

Hamartomas of the Tuber Cinereum: CT, MR, and Pathologic Findings

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The neuroimaging studies, clinical evaluations, and surgical and pathologic findings in five children with biopsy-proved hamartomas of the tuber cinereum were reviewed. Surgical and/or MR findings showed that patients with precocious puberty had pedunculated lesions while those with seizures had tumors that were sessile with respect to the hypothalamus. The radiologic studies included six MR examinations in four patients and CT studies in all five patients. Three children presented with precocious puberty and two with seizures, one of which was a gelastic (spasmodic or hysteric laughter) type of epilepsy. MR studies were obtained both before and after surgery in two patients, only preoperatively in a third patient, and only postoperatively in the fourth child. MR was superior to CT in displaying the exact size and anatomic location of the hamartomas in all cases. The mass was isointense with gray matter on sagittal and coronal T1-weighted images, which best displayed the relationship of the hamartoma to the third ventricle, infundibulum, and mammillary bodies. Intermediate- or T2-weighted images showed signal characteristics of the hamartoma to be isointense (one case) or hyperintense (two cases) relative to gray matter. The difference in T2 signal intensity did not correlate with any obvious differences in histopathology. CT showed attenuation isodense with gray matter, and no calcium. There was no enhancement on CT. There was no enhancement on MR in the one case in which contrast medium was administered. Preservation of the posterior pituitary bright spot was noted on all pre- and postoperative T1-weighted MR scans.

In children presenting with precocious puberty or seizure, MR assessment of the region of the third ventricle is necessary to exclude hypothalamic hamartoma, which appears as a pedunculated or sessile mass that is isointense with gray matter.

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Hamartoma of the tuber cinereum is a rare malformation usually discovered during a workup for precocious puberty or, more rarely, seizures. The CT features of this lesion have been described and are useful in the differential diagnosis [1-5], but MR might be expected to provide better detail of these generally small lesions [6]. To date, MR findings in 31 cases of tuber cinereum hamartoma have been published [7-17], but only 10 of these were biopsy-proved. We report the use of CT and MR (1.5 T) in the workup and management of five children with biopsy-proved hamartomas.

Materials and Methods

We retrospectively reviewed five cases of hypothalamic hamartoma from our neuropathologic files. Four patients had MR studies performed on a GE Signa (Milwaukee, WI) MR system operating at 1.5 T. A multislice, multiecho spin-echo sequence of axial, sagittal, and coronal T1-weighted images, 500/20 (TR/TE), as well as intermediate-weighted (first echo) and T2-weighted (second echo) images, 2500/40, 80, were obtained. Two signal averages were obtained on 3- and 5-mm-thick slices, with a 256 × 128 matrix. In a follow-up MR examination, one patient received IV contrast medium. Patients included three girls and two

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TABLE 1: Hamartoma of Tuber Cinereum: Clinical, CT, MR, Surgical, Histopathologic, and Follow-up Findings

| Case No. | Age (Years) | Sex | Clinical History/ Diagnosis | CT Findings | Macroscopic MR and Surgical Findings | MR Signal Intensity ^a | | | | Pituitary Bright Spot | Pathology ^b | Clinical and Imaging Follow-up |
|----------|-------------|-----|---|--|--------------------------------------|----------------------------------|------------------------------|------------------------------|----|------------------------------|-------------------------------------|--|
| | | | | | | T1 | 1st Echo | Hyperintense | T2 | | | |
| 1 | 5 | F | Precocious puberty, menstruation at 6 mo., axillary/pubic hair at 4½ yr, bone age = 13 yr, increased gonadotropin, increased estrogen, normal neurologic exam | Suprasellar nonenhancing mass | Pedunculated | Isointense | Hyperintense | Hyperintense | | Present | Hamartoma, pial vascular surface | Resolved precocious puberty, postoperative MR showed no residual tumor and mild dilatation of third ventricle |
| 2 | 5 | M | Seizures, 3-mo history of absence of seizures with urination, hyperactivity, normal neurologic exam, normal endocrinologic exam | Suprasellar nonenhancing mass | Sessile | Isointense | Isointense | Hyperintense | | Present | Hamartoma, no pial vascular surface | Controlled seizures at 3 mo on medication, postoperative MR showed residual tumor, no change in signal intensity, no enhancement with contrast on MR |
| 3 | 2 | F | Precocious puberty, 3-mo history of menses, increased estrogen, normal neurologic exam | Nonenhancing parasellar mass subjacent to basilar artery | Pedunculated | Not performed preoperatively | Not performed preoperatively | Not performed preoperatively | | Not performed preoperatively | Hamartoma | Normal endocrinologic exam at 3 yr, postoperative MR showed no evidence of tumor, pituitary bright spot was present |
| 4 | 6 | F | Seizures, infantile laughter/gelastic seizures, normal endocrinologic exam | Suprasellar nonenhancing mass | Sessile, temporal lobectomy | Isointense | Hyperintense | Hyperintense | | Present | Hamartoma | Persistent but decreased frequency of seizures at 1 yr |
| 5 | 6 | M | Precocious puberty, onset over 1 yr; increased gonadotropin; normal neurologic exam | Suprasellar nonenhancing mass | Pedunculated | Not performed preoperatively | Not performed preoperatively | Not performed preoperatively | | Not performed preoperatively | Hamartoma, pial vascular surface | Stable for 6 yr postoperatively |

