

Synchronous Occurrence of a Hemorrhagic Hypothalamic Hamartoma and a Suprasellar Teratoma

Narayanan Anantha Sai Kiran^a Nandita Ghosal^b Sumit Thakar^a

Alangar S. Hegde^a

Departments of ^aNeurosurgery and ^bNeuropathology, Sri Sathya Sai Institute of Higher Medical Sciences, Bangalore, India

Key Words

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Abstract

Hypothalamic hamartomas have been reported to coexist with lesions like Rathke's cleft cyst and arachnoid cysts in the suprasellar or temporo-sylvian regions. This is the first report in indexed literature describing its association with a suprasellar teratoma. A 7-year-old girl presented with long-standing precocious puberty and generalized tonic-clonic seizures and recent-onset raised intracranial pressure. MRI done prior to the onset of symptomatic raised intracranial pressure revealed 2 distinct lesions in the suprasellar region. One was a midline, pedunculated lesion arising from the hypothalamus, with evidence of an old bleed within it. A separate lesion, with a wide base near the tuberculum sellae and a posteriorly directed conical tip, was noted in an adjacent sagittal cut. CT scan done at the time of admission demonstrated a re-bleed in the suprasellar region with blood in the lateral and third ventricles and gross hydrocephalus. The child was taken up for a ventriculoperitoneal shunt followed by complete excision of the lesions. Histopathologic exami-

nation confirmed the pedunculated lesion to be a hypothalamic hamartoma with evidence of hemorrhage, and the other to be a mature teratoma. Postoperative MRI confirmed complete excision of both the lesions. The child reported regression of precocious puberty and remained seizure-free until the last follow-up 6 months after surgery. A hypothesis based on a dysontogenetic mechanism is discussed to explain the unusual occurrence of the dual, seemingly unrelated pathologies. Hemorrhage into the hamartoma was an added oddity in this case.

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Introduction

A non-neoplastic, congenital lesion consisting of heterotopic neural tissue, the hypothalamic hamartoma (HH), commonly presents with gelastic seizures and/or precocious puberty [1–3]. There have been anecdotal reports of its association with other congenital lesions like Rathke's cleft cyst [4] and arachnoid cysts in the suprasellar [5] and temporo-sylvian [6–8] regions. Our report discusses a hitherto undescribed synchronous association of this lesion with a teratoma, another congenital lesion

