The Turkish Journal of Pediatrics 1996; 38: 533-536

HYPOTHALAMIC HAMARTOMA WITH GELASTIC EPILEPSY, PRECOCIOUS PUBERTY AND POLYDACTYLY*

*Güzide Turanlı MD***, *Müjgan Aynacı MD****, *Dilek Yalnızoğlu MD*****
*Yavuz Renda MD******

SUMMARY: Turanlı G, Aynacı M, Yalnızoğlu D, Renda Y. (Neurology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Hypothalamic hamartoma with gelastic epilepsy, precocious puberty and polydactyly. Turk J Pediatr 1996; 38: 533-536.

An entity including gelastic epilepsy, precocious puberty, polydactyly and a hypothalamic hamartoma type IIa is described in a 16-year-old female patient. Polydactyly was detected at birth, she developed precocious puberty at four years of age, and gelastic epilepsy was diagnosed at age seven. The precocious puberty was successfully treated medically and her treatment was discontinued at the age of 10 years, but the gelastic seizures were difficult to control. When the patient was 11 years old, MRI revealed a hypothalamic hamartoma. The combination of these four features is very rare in the literature. *Key words: gelastic epilepsy, hypothalamic hamartoma, precocious puberty, polydactyly.*

Primary tumors of the hypothalamus are less common than other primary, intracranial tumors in childhood[1]. Hamartomas are non-neoplastic malformations and constitute most hypothalamic tumors[2]. Although various associations between hypothalamic hamartoma and gelastic epilepsy have been reported in the literature, the association of hypothalamic hamartoma, gelastic epilepsy, precocious puberty and skeletal abnormalities is very rare[1, 3, 4]. The first case in which all four features have been described was reported in 1994[1]. Here too we present a girl with hypothalamic hamartoma, gelastic epilepsy, precocious puberty and polydactyly.

Case Report

The patient was first admitted to Hacettepe University's Department of Pediatric Endocrinology with symptoms of vaginal bleeding and breast development at four years of age. She was diagnosed with isosexual precocious puberty after laboratory investigations were completed, and was given cyprateron acetate therapy. Treatment was discontinued at the age of 10 years after ensuring that puberty was progressing normally.

* From the Neurology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.
** Pediatric Neurologist, Hacettepe University Faculty of Medicine.
*** Assistant Professor of Pediatrics, Karadeniz Technical University Faculty of Medicine, Trabzon.
**** Fellow in Pediatric Neurology, Hacettepe University Faculty of Medicine.
***** Professor of Pediatrics, Hacettepe University Faculty of Medicine.

At 12 years of age she was admitted to Hacettepe University's Department of Pediatric Neurology with gelastic seizures at a frequency of three to four episodes per day. Since the age of seven she had been experiencing uncontrollable laughing attacks lasting one to two minutes followed by urinary incontinence every two to three weeks. She also had generalized tonic-clonic seizures lastings one to two minutes which had started two years before admission. Aside from mild mental retardation and polydactyly, her physical and neurological examinations were normal on admission. EEG revealed normal background rhythm with left centro-temporo-occipital spike and slow-wave discharges and secondary generalization. Cranial tomography was normal. She was put on carbamazepine therapy, but after three months of treatment no improvement was observed in her seizures. Her magnetic resonance imaging (MRI) revealed a mass in the tuber cinereum. T_1-weighted MRIs demonstrated a hypo-intense hypothalamic mass, 2 cm in diameter, bulging into the floor of the third ventricle, with contact with the mamillary bodies. This lesion was seen observed to be hyperintense on T2-weighted images. There was no abnormality in her cerebral angiography.

Surgery for cranial mass resection was recommended but refused by her family. After a four-year interval with anti-epileptic treatment, she returned to our clinic. At present she is 16 years old and has been receiving carbamazepine therapy for four years, but she experiences one to three laughter episodes every two weeks.

Discussion

Hypothalamic hamartomas are defined as heterotopic and hyperplastic tissue resembling gray matter in various sizes[5]. They usually originate from the tuber cinereum and mamillary bodies[6,7]. They are often associated with cerebral and extracerebral congenital abnormalities such as microgyria, cysts, callosal defects, polydactyly, facial abnormalities and heart defects[8,9]. Nurbhai et al[10] reported an infant with skeletal abnormalities including syndactyly which seems to be the most common skeletal defect occurring with hypothalamic hamartomas. Clinically, hypothalamic hamartomas may be accompanied with precocious puberty, gelastic epilepsy and other type of seizures[7]. MRI is the most sensitive method for detecting hypothalamic hamartomas[11]. In our case, the lesion did not appear on cranial tomography but was detected on MRI.