^a Relative to gray matter.

^b Histologically, all cases had nodular and short lamina of well-formed ganglion cells; mild to moderate gliosis, with widely separated axons, some of which were myelinated.

boys, ranging in age from 2 to 6 years old. Five patients had CT scans, which were acquired on a GE 8800 or 9800 scanner (Milwaukee, WI) both before and after contrast infusion. Three-millimeter-thick slices were obtained through the sella and suprasellar region.

The histologic sections of all five cases were reviewed.

Results

The clinical, CT, MR, surgical, histopathologic, and follow-up clinical and imaging findings in all five patients are summarized in Table 1. The three patients with pedunculated hamartomas presented with precocious puberty and the two with sessile lesions had seizures. All three preoperative MR studies demonstrated lesions isointense with gray matter on T1-weighted images (Figs. 1A, 2A, 2B) and hyperintense relative to gray matter on the second echo of the T2-weighted images (Figs. 1C, 2D, 3C). The presence of myelinated axons on Luxol fast blue stain did not correlate with any T2 shortening in the lesions. The intermediate (first echo) T2-weighted images showed either isointensity (Fig. 2C) or hyperintensity (Figs. 1B and 3B) relative to gray matter (Table 1). There was no contrast enhancement in the one case in which it was administered (Fig. 2E). There was no contrast enhancement on CT scanning (Fig. 3A), and no calcium was seen in any of the five cases. The posterior pituitary bright spot was present on all pre- and postoperative MR studies.

Discussion

Tuber cinereum is descriptively named for the region including the small bilateral protuberances of gray matter, the middle hypothalamic nuclei located between the infundibular stalk and the large, prominent mammillary bodies. An important efferent pathway from these nuclei is the tuberoinfundibular tract. Evidence suggests that these axons carry secretory granules, containing releasing hormones, allowing modulation of gonadotropins [18].

Hamartomas of the tuber cinereum are congenital, nonneoplastic heterotopias. Grossly, they may be pedunculated (Fig. 3) or broader-based, involving more of the hypothalamus (Figs. 1, 2, 4A). The first case was described in 1934 [19]. Histologically, the hamartoma closely resembles normal gray matter (Fig. 4B), and some neurons are reminiscent of those found in the adjacent hypothalamus. Some of the axons are myelinated. A variable amount of fibrillary gliosis may be found [20]. The pathologic changes seen in these masses are less striking than the gliotic nodules of tuberous sclerosis or the ganglion cell neoplasms. The latter are noted for abnormal neurons, a frequently prominent glial component, desmoplasia, and calcification.

The hamartoma in each of our cases most closely resembled gray matter in its signal characteristics on T1-weighted images. Similar MR findings have been reported by Hahn et al. [8] in two biopsy-proved cases imaged at 1.5 T. In eight other reports of biopsy-proved hamartomas [10, 12–15, 21] imaged at other or undisclosed field strengths, the tumors were isointense with gray matter in six cases [10, 12–15] and had areas of hyperintensity in two cases [21] on T1-weighted images. It has been suggested [10] that optic and hypothalamic gliomas tend to have prolonged T1 relaxation (hypointensity). Solid craniopharyngiomas also tend to be hypointense on T1-weighted scans, while cystic craniopharyngiomas often have prolonged T1, a possible characteristic differentiating these from noncystic hypothalamic hamartomas [10]. In the postoperative evaluation of these patients, T1-weighted images are the most helpful in outlining the anatomy of the floor of the third ventricle and the suprasellar cistern.

