AJNR

Hamartoma of the tuber cinereum: a comparison of MR and CT findings in four cases.

E M Burton, W S Ball, Jr, K Crone and L M Dolan

AJNR Am J Neuroradiol 1989, 10 (3) 497-501
http://www.ajnr.org/content/10/3/497

Hamartoma of the Tuber Cinereum: A Comparison of MR and CT Findings in Four Cases

Edward M. Burton[1,2]
William S. Ball, Jr.[1]
Kerry Crone[3]
Lawrence M. Dolan[4]

Hamartoma of the tuber cinereum is a well-recognized cause of central precocious puberty. We report three patients with an isodense, nonenhancing mass within the interpeduncular cistern identified by CT. In a fourth patient, the CT scan was normal. MR imaging was obtained in all cases and demonstrated a sessile or pedunculated mass of the posterior hypothalamus arising from the region of the tuber cinereum. The smallest mass was 2 mm in diameter and was found in the patient in whom the CT scan was normal. The signal intensity of the masses was generally homogeneous and isointense relative to gray matter on T1- and intermediate-weighted images, and hyperintense on T2-weighted images.

MR imaging accurately diagnoses hypothalamic hamartomas, identifies small hamartomas of the tuber cinereum more sensitively than CT does, and provides optimal imaging for serial evaluation while the patient is being treated medically.

Central (neurogenic or true) precocious puberty is caused by premature activation of the hypothalamic-pituitary axis, resulting in sexual maturation prior to age 7½ years in females and age 9 years in males. Hamartoma of the tuber cinereum is a well-recognized cause of central precocious puberty [1, 2], with approximately 90 cases previously reported in the radiologic literature [3–9]. There are, however, few reports describing its appearance on CT [6–12] and MR imaging [9, 13]. We report four cases of hypothalamic hamartoma causing precocious puberty, and describe their pertinent CT and MR characteristics.

Materials and Methods

Between January 1, 1986, and January 1, 1988, we evaluated seven patients ages 3–8 years old with precocious puberty and a CNS lesion by cross-sectional radiographic imaging. Five of these children were female and two were male. Two females had neurofibromatosis and one male had a hypothalamic glioma. Three females and one male had a hypothalamic hamartoma. Of these four patients, three had CT examinations with a GE 9800 scanner. The fourth child was evaluated with a Siemens DR3 scanner. In each case, direct coronal imaging (1–1.5-mm-thick sections) was performed from the anterior clinoid processes to the basilar artery after administration of IV contrast material (2 ml/kg). MR imaging (3-mm-thick sections) in the axial and coronal projections was performed on three children by using a 1.5-T GE magnet and on one child with a 1.0-T Siemens magnet. Pulse sequences of short TR/short TE, 550–600/17–20 (TR range/TE range), long TR/short TE, 2000–2500/20–35, and long TR/long TE, 2000–2500/100–120, generated T1-weighted, intermediate-weighted, and T2-weighted images, respectively.

In three children (cases 1–3), a luteinizing hormone-releasing hormone (LHRH) stimulation test was performed by the IV administration of 100 μg of LHRH* followed by radioimmunoassay measurement of follicle stimulating hormone (FSH) and luteinizing hormone (LH) every 15 min for 60 min.

Received July 18, 1988; accepted after revision November 5, 1988.

This work was supported in part by USPHS grant RR00123 from the General Clinical Research Centers Branch, Division of Research Resources, National Institutes of Health.

[1] Department of Radiology, Children's Hospital Medical Center, Cincinnati OH 45229.

[2] Present address: Department of Radiology, LeBonheur Children's Medical Center, 848 Adams Ave., Memphis, TN 38103. Address reprint requests to E. M. Burton.

[3] Department of Neurosurgery, Children's Hospital Medical Center, Cincinnati, OH 45229.

[4] Department of Endocrinology, Children's Hospital Medical Center, Cincinnati, OH 45229.

AJNR 10:497–501, May/June 1989
0195–6108/89/1003–0497

* Ayerst, New York, NY.

Results

In three children (cases 1–3), the LHRH stimulation test produced marked elevation of FSH and LH, documenting central precocious puberty. The hamartoma in case 4 was proved by biopsy.

The characteristic features on CT and MR for each case are described in Table 1. The masses were 2–30 mm (mean, 14.3 mm) in greatest dimension. CT revealed three of the four hamartomas (cases 1, 2, and 4). In the third case, a 2-mm hamartoma was not detected on CT, even in retrospect. Of the three cases identified on CT, the mass appeared homogeneous and either isodense (Fig. 1A) or hypodense (Fig. 3A) relative to gray matter on the precontrast examination. In no case was there enhancement, fat, or calcification. In two patients (cases 1 and 2), CT clearly showed the mass arising from the floor of the hypothalamus.