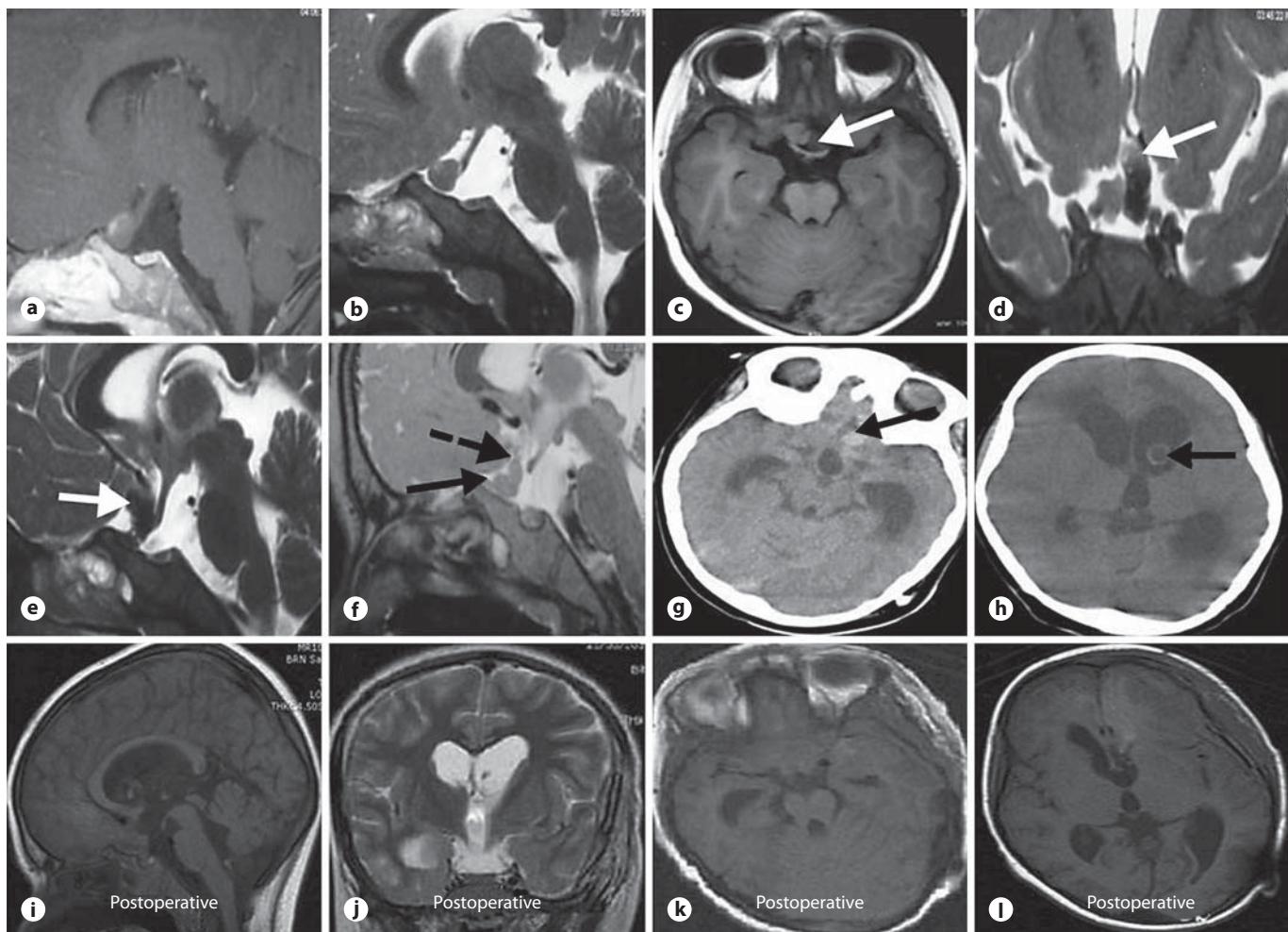


Fig. 1. Mid-sagittal **a** T₁ contrast and **b** T₂-WI showing the iso-intense, pedunculated lesion arising from the region of the hypothalamus. **c–e** Axial T₁ plain (**c**), coronal T₂ (**d**), sagittal T₂-WIs (**e**) showing a large circumscribed area of T₁- and T₂-hypointensity (solid white arrows in **c–e**) in the hypothalamic lesion suggestive of an old bleed. **f** Sagittal T₂-WI in a cut adjacent to that of the hypothalamic lesion, showing a separate, iso-intense lesion with a wide base (solid black arrow) in the region of the tuberculum

sellae, and the narrow tip (broken black arrow) directed postero-superiorly. **g, h** Plain CT scan done at the time of admission showing re-bleed with blood in the suprasellar region (arrow in **g**)/left lateral ventricle (arrow in **h**) and gross hydrocephalus with periventricular ooze. **i–l** Postoperative MR images, **i** sagittal T₁, **j** coronal T₂, and **k, l** axial T₁-WIs confirming total excision of the lesions and resolution of hydrocephalus.

with a predilection for the suprasellar region [9, 10]. Such an occurrence helps in clarifying its dysontogenetic pathogenesis [4–8].

Case Report

A 7-year-old girl presented with a history of multiple episodes of generalized tonic-clonic seizures and precocious puberty from 3 years of age and headache with vomiting for 1 week prior to admission. On examination, she was conscious and oriented, but

very irritable. Other than papilledema on fundoscopy, her neurological examination was unremarkable. Systemic examination revealed the presence of secondary sexual characteristics. Her hormonal profile (T₃, T₄, TSH, cortisol, prolactin and growth hormone) was normal. Magnetic resonance imaging (MRI) done prior to the onset of symptomatic raised intracranial pressure revealed two distinct lesions in the suprasellar region (fig. 1a–f). One was a centrally located, pedunculated lesion arising from the hypothalamus which was predominantly iso-intense on T₁- and T₂-weighted images (WI) (fig. 1a, b). A larger, circumscribed area of T₁- and T₂-hypointensity, suggestive of an old bleed (fig. 1c–e), was noted inside this lesion. Seen in an adjacent sagittal cut was a