We found that the hamartoma may be isointense, slightly hyperintense, or markedly hyperintense relative to gray matter on the intermediate echo, but it was always hyperintense in relation to gray matter on the second echo of T2-weighted images. Although a variance in myelinated axons and the effect of myelin on T2 shortening [22] and the presence of gliosis could affect the variability of the T2 signal, it was not

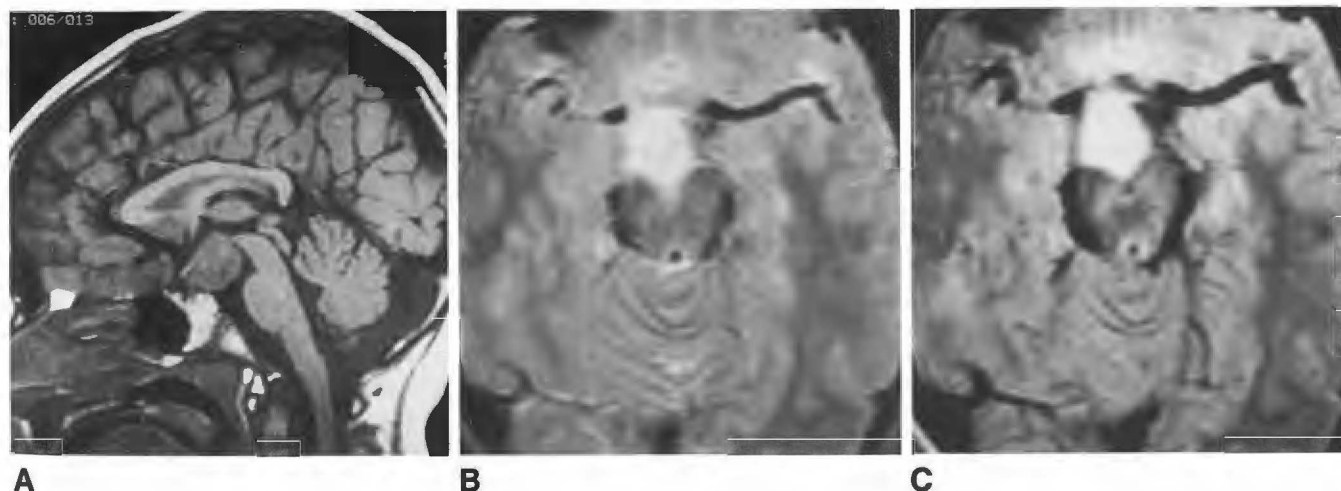


Fig. 1.—Case 4.

A, Sagittal T1-weighted MR image shows sessile hamartoma in typical third ventricular location, isointense with gray matter, infiltrating the floor of the hypothalamus. Posterior pituitary bright spot is present.

B and C, Axial T2-weighted MR images, first echo (B) and second echo (C), show that signal intensity has increased markedly with respect to gray matter.

