Successful resection of a hypothalamic hamartoma and a Rathke cleft cyst

Case report

YU-TZE NG, M.D., F.R.A.C.P., JOHN F. KERRIGAN, M.D., ERIN C. PRENGER, D.O., WILLIAM L. WHITE, M.D., AND HAROLD L. REKATE, M.D.

Departments of Pediatrics, Neurology, Neuroradiology, and Neurosurgery, Barrow Neurological Institute, St. Joseph’s Hospital, Phoenix, Arizona

The authors report the case of a 12-year-old girl with Pallister–Hall syndrome, long-standing refractory, symptomatic epilepsy, mental retardation, and panhypopituitarism in whom two rare, deep midline lesions were detected. She underwent successful transsphenoidal resection of the Rathke cleft cyst and transcallosal resection of the hypothalamic hamartoma within a 4-day period without complications. Neuropathological studies confirmed the neuroimaging diagnoses for the two lesions. The patient has been seizure free for 6 months postoperatively.

KEY WORDS • hypothalamic hamartoma • transcallosal resection • Rathke cleft cyst • Pallister–Hall syndrome • pediatric neurosurgery

HAMARTHOMAS of the tuber cinereum are congenital malformations consisting of tumorlike masses of neuronal tissue in an ectopic location.1 Hypothalamic hamartomas are estimated to occur in approximately one in 1 million births. They often result in a mixed seizure disorder (typified by gelastic or laughing seizures), mental retardation, precocious puberty, and behavioral problems. Pallister–Hall syndrome is a rare disorder that can occur either spontaneously or be inherited in an autosomal-dominant fashion.6 It is associated with polydactyly, midline defects (including dysmorphic facial features), hypothalamic hamartomas, and imperforate anus.6 Rathke cleft cysts are congenital, nonneoplastic sellar and suprasellar cysts derived from the remnants of the Rathke pouch that is found during routine autopsy examinations in 13 to 22% of cases.2 The incidence of symptomatic Rathke cleft cysts is clearly lower than that of asymptomatic Rathke cleft cyst. The most common symptoms are headache, visual disturbances, and endocrinological symptoms.3,4,5

Case Report

History and Examination. This 12-year-old girl with Pallister–Hall syndrome, including positive genetic testing for associated Gli3 mutation,7 presented with a history of refractory, symptomatic epilepsy beginning at 3 months of age. She was experiencing frequent gelastic (3–50 times per day) and complex partial seizures and infrequent generalized tonic–clonic and drop seizures. Her seizures were poorly controlled with the use of three antiepileptic drugs; five other antiepileptic drugs had failed to be beneficial previously. She also had a history of mental retardation, behavioral problems, panhypopituitarism, precocious puberty, imperforate anus, and polydactyly. The patient’s family history was significant—a younger brother also suffered from Pallister–Hall syndrome (although neither parent demonstrated any phenotypic features of Pallister–Hall syndrome) and hypothalamic hamartoma without a Rathke cleft cyst.

The patient underwent brain MR imaging studies that demonstrated two prominent midline lesions—a hypothalamic hamartoma and a Rathke cleft cyst just anterior to it (Fig. 1).

Operation. A frameless stereotactic transsphenoidal microsurgical excision of the Rathke cleft cyst was performed through the right nostril. The cyst contained a thick, clear, mucoid liquid and a few opaque chunks of amorphous solid material. There was no cerebrospinal fluid leakage. The sella turcica was left open as a potential drain for possible cyst recurrence. No apparent residue of the Rathke cleft cyst was detected on the postoperative MR image.