In all cases, MR revealed the presence of a hamartoma, as well as the continuity of the hamartoma with the tuber cinereum of the hypothalamus (Figs. 1B, 2, and 3B). In each case, the signal intensity was homogeneous and isointense relative to gray matter on the T1-weighted images, with minimal increase in signal on the intermediate-weighted images. Small hamartomas were difficult to identify on T2-weighted images because of the presence of bright signal from the surrounding CSF in the interpeduncular cistern (Fig. 1C). The signal intensity of the largest hamartoma (case 4) was clearly hyperintense on the T2-weighted images (Fig. 3C).

In each case, the remainder of the hypothalamus, seen to greatest advantage on the direct coronal projection, appeared normal in signal. Displacement of the floor and lateral walls of the third ventricle was minimal, and was noted only in those hamartomas larger than 10 mm in diameter. Despite minimal compression of the anterior surface of the midbrain and pons in case 2, the signal intensity of these areas remained normal. The anterior pituitary gland and neurohypophysis were normal in signal intensity. Pituitary gland height was 5.0–6.6 mm (mean, 5.65 mm).

Discussion

Normal pubertal development is the result of gradual withdrawal of the influence of inhibitory factors on the hypothalamus, resulting in the pulsatile release of LHRH and subsequent activation of the pituitary-gonadal axis. Precocious puberty is due to premature dysinhibition of the hypothalamus. Processes known to disrupt the inhibitory signals of the hypothalamus include congenital or acquired brain dysfunction, trauma [14], and masses in the region of the hypothalamus [15]. Although hypothalamic glial tumors [8, 15] and gangliogliomas [15, 16] have rarely been reported in association with precocious puberty, the hamartoma of the hypothalamus is the only central process suspected to produce and release LHRH and, thus, initiate precocious puberty.

Although history, physical examination, and the LHRH stimulation test may aid in the diagnosis of central precocious puberty, cross-sectional images are required to confirm the presence of a CNS lesion [1]. Imaging of the brain is necessary in all children with isosexual precocious puberty. One-half to 94% of males with central precocious puberty are reported to have a demonstrable lesion [3, 8]. In females with central precocious puberty, the incidence of definable anatomic abnormalities is reported to be from 22% to 49% [4, 8, 17]. In our series, three of four patients were female.

Hypothalamic hamartomas are described as sessile or pedunculated masses attached to the posterior hypothalamus between the pituitary stalk and the mamillary bodies, in the region of the tuber cinereum. Resembling "collar buttons" [11], they are 0.4–4 cm in diameter, and are composed primarily of neural tissue histologically similar to the normal hypothalamus [1, 2, 18]. Microscopically, they are represented by neurons of variable size supported by a normal complement of neuroglia [1, 2]. They are characterized by a lack of invasiveness, stability in size over time, and imaging characteristics similar to normal gray matter on CT [8–12].

The appearance of hypothalamic hamartomas on CT is that of a well-defined nonenhancing isodense mass localized to the tuber cinereum and interpeduncular cistern. Calcification [8, 11], fat [19], cyst formation [20], and contrast enhancement have been reported, but are unusual findings. Small hamartomas, undetected by thin-section direct coronal CT, may be revealed by MR imaging. The location of the mass and stability in size are consistent with the diagnosis of hypothalamic hamartoma of the tuber cinereum.

On MR, hamartomas typically appear isointense relative to gray matter on T1-weighted images. Areas of bright signal intensity due to short T1 relaxation times may indicate the presence of fat within the tumor [19]. A minimal increase in signal intensity occurs on the intermediate-weighted images. The signal intensity of T2-weighted images is homogeneous,

TABLE 1: Hypothalamic Hamartoma: CT and MR Characteristics

Case No.	Age (years)	Gender	Tumor Length	CT		MR			
				Precontrast	Enhancement	T1WI	IWI	T2WI	Homogeneity
1	2.5	F	8.2 mm	Homogeneously isodense	No	Isointense to gray matter	Minimally hyperintense	NS	Yes
2	6.5	F	17.0 mm	Homogeneously isodense	No	Isointense to gray matter	Minimally hyperintense	NS	Yes
3	1.5	F	2.0 mm	Not visualized	–	Isointense to gray matter	Minimally hyperintense	NS	Yes
4	4	M	30.0 mm	Homogeneously hypodense	No	Isointense to gray matter	Minimally hyperintense	Hyperintense	Yes

Note.—T1WI = T1-weighted image, IWI = intermediate-weighted image, T2WI = T2-weighted image, NS = not seen due to hyperintense CSF.