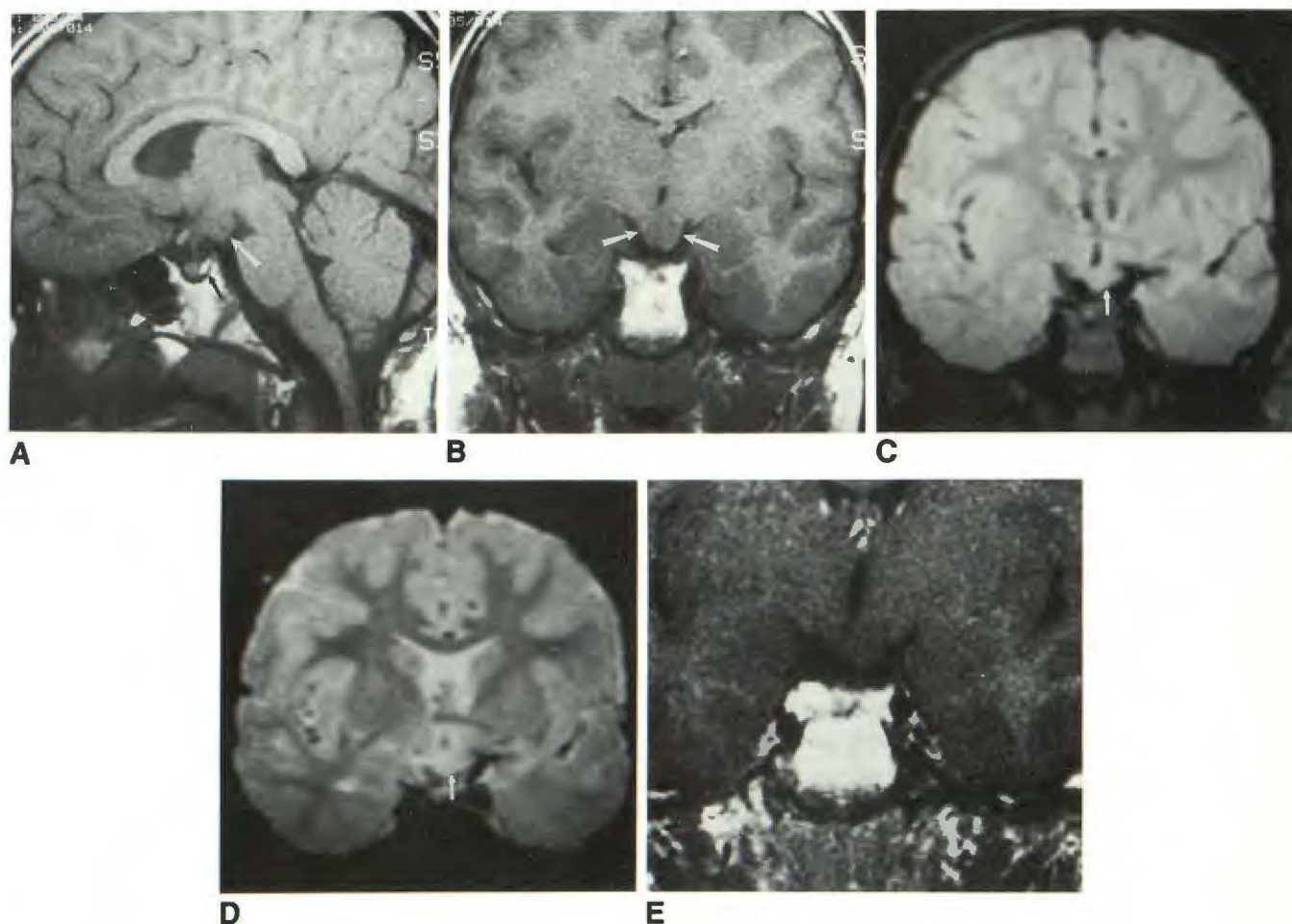


Fig. 2.—Case 2.

A, Sagittal T1-weighted MR image (500/20) shows 1.5-cm sessile mass with signal intensity isointense with gray matter. Mass is diffusely attached to and originating from the tuber cinereum (white arrow). Infundibular and optic recesses of third ventricle are obliterated, but posterior pituitary bright spot is preserved (black arrow).

B and C, Coronal T1-weighted (B) and first-echo T2-weighted (C) MR images reveal that the tumor has signal characteristics isointense with gray matter, has a broad base of attachment, and projects from left side of hypothalamus into suprasellar cistern (white arrows).

D, Coronal second-echo T2-weighted MR image shows the tumor to be hyperintense relative to gray matter (arrow).

E, Contrast-enhanced MR image (500/20) shows no tumor enhancement.

obvious from the comparison of histopathology and MR images in the present series why the lesion in case 2 (Fig. 2C) was isointense and the lesions in cases 1 (Fig. 3B) and 4 (Fig. 1B) were hyperintense relative to gray matter on the T2-weighted first-echo image.

Although hamartomas are benign and represent heterotopic rests of cells, all biopsied cases in the literature [10, 12–15, 21], including ours, had increased T2 signal on the second-echo image (Figs. 1C, 2D, 3C), which may make distinguishing hamartoma from glioma difficult. In fact, in a series of 59 suprasellar masses, MR signal characteristics were nonspecific in 70% of cases [15]. Thus, distinguishing hamartoma from glioma by T2 MR signal intensity may be somewhat limited, but isointensity relative to gray matter on the intermediate- or first-echo T2-weighted images may be more indicative of hamartomas.

On enhanced CT, the hamartoma appears as an isodense mass without definite enhancement, reflecting an intact blood-brain barrier. In our only MR case in which contrast material was administered, no enhancement was present (Fig. 2E). Histologically, tumor neovascularity was not present.

