



## Case report

## Bilateral sixth cranial nerve palsy, the first presenting feature of hemorrhagic apoplexy of pituitary macroadenoma: A case report

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## ABSTRACT

**Introduction and importance:** We report on apoplexy of undiagnosed pituitary macroadenoma presenting as sudden onset bilateral sixth nerve palsy.

**Case presentation:** A 36-year-old male patient presented with a complaint of sudden onset diplopia for one week associated with chronic headache for two years. On further investigations, isolated bilateral sixth cranial nerve palsy was found to cause diplopia in lateral gaze and at distance. Magnetic resonance imaging of the brain showed a well-defined lobulated mass of 19 × 22 × 24 mm in the sellar and suprasellar region with hemorrhage, compressing optic chiasma superiorly with extension into the superior cavernous sinus compartment on the left side. The neurosurgery team excised the tumour through an endoscopic endonasal transsphenoidal approach. Abducens nerve palsy recovered within one week.

**Clinical discussion:** In our case diplopia due to bilateral sixth cranial nerve palsy was the first clinical presentation of hemorrhagic apoplexy of pituitary macroadenoma which is a potentially life-threatening condition. There was no other significant ocular symptoms. High index of suspicion, prompt diagnosis and multidisciplinary team management resulted into favourable outcome.

**Conclusion:** Sudden onset diplopia and isolated bilateral sixth nerve palsy should be added to the spectrum of clinical presentations of hemorrhagic apoplexy of previously undiagnosed pituitary macroadenoma.

## 1. Introduction

Pituitary adenomas are benign, slow-growing lesions arising from the secretory cells of the anterior pituitary gland. The prevalence of pituitary adenomas is around 20 % [1]. They are the most common cause of sellar masses after the third decade of life. They present with neuro-ophthalmic manifestations that arise due to endocrinological or mass effects on the adjacent chiasma [2]. The most common ocular symptoms due to pituitary macroadenoma are visual field defects [3], incidence of ocular palsy occurring with pituitary tumors is rare [4]. Extraocular muscle palsy in pituitary tumors generally indicates compression of the cavernous sinus wall or direct extension of the pituitary adenoma into the cavernous sinus [4]. Compression of cavernous sinus wall in pituitary tumors occurs mainly due to pituitary apoplexy, and results in acute onset of headache, nausea, vomiting, ophthalmoplegia, visual loss, and

even hypopituitarism [1]. Third cranial nerve palsy is most common in space occupying pituitary tumors due to its anatomical location and sixth cranial nerve involvement is rare [5,6]. We describe a case of bilateral sixth cranial nerve palsy due to haemorrhagic apoplexy in a large pituitary macroadenoma. Prompt diagnosis and management by a multidisciplinary team lead to fast recovery of abducens nerve palsy without any significant consecutive pituitary insufficiency.

## 2. Presentation of case

A 36-year-old male presented to emergency department of All India Institute of Medical Sciences (AIIMS), Rishikesh, India, with complaints of sudden onset diplopia for one week and a headache for two weeks. The complaints of chronic headache were there from last two years, localized to the left retroorbital and occipital region. There was a history