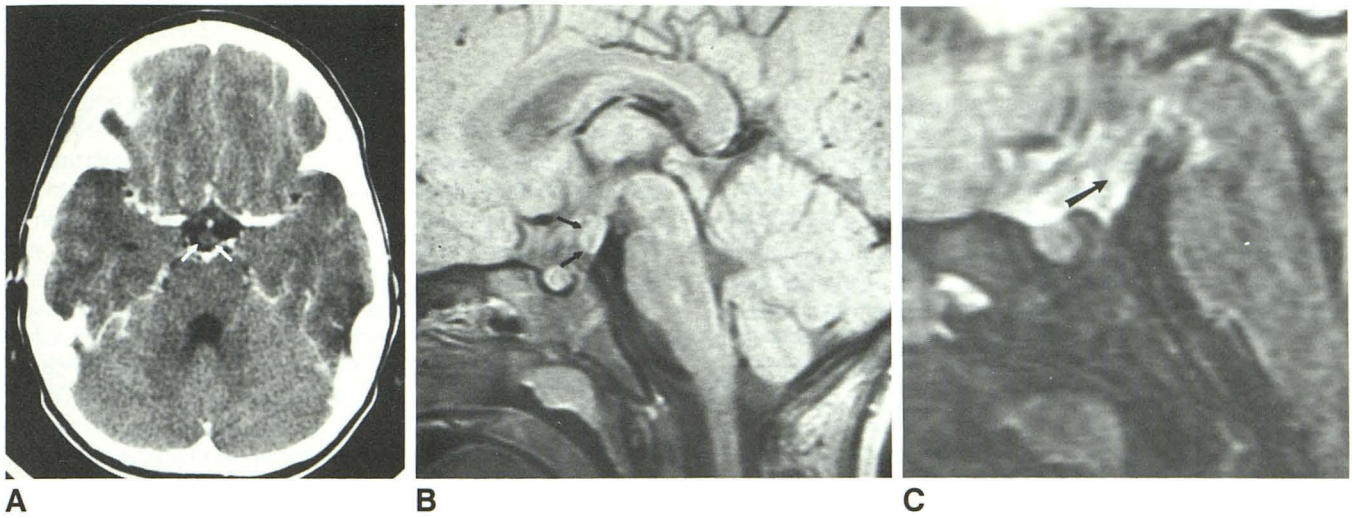

Fig. 1.—Case 1.

A, CT scan shows isointense, nonenhancing mass (*arrows*) lying between pituitary stalk and basilar artery.

B, On T1-weighted MR image, mass appears isodense (*arrows*). Its attachment to tuber cinereum and pedunculation into interpeduncular cistern is optimally demonstrated.

C, On T2-weighted MR image, there is difficulty in identifying the mass because of surrounding hyperintense CSF (*arrow*).

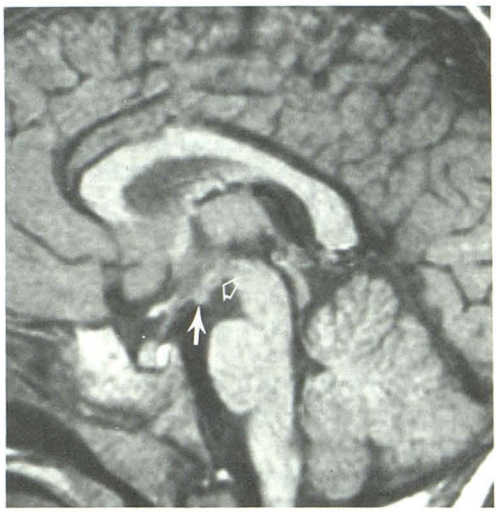

Fig. 2.—Case 3. T1-weighted MR image shows 2-mm isointense mass arising from tuber cinereum (*closed arrow*) lying anterior to mamillary bodies (*open arrow*). This mass was not identified on CT.