distinct lesion which was iso-intense on T₁- and T₂-WIs (fig. 1f). It had a wide base near the tuberculum sellae and a conical tip directed postero-superiorly. Neither of the lesions enhanced significantly with contrast. There was no evidence of intraventricular hemorrhage or hydrocephalus in these MR images. CT scan done at presentation with raised intracranial pressure revealed a recent bleed in the suprasellar region (fig. 1g), blood in the lateral (fig. 1h) and third ventricles near the region of the foramina of Monro, and resultant gross hydrocephalus (fig. 1g, h).

The patient underwent a ventriculo-peritoneal shunt and a follow-on left pterional approach and excision of the lesions. At surgery, there was evident xanthochromia in the sylvian fissure and suprasellar region. Two distinct lesions were noted in the suprasellar region. The larger, pedunculated lesion arising from the hypothalamus was greyish and firm, and contained greenish material which was corresponding to the large, circumscribed, T₁- and T₂-hypointense area (arrows in fig. 1c–e) on the MRI. Adjacent to this lesion was a smaller, whitish structure with a wide base attached to the dura in the region of the tuberculum sellae, and a tapering, conical free-end posteriorly (fig. 2). The pituitary stalk was seen separately. Both the lesions were completely excised.

On light microscopy, the first lesion arising from the hypothalamus demonstrated glial tissue with neurons lying singly and in clusters, with evidence of dysmorphism (fig. 3a). Hemosiderin, suggestive of hemorrhage (fig. 3b), was noted in this lesion. The greenish material contained fibrin with hemosiderin. These features were consistent with the diagnosis of an HH with bleed. Sections from the adjacent dural-based lesion showed a mature teratoma, as evidenced by the presence of seromucinous and intestinal glands, adipose tissue, respiratory epithelium and a fragment of cartilage (fig. 3c–e).

Her symptoms of raised intracranial pressure subsided following the shunt surgery. A postoperative MRI revealed significant decrease in ventricular size and no residual lesion (fig. 1i–l). At a follow-up visit 6 months after definitive surgery, she had remained seizure-free while her symptoms of precocious puberty had demonstrated significant regression.

Discussion

The HH is a congenital lesion that arises from the tuber cinereum or mammillary bodies. Mostly sporadic, a few of its cases (10%) have been reported in association with malformation syndromes like that of Pallister-Hall, McKusick-Kaufman, and Bardet-Biedl [2, 4]. Amongst its reported lesional, intracranial associations are Rathke's cleft cyst [4] and arachnoid cysts, either in the suprasellar region [5] or in the temporo-sylvian region [6–8]. Adding to this small list is our report of a suprasellar teratoma.

Another rare dysembryonic lesion, the teratoma, represents 0.5% of all intracranial tumors [9]. Common sites of predilection include the pineal, suprasellar and hypothalamic regions. It is classified into mature, immature and malignant types based on histology [9, 10]. Amongst the unusual pathologies reported to have occurred con-

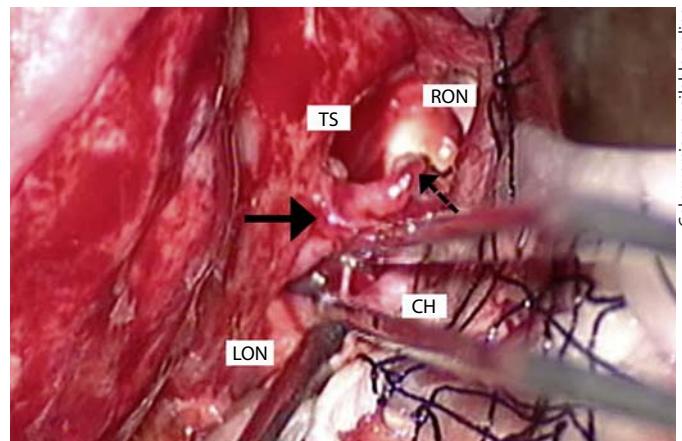


Fig. 2. Intraoperative picture taken after excision of the HH showing the teratoma with a wide dural base (solid arrow) in the region of the tuberculum sellae (TS), and a free pointed tip (broken arrow) directed posteriorly. LON = Left optic nerve; RON = right optic nerve; CH = optic chiasm.