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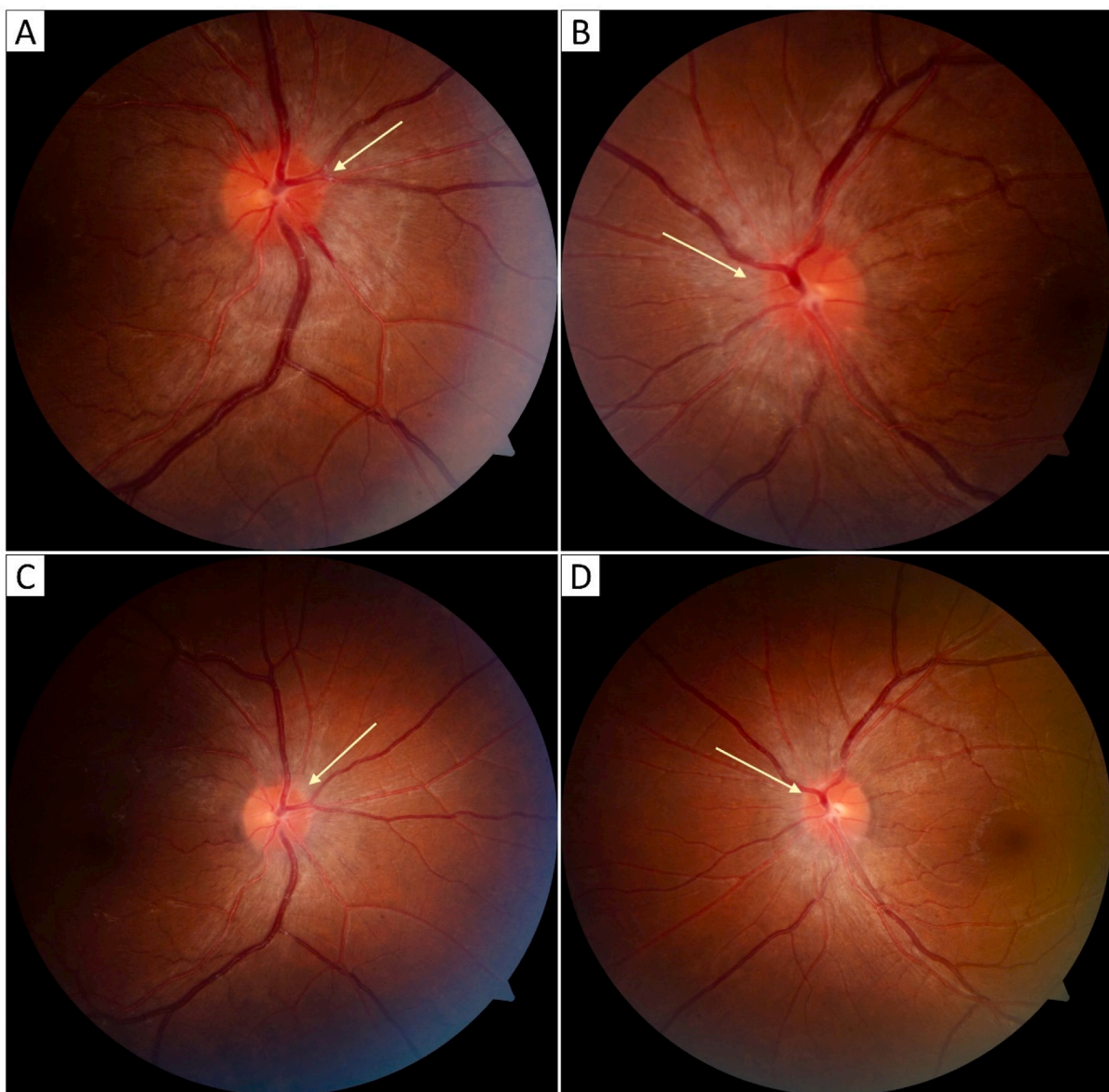
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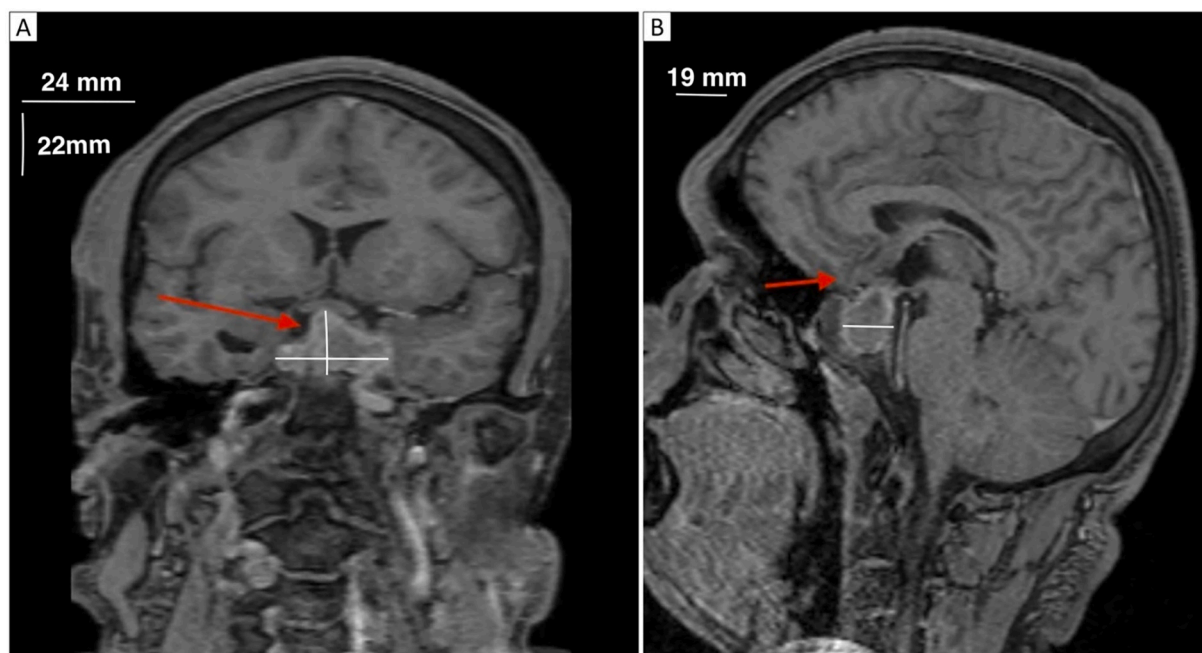
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**Fig. 1.** Clinical nine gaze photograph (A-I) depicting right esotropia in primary position (1E) with limitation of abduction in both eyes, right (A, D, G) more than left (C, F, I), rest of the movements are full & free (B, H) suggestive of bilateral abducens nerve palsy.