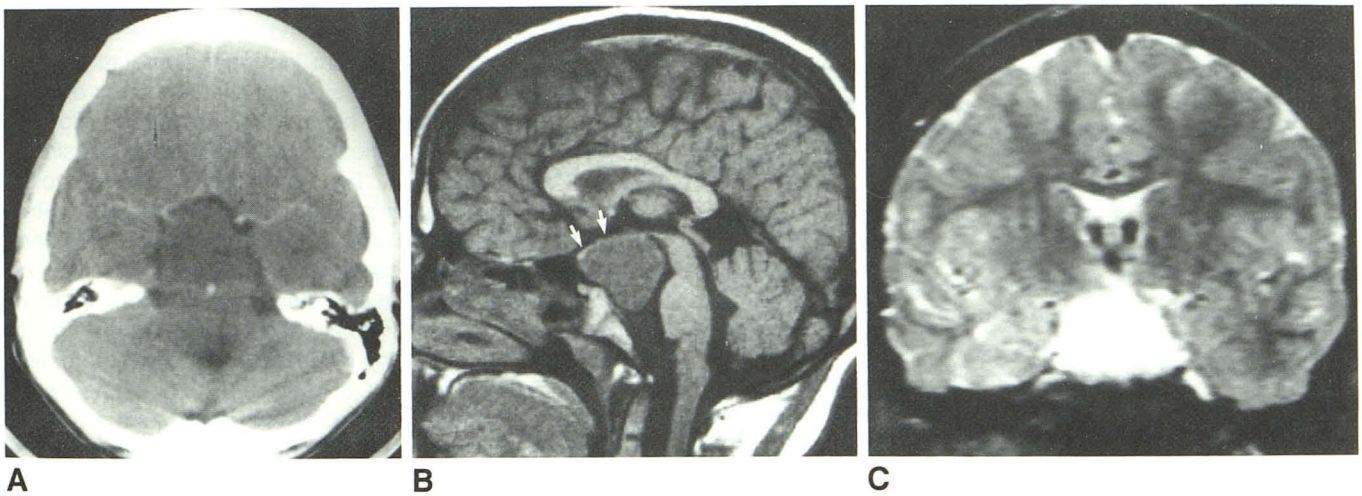

Fig. 3.—Case 4.

A, Contrast-enhanced CT scan shows mildly hypodense, nonenhancing mass occupying much of the suprasellar and interpeduncular cisterns.

B, Sagittal T1-weighted MR image, 550/17, shows that mass arises from floor of third ventricle (hypothalamus) and displaces pituitary stalk and optic chiasm (*arrows*) anteriorly.

C, On T2-weighted MR image, 2500/120, mass remains homogeneous but is hyperintense. A hypothalamic hamartoma was proved at biopsy. [Courtesy of Dr. James Simmons, Memphis, TN.]

but hyperintense relative to gray matter. The hyperintensity of small hamartomas depicted on T2-weighted images results in decreased conspicuity because of the inability to discern the mass from the hyperintensity of CSF in the surrounding interpeduncular cistern. Rarely, the signal intensity of large hamartomas on T2-weighted images is inhomogeneous because of necrosis, fat, or calcification. Thus, hamartomas are most easily visualized on T1- and intermediate-weighted images. As illustrated by case 3, MR imaging appears to be more sensitive than CT in the detection of small hamartomas. Owing to its capacity for orthogonal imaging, MR is more accurate in the identification and anatomic delineation of large hamartomas (case 4).

Both CT and MR are invaluable in differentiating hamartomas of the tuber cinereum from other suprasellar masses in children. Craniopharyngiomas are often cystic (85%), contain calcification (80%), and are more commonly located directly above or extending into the sella turcica. Even with involvement of the floor of the hypothalamus, isolation of a craniopharyngioma to the interpeduncular cistern is rare. Because of their solid and cystic components, craniopharyngiomas may show a variety of appearances on MR [21, 22]. In general, solid craniopharyngiomas are hypointense on T1- and hyperintense on T2-weighted images. In addition, the prolonged T1- and T2-relaxation of a craniopharyngioma cyst clearly distinguishes it from a solid hamartoma.

Optic chiasmatic gliomas are typically isodense or hypodense on CT and demonstrate marked contrast enhancement, mass effect, and, occasionally, calcification. Optic gliomas arise anterior or lateral to the tuber cinereum within the optic chiasm or optic tracts. On MR, they are most frequently hypointense on T1-weighted images, and hyperintense on intermediate- and T2-weighted sequences [23]. Enlargement of the optic nerves, optic chiasm, or optic tracts supports the diagnosis of an optic pathway glioma rather than a hamartoma. Intracranial germinomas are unusual in childhood, but may present as a suprasellar mass. On noncontrast CT, they appear isodense or hypodense, and enhance moderately after IV contrast administration. Although there is limited experience with suprasellar germinomas on MR, occasional reports have described them as homogeneous masses that are isointense on T1- and T2-weighted images [22]. A negative LHRH stimulation test, growth on sequential examinations, and lack of clinical signs of precocious puberty support the diagnosis of germinoma.