comitantly with a teratoma are an interparietal encephalocele [11] and spinal dysraphism [12–14]. These unusual associations, like those of the HH, suggest a common genetic basis for pathologies of seemingly different origin.

The mechanism of development of the HH is largely unclear, resulting in the generation of several hypotheses [3]. One hypothesis relates to the ectopic localization of otherwise normal cellular elements secondary to defects in cell-cell recognition and cell-matrix interference, mechanisms that normally guide neuronal migration along radial glial cells. The absence of appropriate migratory and proliferative stimuli results in local structural abnormalities and an ensuing HH. A second hypothesis is related to an abnormal proliferative potential of normally positioned hamartomatous cells. Rarely, this proliferative phenotype persists, resulting in a hypothalamic hamartoblastoma with more primitive and immature neuronal and glial elements [2].

Teratomas in the central nervous system are typically located in midline structures, supporting the theory that they originate from pluripotent cell rests at the sites of early neural tube closure [9, 10, 12–14]. Well-known associations of teratomas in the spinal cord with dysraphic congenital spinal malformations such as spina bifida, syrinx, dermal sinus, split cord, meningomyelocele and lipomeningomyelocele suggest an embryogenetic error related to dysfunction of genetic and cellular inductive mechanisms [12–14].

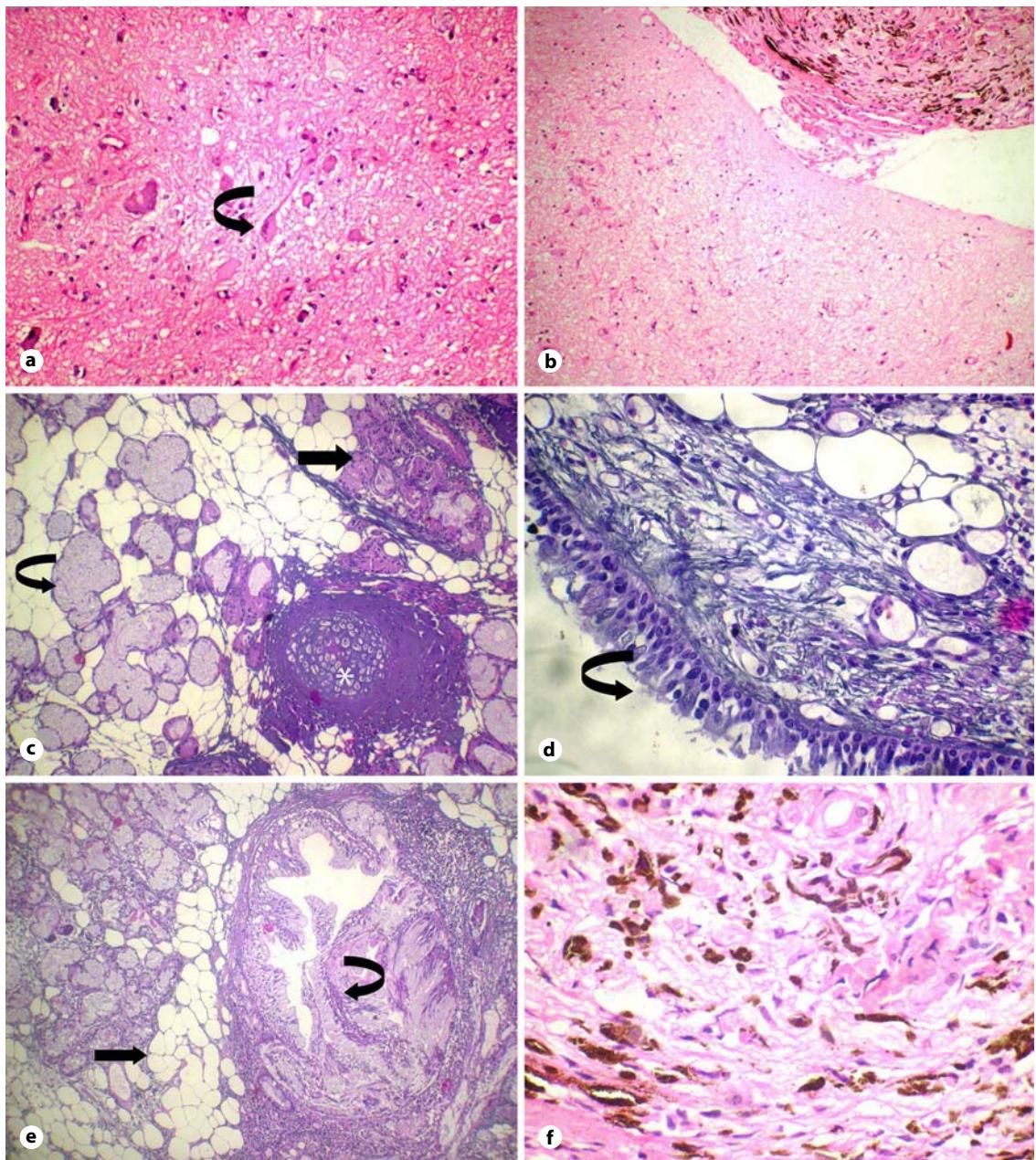


Fig. 3. Paraffin section showing **a** HH, with clustering of neurons (curved arrow), **b** hemosiderin pigment in one part of the hamartoma. Paraffin section of the distinct, dural-based lesion showing a mature teratoma with **c** seromucinous glands (straight and curved arrows), cartilage (asterisk), **d** respiratory epithelium (curved arrow), and **e** fat (straight arrow) with intestinal glands. **f** Brownish granular hemosiderin pigment in the hamartoma (hematoxylin and eosin: **b, c, e** $\times 100$; **a, d, f** $\times 400$).

In our case, a genetic error causing defective cell-cell recognition and abnormal neuronal migration may have resulted in two different midline pathologies as part of an ontogenetic derangement. Abnormal neuronal migration and ectopic localization of relatively normal tissue would