While CT suggested the preoperative diagnosis in all five patients, two of the five underwent water-soluble contrast CT cisternography to confirm the findings. MR as a noninvasive technique was unequivocally positive in the three instances in which it was obtained preoperatively (cases 1, 2, 4). In addition, MR with its direct multiplanar capabilities has the advantage of allowing for the evaluation of any associated intracranial congenital abnormalities [23]. Diebler and Ponsot [1] and Naidich and Zimmerman [2] have reported associated congenital anomalies with midline hamartomas; including callosal agenesis, optic malformation, and hemispheric dysgen-

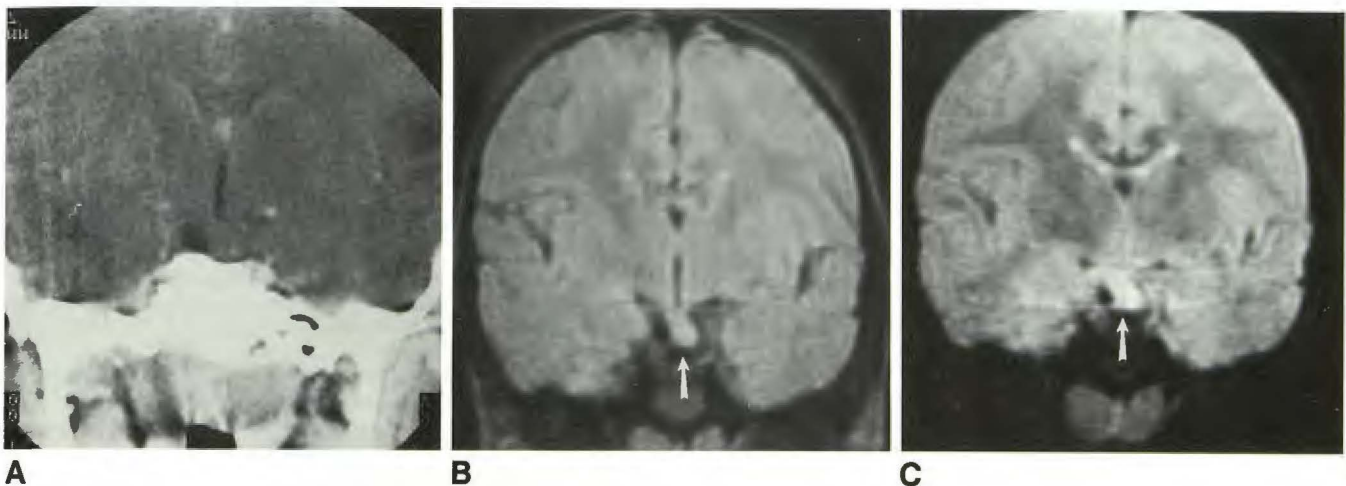
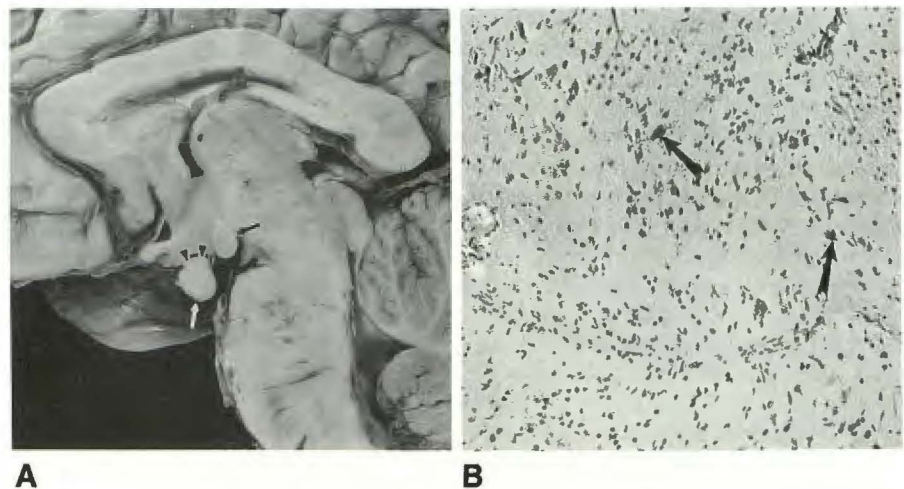


Fig. 3.—Case 1.
A, Coronal CT scan with contrast infusion reveals the relationship of the mass to the hypothalamus and floor of the third ventricle.
B and C, Coronal T2-weighted MR images, first echo (2500/40) (**B**) and second echo (2500/80) (**C**), show pedunculated mass that is slightly hyperintense relative to gray matter (arrows).