Hypothalamic gliomas and gangliogliomas appear inhomogeneous and demonstrate minimal to moderate contrast enhancement on CT [24, 25]. Cyst formation, necrosis, and calcification are more common features of gliomas, compared with hamartomas. Heterogeneous signal intensity and prolonged T1- and T2-relaxation times differentiate hypothalamic glioma or ganglioglioma from hamartoma. Difficulty may arise in distinguishing a sessile hamartoma from a mildly hypercellular, low-grade hypothalamic glioma by CT or MR. Such lesions may require careful sequential evaluation of growth of the lesion. Further, while the appearance of a pedunculated mass in the interpeduncular cistern is typical of a hamartoma, it would be atypical for a germinoma, hypothalamic glioma, or ganglioglioma.

As a result of current neuroradiologic imaging and recent elucidation of LHRH physiologic control of LH and FSH secretion, the management of patients with a hypothalamic hamartoma appears less controversial than in the past. Prior to the advent of high-resolution CT and MR, surgical exploration of interpeduncular lesions was undertaken for diagnosis and therapy. With current endocrinologic testing and noninvasive imaging, a diagnosis of hamartoma can be made with a high degree of probability. Despite a lack of pathologic proof in three of our cases (cases 1–3), their typical appearance on MR and a positive LHRH stimulation test were consistent with the diagnosis of hamartoma, and did not require surgical confirmation. Their diagnosis is supported by lack of interval growth for 6–12 months. We recommend neuroimaging by MR at frequent intervals, with referral for surgical intervention only if the lesion enlarges or undergoes change, suggesting malignancy. Currently, we reevaluate patients with a suspected hypothalamic hamartoma by MR at 6-month intervals for the first year and at yearly intervals thereafter. We have noted no change in size of the hamartomas while patients received hormonal suppressive therapy.

Surgery has an even more restricted role in the management of the physiologic characteristics of precocious puberty. Recent reports demonstrate poor correlation between the size of the hamartoma, extent of its removal, and postoperative resolution of symptoms [26]. A more physiologic approach to treatment with LHRH-agonist offers considerable promise [5]. For these reasons, current data do not support a primary role for surgery in the treatment of hypothalamic hamartomas. Surgery should be reserved for lesions uncharacteristic of hamartoma or large masses producing neurologic deficit. Finally, surgical intervention should be considered for patients in whom medical management fails to control neuroendocrine dysfunction [27, 28].

In summary, changes in indications for surgery of hamartomas of the tuber cinereum and successful medical management for neuroendocrine dysfunction emphasize the importance of precise neuroradiologic imaging in the diagnosis of this disorder. In a child with isosexual precocious puberty, a positive LHRH stimulation test and a homogeneous mass, arising within or extending from the tuber cinereum into the suprasellar cistern, with typical signal characteristics on MR, are virtually diagnostic of a hamartoma. Low-grade gliomas, gangliogliomas, and germinomas rarely may arise in a similar location, but can usually be distinguished from a typical hamartoma by differences in signal characteristics, a negative LHRH stimulation test, and by demonstration of interval growth on sequential examinations. Although CT may be helpful in differentiating atypical lesions, MR is more sensitive in identifying small hamartomas, defining the site of origin of the tumor, and in providing information regarding the extent of involvement by the mass. In addition to its greater sensitivity, the lack of ionizing radiation promotes MR as the imaging standard for sequential evaluation in this selected group of children.

ACKNOWLEDGMENTS

We thank Juanita Hunter and Patty Felix for preparing the manuscript, Laura Burton for editing it, and Robert Kaufman for reviewing it.