**Fig. 2.** Colour fundus photograph showing grade 2 papilledema in both right (A) and left eyes (B) at the time of presentation and grade 1 papilledema in both right (C) and left eyes (D) after two weeks of surgery (yellow arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



**Fig. 3.** Post contrast T1 weighted coronal (A) and sagittal view (B) of magnetic resonance images of brain depicting heterogeneously enhancing mass lesion of  $19 \times 22 \times 24$  mm in sella and suprasellar area abutting cavernous segment of bilateral internal carotid artery and, the lesion is extending into superior compartment of cavernous sinus (red arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

of irrelevant talking and snoring for the past two days noticed by his wife. He was on tablet thyroxine  $75 \mu\text{g}$  (Thyroicp, Cipla Ltd., Mumbai, India) for the last year. There was no history of hypertension, diabetes mellitus, tuberculosis, or trauma. On examination, the best-corrected visual acuity was 6/6 in both eyes. Pupillary reflexes, colour vision, contrast sensitivity, corneal sensation, and anterior segment examination were within normal limits in both eyes. On the Hirschberg test [7], 15-degree of right esotropia was noted in primary gaze (Fig. 1E). On the cover-uncover test, he had an alternate convergent squint. Extraocular motility evaluation revealed limited abduction of both eyes, the right side affected (Fig. 1A, D, G) more than the left side (Fig. 1C, F, I). Ocular movements in the rest of all other directions were full and free (Figure 1).

On prism bar cover test (PBCT) with right eye fixing, there was 40 prism diopter (PD) of left esotropia on near fixation, which increased to 50 PD on distant fixation. On PBCT with left eye fixing, there was a right esotropia of 30 PD at near and 40 PD at distant fixation. Diplopia charting with red-green glasses revealed horizontal uncrossed binocular diplopia increasing in lateral gazes and at distance fixation. Posterior segment examination with indirect ophthalmoscope revealed grade 2 papilledema (on the Frisén scale) [8] in both eyes (Fig. 2A, B, yellow arrows). Visual fields 120–2 were within normal limits in both eyes.

