nerve and chiasm.

3.6. Differential diagnoses

Differential diagnoses of pituitary adenoma will include other brain tumours, such as craniopharyngioma, meningioma, glioma etc.

3.7. Pituitary apoplexy

Pituitary apoplexy (stroke) is a sudden onset haemorrhage or infarction in the pituitary tumour and is a life-threatening condition[13]. It can occur spontaneously or after head trauma. The presenting clinical feature will be sudden onset headache, associated with a rapidly worsening visual field defect. There can be associated ophthalmoplegia and diplopia due to cranial nerve involvement in the cavernous sinus. There will be associated hypopituitarism leading to any type of hormonal deficiency (predominantly adrenal insufficiency). Cortisol deficiency is the most serious deficiency as it can lead to life threatening hypotension.

3.8. Neuroimaging

Contrast enhanced MRI (CEMRI) is the technique of choice for evaluating the pituitary gland. It is preferred over CT scan because of the advantages of providing superior contrast differentiation of soft tissues and not exposing the subject to potentially harmful ionising radiation. Adenomas appear hypointense on T1-weighted images and can be made hyperintense by gadolinium staining or on T2-weighted images[6]. The radiological picture shows “snowman like appearance” due to intra-sellar and supra-sellar mass of the tumor.

3.9. Optical coherence tomography (OCT)

The damage to retinal nerve fiber layer (RNFL) and macular ganglion cell layer (GCL) due to compression can be quantified by OCT analysis. The pattern of the optic atrophy correlates with the OCT analysis.

3.10. Treatment

Prolactinoma: Majority are treated medically with dopamine agonists (example: cabergoline)[14]. Serum prolactin levels usually normalise within weeks in 80 to 90 per cent of patients and tumour shrinkage occurs in about 70 per cent of patients within three to six months. Changes in visual fields can be noted within days after starting therapy. Surgery can be used if dopamine agonists are not tolerated or do not work.[15,16]

Other Pituitary Adenomas: In general, surgery is used to treat most other types of pituitary adenomas, although medical therapy or radiation can be used in some cases.

Trans-sphenoidal surgical resection is considered first line of the treatment. The endoscopic trans-nasal trans-sphenoidal techniques allows a simpler and more direct approach to the sella[17–20], resulting in wider

panoramic view of the surgical field, increased patient comfort, decreased use of nasal packing, decreased patient morbidity.[21–23] Other approaches include microscopic sublabial trans-sphenoidal technique and open pterional craniotomy with trans-sylvian approach. Recovery of pituitary function often occurs very soon after the procedure.[24] Visual acuity improves by 68 per cent on average (range 45 to 91 per cent), while improvement in visual field sensitivity is more marked at 84 per cent on average (range 73 to 96 per cent). Recurrence of pituitary adenoma after complete surgical resection can occur within four years in 10 to 25 per cent of patients. Periodic hormonal testing and repeat MRI imaging are recommended annually.[25–29]

Radiotherapy can be used as an adjuvant treatment to obtain a better disease control. Treatment doses in the range of 12-15 Gy is delivered in a single fraction or in multiple fractions. It can prevent further adenoma growth in more than 95% of adenomas. However, rates of radiation-induced hypopituitarism are quite significant.

3.11. Rate of recovery of visual function after surgery

Visual prognosis depends on the chronicity of the disease. An old lesion which has already incited ganglion cell axons death has a poor visual prognosis. However, visual acuity recovers very rapidly following removal of the compressive tumour, particularly during the day. A gradual improvement in visual acuity continues over the next few months.[30–32]

4. Conclusion

Pituitary adenomas have a varied presentation ranging from subtle to aggressive manifestations. The early diagnosis by good clinical assessment and neuroimaging is mandatory. Early multi-disciplinary approach of the management is vital in these cases.

5. Patient Concern

Patient has given written consent to publish his case, with the hidden identity.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Shrinkhal, Assistant Professor

Arvind Kumar Suman, Assistant Professor

Suyash Singh, Associate Professor

Shruti Gupta, Associate Professor

Arijit Jotdar, Assistant Professor

Dhruv Kapoor, Senior Resident

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