have resulted in the HH on one hand, while misplaced pluripotent cells and a subsequently disordered organogenesis would have resulted in the teratoma on the other.

Although atypical features like cystic change [3, 15] and the presence of fat [16] have been reported in the HH,

hemorrhage has not been documented as yet. Lesions in the hypothalamic region rarely reported to have bled are pilocytic astrocytomas, pilomyxoid astrocytomas and fibrillary astrocytomas [17–23]. Possible causes of tumor-related hemorrhage include endothelial proliferation and obstruction of the tumor vessels causing necrosis and hemorrhage, disruption of vessels by tumor expansion, tumor infiltration into vessels, or abnormal tumor vascularity [17–24]. Hemorrhage in a hamartoma is rare, with isolated reports in sites like the retina and intestine [25, 26]. A postulated mechanism of hemorrhage in such cases is related to the impingement of surrounding blood vessels by the lesion. In our case, it is conceivable that the significantly sized hamartoma may have impinged on some vessel(s) in the capillary-rich suprasellar region to have caused the recurrent bleeds.

Although gelastic seizures are the prototypic seizures in a case of an HH, other seizure types, including generalized seizures, are known to develop secondary to the spread of seizure activity from the mammillary bodies to the thalamus and cortex via the mammillothalamic tract

[27]. While confirming the intrinsic epileptogenic potential of these lesions by depth electrode placement, Shim et al. [28] reported good control of all HH-associated seizures after disconnection/excision of the lesion. This would explain the disappearance of the generalized seizures in our case following complete resection of the HH.

Conclusion

This first-of-its-kind report describes the coexistence of a mature suprasellar teratoma with an HH. An additional unreported feature in the case was the evidence of bleed into the hamartoma. A hypothesis is proposed to explain the concurrent occurrence of the hamartoma with the dysontogenetic lesion.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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