Based on the above clinical findings, the provisional diagnosis was bilateral acquired sixth cranial nerve palsy. As the patient had a history of chronic headache and hypothyroidism, he was referred to the endocrinology department of AIIMS, Rishikesh, India for further evaluation. The blood investigations were suggestive of hypopituitarism with mild hyperprolactinemia (serum testosterone- $7.0 \text{ ng/dl}$ , basal cortisol- $0.50 \text{ IU/ml}$ , serum prolactin- $72 \text{ ng/ml}$ ) and hypothyroidism (TSH -  $0.07 \text{ pg/ml}$ , FT3- $1.53 \text{ pg/ml}$ , FT4- $0.5 \text{ pg/ml}$ ). Magnetic resonance imaging of the brain revealed well defined lobulated mass of  $19 \times 22 \times 24$  mm in the sellar and suprasellar region with hemorrhage, compressing optic chiasma superiorly with extension into superior cavernous sinus compartment, suggestive of pituitary macroadenoma with apoplexy with superior cavernous sinus compartment involvement (Fig. 3A, B, red arrows).

Thus, bilateral lateral rectus palsy due to pituitary macroadenoma with apoplexy was found as the underlying cause of binocular diplopia.

Because of acute presentation, the neurosurgery team excised the tumour through an endoscopic endonasal transsphenoidal approach. Histopathological examination of the excised tissue revealed predominantly hemorrhagic necrosis (Fig. 4A, red arrows) along with a few interspersed small uniform nuclei (Fig. 4A, green arrows) on Hematoxylin and Eosin staining. Immunohistochemistry revealed positive staining for growth hormone (Fig. 4B, black arrow), negative staining for follicle-stimulating hormone, and luteinizing hormone (Fig. 4C and D, respectively).

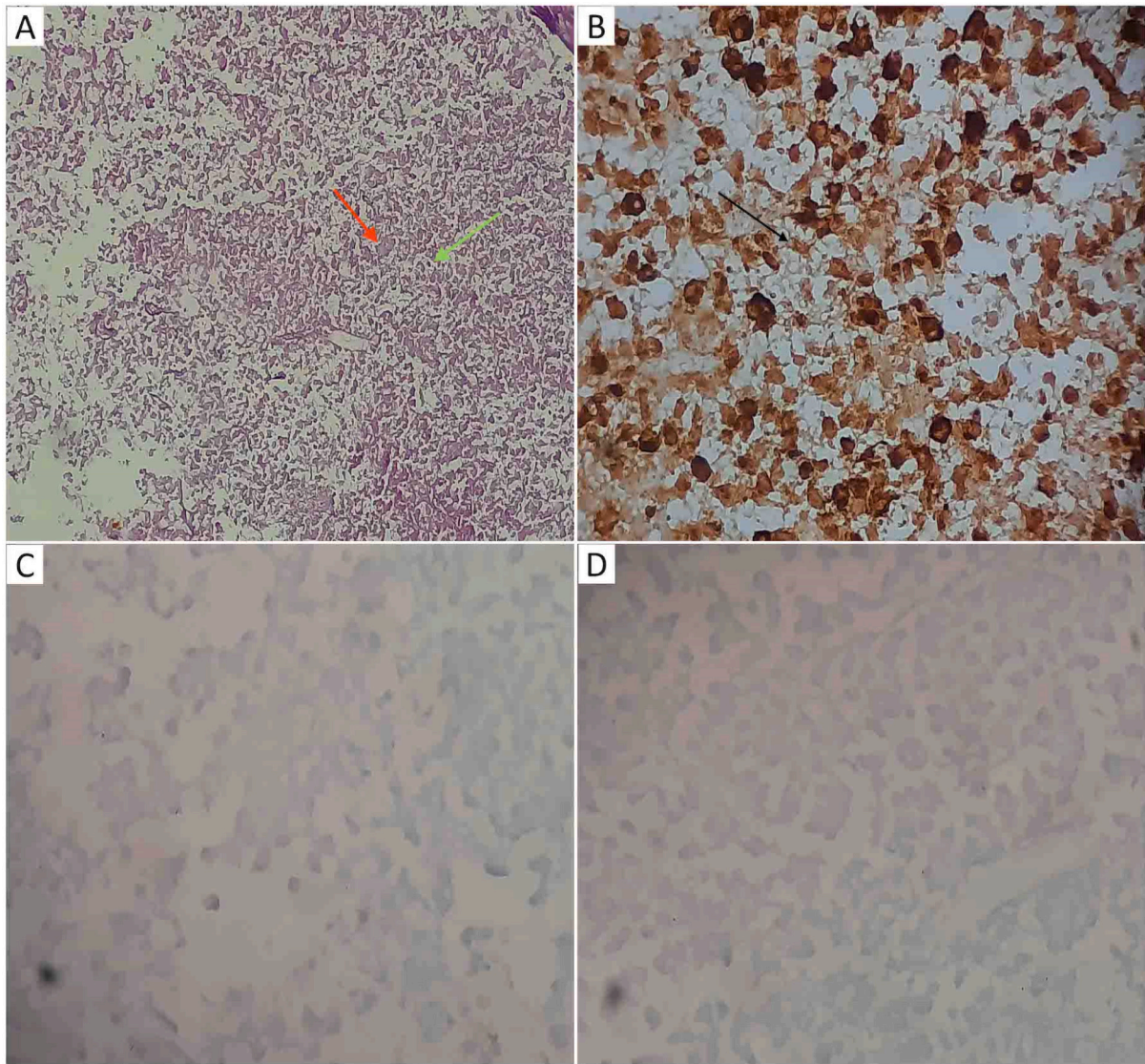
Ocular symptoms resolved, and extraocular movements were full and free in all gazes (Fig. 5: 5A-5I); Grade 2 papilledema reduced to Grade 1 papilledema (on the Frisén scale, Fig. 2C, D, yellow arrows) within one week of surgery.