Fig. 4.—Gross and histologic findings of hypothalamic hamartoma.

A, Sagittal section, whole brain. This hamartoma of the tuber cinereum (white arrow) was incidentally discovered at autopsy. Note pedunculated attachment to the tuber cinereum (arrowheads). Mammillary body is seen posteriorly (black arrow). Note also the normally developed corpus callosum and lack of microgyria.

B, Photomicrograph of case 2 shows well-defined but disorganized mass of CNS tissue, including scattered mature central ganglion cells (arrows) with mild gliosis. With Luxol fast blue stain, several axons were shown to be myelinated. (H and E $\times 130$)



esis (heterotopias and microgyria), suggesting an insult occurring around the first month of gestation [1]. They refer to the hamartomas and congenital anomalies as a dysraphic syndrome. None of the five cases in our series displayed any associated intracranial congenital anomalies.

Clinical presentations in our five patients reflect the experience previously reported in the literature: precocious puberty and/or seizures. The mechanism whereby a hamartoma causes precocious puberty has not been clarified. One hypothesis suggests that the inhibitory pathways from the hypothalamus to the posterior pituitary and infundibulum are interrupted by mechanical compression [20, 24]. The fact that precocious puberty occurs with other lesions around the hypothalamus, such as glioma, supports this theory. Other cases seem to point to a direct neurosecretory role by the hamartoma itself [25–27]. Absence of the posterior pituitary bright spot on MR images has been reported to be associated with interruption of the stalk with resultant diabetes insipidus

[28, 29]. In all of our cases, the bright MR signal of the posterior pituitary on T1-weighted images was preserved, even when the infundibular recess was obliterated, the stalk was compressed, and hormonal evidence of precocious puberty existed (Figs. 1A and 2A). This observation could be interpreted as indicating that (1) gonadotropin-releasing-factor neurons are more resistant to compression than are vasopressin neurons, (2) only complete transection of the stalk results in loss of the posterior pituitary signal, (3) the tumor does affect the pituitary stalk but the mechanism for precocious puberty is neurosecretion from the hamartoma itself, and (4) the posterior pituitary bright spot signal has no relationship with the hypothalamic gonadotropin-releasing-factor neurons.

Some reports have found that seizures are associated with larger lesions [1]. Two of our patients (cases 2 and 4), both with large lesions, presented with seizures. The size of these hamartomas was approximately the same as that in the

patient in case 1, who had precocious puberty. Hypotheses for the seizures include (1) interconnection of the hamartomatous neurons with those of the limbic system or (2) association of the seizures with midline abnormalities or hemispheric malformations. One of our patients' seizures consisted of absence states, while the other patient with seizures had the rarer, but virtually pathognomonic, gelastic epilepsy, resulting in spasmodic laughter, which has been reported with hamartomas [1]. The onset of this type of laughter in infancy, its frequency, and its character, distinguish it from the epileptic laughter associated with temporal lobe seizures [11]. The mechanism for this ictal laughter is unclear, representing either mechanical stimulation of the floor of the third ventricle by the tumor, causing epileptic discharge from the hypothalamus, or some kind of automatism or release phenomenon [11]. Temporal lobe epilepsy can also be associated with laughter.

Postoperative MR imaging showed no tumor in two cases in which pedunculated lesions were resected (cases 1 and 3), suggesting that a careful microsurgical approach to these lesions can result in total resection and excellent clinical outcome. This series, as well as other sporadic reports [3, 24, 30], refutes the position that no case has been published in which this mass has been completely or partially removed [1]. Exophytic lesions, associated with precocious puberty, lying anterior to the basilar artery can be resected, resulting in the amelioration of symptoms. Pedunculated, prepontine masses may be diagnosed preoperatively with more confidence, but intrinsic lesions may need biopsy to differentiate hamartomas from gliomas.

In summary, in children presenting with precocious puberty or seizures, masses of the third ventricle with MR signal characteristics suggestive of gray matter should lead to a confident preoperative diagnosis of tuber cinereum hamartoma.

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