Three days later, the patient underwent transcallosal resection of the hypothalamic hamartoma using the approach
originally described by Rosenfeld, et al., with some modifications. Using a frameless stereotactic guidance system, an approach approximately 2 cm in length was made in the anterior portion of the corpus callosum. The two leaves of the septum pellucidum were separated, providing access to the third ventricle where the hamartoma could be seen bulging from the floor. The hamartoma arose from the lateral wall of the left side of the third ventricle and was visible as a distinct, light-gray mass. The hamartoma was removed using a combination of pituitary rongeurs and an ultrasonic aspirator. At the end of the procedure, the pial surface of the interpeduncular cistern was visible. An extra-ventricular drain tube that was left in situ was removed a few days later. Figure 2 demonstrates the sites of the resected lesions on postoperative brain MR images.

Neuropathological Studies. The first resected lesion contained acellular proteinaceous debris consistent with a Rathke cleft cyst. The second lesion demonstrated the features that typically confirm the diagnosis of hypothalamic hamartoma—diffusely distributed normal-appearing neurons of various sizes admixed with variably prominent astrocytes.

Postoperative Course. The patient’s recovery was uncomplicated and diabetes insipidus did not develop. She experienced no seizures postoperatively and at the 6-month follow-up examination remained seizure free.

Discussion

We report on the successful resection of two rare, deep midline brain lesions in a unique case. Although we are unaware of an embryological basis for the occurrence of these two rare lesions in one patient, it is probable that the association of Pallister–Hall syndrome with midline defects contributed to this clinical phenotype. In three separate reports from Japan, however, authors describe large left temporosylvian arachnoid cysts associated with hypothalamic hamartomas. From the findings of these reports one might infer that the two lesions in the present case are genetic in origin.

The transsphenoidal route of resection of Rathke cleft cysts is the most widely used approach. Resection of hypothalamic hamartomas was previously considered to be too difficult technically and also unlikely to influence the seizure outcome. More recently, evidence that the hypothalamic hamartoma itself is intrinsically epileptogenic and responsible for the mixed seizure disorder has been increasing; that surgical removal of the lesion can lead to prolonged seizure remission further supports this position. Various therapies have been tried, with limited success to control the seizures. These have included vagal nerve stimulation, gamma knife surgery (probably the most successful), stereotactic destruction of the lesion by using radiofrequency, and even therapy with a gonadotropin-releasing hormone analog.

Multiple surgical approaches and techniques have been used and described in the resection of hypothalamic hamartomas, including subfrontal, transsylvian, subtemporal, frontotemporal, perialar craniotomy, interhemispheric, and transcallosal approaches. Many of these methods are associated with high complication rates including capsular and thalamic infarcts (with associated hemiparesis), third cranial nerve palsies, and memory loss. Moreover, these procedures often do not result in adequate resection of the tumor with persisting seizure activity.

We have performed many resections of hypothalamic hamartomas via orbitozygomatic approaches and have found that the transcallosal approach is much more likely to yield positive results in seizure management and behavioral improvement. Although we always attempt to remove as much of the hamartoma as possible, we believe that it is the disconnection of the hamartoma from the hypothalamus that is crucial, as evidenced by this patient’s positive outcome despite incomplete removal of the le-
Disconnection is difficult to accomplish using an approach from below such as the subfrontal approach. It would have been difficult or impossible to access the Rathke cleft cyst via the trans–third ventricle approach and impossible to disconnect the hamartoma via the trans-sphenoidal approach. After much thought and discussion, the decision was made to remove the two lesions separately. The main risks involved are loss of short-term memory resulting from damage to the fornices or direct injury to the hypothalamus, which can cause appetite changes or diabetes insipidus.

Rosenfeld, et al., described excellent results in several patients in whom resection of hypothalamic hamartomas was performed via a transcallosal–interforniceal route to the third ventricle by using a microsurgical technique and frameless stereotaxy. We present a case of successful transcallosal resection of a hypothalamic hamartoma and provide further support that the transcallosal–interforniceal route of resection of such tumors is effective, safe, and possibly the best approach for resection of this lesion.

References

Figure 2. Upper: A T2-weighted MR image demonstrating the two resected lesions (black arrow) and the optic chiasm (white arrow). Lower: Coronal T2-weighted MR image revealing the partially resected hypothalamic hamartoma.