The patient was discharged on tablet thyroxine  $75 \mu\text{g}$  (Tab Thyroicp, Cipla Ltd., Mumbai, India) once a day, tab desmopressin  $0.05 \text{ mg}$  (Tab Minirin, Ferring Pharmaceuticals Pvt. Ltd., Thane, India) sublingually twice a day, and tab prednisolone  $5 \text{ mg}$  (Tab Wysolone, Pfizer Ltd., Chennai, India) at 8 am and  $2.5 \text{ mg}$  at 5 pm. After six months of follow up there were no ophthalmic symptoms, and serum insulin-like growth factor 1 (somatomedin-c) was  $138 \text{ ng/ml}$  (normal reference range-  $63.4$ - $223 \text{ ng/ml}$ ).

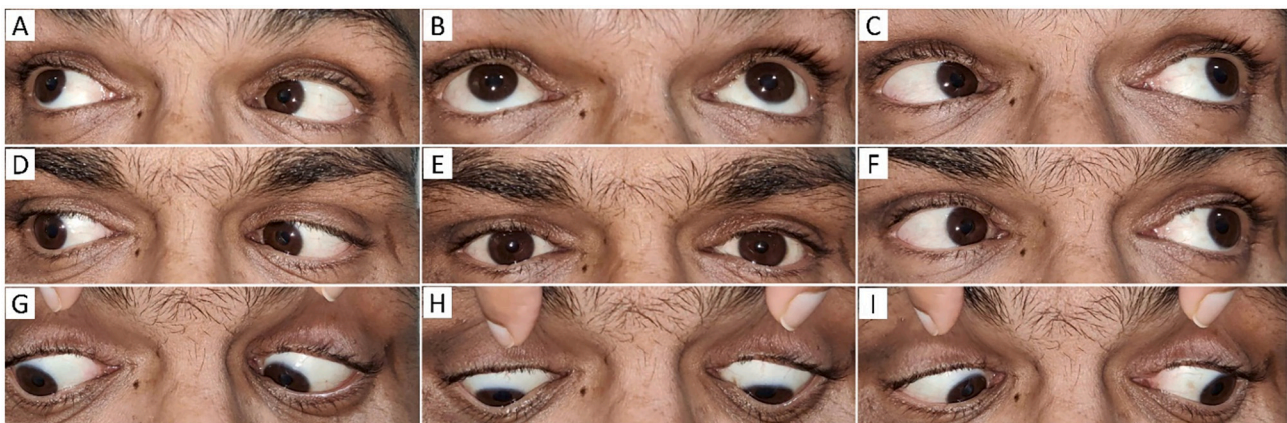
The work has been reported in the line of SCARE 2020 criteria [9].