REFERENCES

1. Judge DM, Kulin HE, Page R, et al. Hypothalamic hamartoma: a source of luteinizing hormone-releasing factor in precocious puberty. *N Engl J Med* **1977**;296:7–10
2. Hochman HI, Judge DM, Reichlin S. Precocious puberty and hypothalamic hamartoma. *Pediatrics* **1981**;67:236–244
3. Zuniga OF, Tanner SM, Wild WO, Mosier D Jr. Hamartoma of CNS associated with precocious puberty. *Am J Dis Child* **1983**;137:127–133
4. Cacciari E, Frejaville E, Cicognani A, et al. How many cases of true precocious puberty in girls are idiopathic? *J Pediatr* **1983**;102:357–360
5. Styne DM, Harris DA, Egli CA, et al. Treatment of true precocious puberty with a potent luteinizing hormone-releasing factor agonist: effect of growth, sexual maturation, pelvic sonography, and the hypothalamic-pituitary-gonadal axis. *J Clin Endocrinol Metab* **1985**;61:142–151
6. Nakagawa N, Takahashi M, Kohrogi Y, Kodama T, Matsukado Y. Neuroradiologic findings of hypothalamic hamartoma with emphasis on computed tomography. *J Comput Tomogr* **1986**;10:77–83
7. Breningstall GN. Gelastic seizures, precocious puberty, and hypothalamic hamartoma. *Neurology* **1985**;35:1180–1183
8. Rieth KG, Comite F, Dwyer AJ, et al. CT of cerebral abnormalities in precocious puberty. *AJNR* **1987**;8:283–290
9. Hahn FJ, Leibrock LG, Huseman CA, Makos MM. The MR appearance of hypothalamic hamartoma. *Neuroradiology* **1988**;20:65:68
10. Diebler C, Ponsot G. Hamartomas of the tuber cinereum. *Neuroradiology* **1983**;25:93–101
11. Lin S-R, Bryson MM, Gobien RP, et al. Radiologic findings of hamartomas of the tuber cinereum and hypothalamus. *Radiology* **1978**;127:697–703
12. Mori K, Handa H, Takeuchi J, et al. Hypothalamic hamartoma. *J Comput Assist Tomogr* **1981**;5:519–521
13. Berkovic SF, Andermann F, Melanson D, et al. Hypothalamic hamartomas and ictal laughter: evolution of a characteristic epileptic syndrome and diagnostic value of magnetic resonance imaging. *Ann Neurol* **1988**;23:429–439
14. Shaul PW, Towbin RB, Chernausek SD. Precocious puberty following severe head trauma. *Am J Dis Child* **1985**;139:467–469
15. Pescovitz OH, Comite F, Hench K, et al. The NIH experience with precocious puberty: diagnostic subgroups and response to short-term luteinizing hormone-releasing hormone analog therapy. *J Pediatr* **1986**;108:47–54
16. List CF, Dowman CE, Bagchi BK. Posterior hypothalamic hamartomas and gangliogliomas causing precocious puberty. *Neurology* **1958**;8:164–174
17. Lyon AJ, DeBruyn R, Grant DB. Isosexual precocious puberty in girls. *Acta Paediatr Scand* **1985**;74:950–955
18. Richter RB. True hamartoma of the hypothalamus associated with pubertas praecox. *J Neuropathol Exp Neurol* **1951**;10:368–383
19. Kortman KE, Bradley WG Jr. Supratentorial neoplasms. In: Stark DD, Bradley WG Jr, eds. *Magnetic resonance imaging.* St. Louis: Mosby, **1988**:410–411
20. Weinberger LM, Grant FC. Precocious puberty and tumors of the hypothalamus. *Arch Intern Med* **1941**;67:762–792
21. Pusey E, Kortman KE, Flannigan BD, et al. MR of craniopharyngiomas: tumor delineation and characterization. *AJNR* **1987**;8:439–444, *AJR* **1987**;149:383–388
22. Brant-Zawadzki M, Kelly W. Brain tumors. In: Brant-Zawadzki M, Norman D, eds. *Magnetic resonance imaging of the central nervous system.* New York: Raven, **1987**:168–170, 172
23. Albert A, Lee BCP, Saint-Louis L, et al. MRI of optic chiasm and optic pathways. *AJNR* **1986**;7:255–258
24. Yamada H. Brain tumors. In: Yamada H, ed. *Pediatric cranial computed tomography.* New York: Igaku-Shoin, **1983**:243
25. Nass R, Whelan MA. Gangliogliomas. *Neuroradiology* **1981**;22:67–71
26. Sata M, Vshio Y, Arita N, Mogami H. Hypothalamic hamartoma: report of two cases. *Neurosurgery* **1985**;16:198–206
27. Keyuma Y, Kato E, Sekido K, Kuwubara T. Hypothalamic hamartoma successfully treated by operation. *J Neurosurg* **1985**;62:288–290
28. Price RA, Lee PA, Albright AL, et al. Treatment of sexual precocity by removal of a luteinizing hormone-releasing hormone secreting hamartoma. *JAMA* **1984**;251(17):2247–2249