### 3. Discussion

Pituitary apoplexy (PA) is a potentially life-threatening condition which may have highly variable presentation in the form of sudden onset headache, nausea, vomiting, visual disturbances, diplopia, hypopituitarism, and impaired consciousness. Headache, nausea and vomiting is mainly due to meningeal irritation, raised intracranial pressure, and adrenaline insufficiency. Visual disturbances are mainly due to optic nerve and chiasmal compression [1,3,4]. Surgical decompression is indicated in cases with acute, severe, progressive visual and neurological manifestations, whereas the patients with mild stable clinical presentation are managed conservatively [10]. Isolated acute cranial nerve palsies due to PA indicates a milder form of chronic disorder. The lateral expansion of the pituitary adenoma can involve III, IV, V, VI cranial



**Fig. 4.** A – Histopathological slide (10×) with Hematoxylin and Eosin staining showing predominantly hemorrhagic necrosis (red arrows) along with a few interspersed small uniform nuclei (green arrows). B - Immunohistochemistry slide showing positive staining for GH (Growth hormone) (black arrow). C – IHC (Immunohistochemistry) slide showing negative staining for FSH (Follicle Stimulating Hormone). D – IHC (Immunohistochemistry) slide showing negative staining for LH (Luteinizing hormone). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



**Fig. 5.** Clinical nine gaze photographs showing orthophoria in primary position (E) with no limitation in abduction in side gazes in both eyes showing complete recovery of abduction limitation on both right and left sides (A-D, F-I).

nerves while superior expansion results in dysfunction of the optic nerve and optic chiasm. The oculomotor nerve is more susceptible to laterally transmitted pressure by expanding the pituitary mass, because of its anatomical location [5,6]. Abducens nerve is often spared because of its more central position within the cavernous sinus. It runs lateral to the internal carotid artery but medial to the third, fourth, and first and second divisions of the fifth cranial nerves [11].

The rare presentation of bilateral isolated sixth cranial nerve with papilledema without any complaints of headache, nausea, vomiting and visual field defect in the index case can be explained by the growth pattern of the growth hormone (GH) positive pituitary adenoma that tends to have lateral or infrasellar invasion [12]. This invasion pattern of GH secreting adenomas is generally found originating from the lateral wings of the pituitary gland due to the presence of somatotroph cells at this location [13].

Further, it has been reported that these isolated nerve palsies without a visual field defect have a better prognosis than those presenting with visual field defects if diagnosed and treated appropriately [14]. Acute presentation in our case with radiological signs of apoplexy guided us for prompt surgical intervention, which in turn lead to favourable visual outcome without any significant hormonal disturbance.

This case report emphasizes the importance of ocular symptoms in diagnosing life-threatening complications of pituitary macroadenoma and also on the recognition of the rare, atypical presentations (bilateral sixth cranial nerve palsy) of pituitary apoplexy, which can develop before the diagnosis of pituitary adenoma is established, and visual field is affected.

#### 4. Conclusion

Pituitary apoplexy can present as isolated bilateral sixth cranial nerve palsy without any signs or symptoms of increased intracranial pressure, or any visual field defects. A high index of suspicion, early diagnosis and appropriate management can improve the visual outcome, relieve the symptoms, accelerate the recovery of ophthalmoplegia, and prevent the potentially severe consequences of hormonal disturbances and the mass effect.

#### Patient's perspective

The patient was satisfied with the overall team management, both medical and surgical. After 6 months of follow up, he was asymptomatic.

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None.

#### Ethics approval

AIIMS/IEC/22/334 dated 21/07/2022.

#### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contribution

Anupam Singh: Conceptualization, Methodology, Software, Writing, Editing.  
Mitali Khurana: Data curation, Writing- Original draft preparation.  
Himani pal: Data curation, Writing- Original draft preparation.  
Shweta Azad: Visualization, Investigation.  
Rakesh K Sihag: Patient management, Supervision, Writing, Editing.  
Barun Kumar: Software, Validation, Writing- Reviewing and Editing.

#### Research registration

N/A.

#### Guarantor

Anupam Singh accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controls the decision to publish.

#### Declaration of competing interest

None declared.

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