Abnormal neuronal connections or independent endocrine activity of hypothalamic hamartomas may result in precocious puberty[12-14]. The pathogenesis of gelastic epilepsy has been described as mechanical compression the mamillary bodies and/or pathological neuronal connections to the hypothalamus and limbic system[2].

Uncontrollable pathological laughter may result from several causes, such as bilateral cortico-bulbar lesions, multiple sclerosis, amyotrophic lateral sclerosis, bilateral frontal lobe disease, hysterical laughter and hebephrenic schizophrenia.

The criteria for gelastic epilepsy were described by Gascon and Lombroso[15] in 1971. Thesė criteria are: stereotypical recurrence, the absence of external precipitating factors, concomitance of other epileptic manifestations, the presence of ictal and interictal EEG abnormalities, and the absence of other causes of pathological laughter. All of these criteria were also present in our patient.

Valdueza et al.[2] classified hypothalamic hamartomas into two groups and types Ia, Ib and IIa, IIb according to their localizations, type of attachment, extent of hypothalamic displacement and size. Type Ia and Ib lesions are characteristically medium in size, either asymptomatic or associated with precocious puberty. There is no hypothalamic displacement. Type Ia originates from the tuber cinereum, and Ib from the mamillary body.

Type IIa hamartomas are usually larger than 1.5 cm, their attachment is sessile, and they are localized on the tuber cinereum or mamillary body. They result in slight hypothalamic displacement. Patients usually suffer from mixed seizures (gelastic, other seizures and memory disturbances). Our patient was classified as type IIa with the presence of generalized tonic-clonic and gelastic seizures and the absence of hypothalamic displacement on MRI. In type IIb hypothalamic displacement is marked. The prognosis is poor and control of seizures is difficult in these patients. Precocious puberty can be managed medically with a good effect[1]. According to Valdueza et al.[2], the surgical approach is a realistic alternative in certain cases, including large and broad-based type IIb hamartomas associated with gelastic epilepsy and behavioral disorders. Medical therapy controlled precocious puberty in our patient but the treatment was unable to control her gelastic seizures.

REFERENCES

1. Minns RA, Stirling HF, Wu FC. Hypothalamic hamartoma with skeletal malformations, gelastic epilepsy and precocious puberty. Dev Med Child Neurol 1994; 36: 173-182.
2. Valdueza JM, Cristante L, Dammann O, et al. Hypothalamic hamartomas: with special reference to gelastic epilepsy and surgery. Neurosurgery 1994; 34: 949-958.
3. Richter RB. True hamartoma of the hypothalamus associated with pubertas praecox. J Neuropathol Exp Neuropathol Exp Neurol 1951; 10: 368-383.
4. Williams M, Schutt W, Savage D. Epileptic laughter with precocious puberty. Arch Dis Child 1978; 53: 965-966.
5. Russell DS, Rubinstein LJ. Pathology of Tumours of the Nervous System (5th ed). Baltimore: Williams-Wilkins; 1989: 710-714.
6. Takeuchi J, Hande H, Miki Y, et al. Precocious puberty due to a hypothalamic hamartoma. Surg Neurol 1979; 11: 456-460.
7. Zuniga OF, Tanner SM, Wild WO, Mosier HDJr. Hamartoma of CNS associated with precocious puberty. Am J Dis Child 1983; 137: 127-138.
8. Schmidt E, Hallervorden J, Spotz H. Die enitstchung der hamartoma is hypothalamus mit und ohne pubertas praecox. Dtsch Z Nervenheilk 1958; 177: 253-262.

9. Somer M, Lindahl E, Perheentupa J. Precocious puberty associated with oral-facial-digital syndrome type I. Acta Paediatr Scand 1986; 75: 672-675.
10. Nurbhai MA, Tomlinson BE, Lorigan-Forsythe B. Infantile hypothalamic hamartoma with multiple congenital abnormalities. Neuropathol Appl Neurobiol 1985; 11: 61-70.
11. Marliani AF, Tampieri D, Melancon D, et al. Magnetic resonance imaging of hypothalamic hamartomas causing gelastic epilepsy. Canadian Ass Radiologist J 1991; 42: 335-339.
12. Marcuse PM, Burger RA, Salmon GW. Hamartoma of the hypothalamus. Report of two cases with associated developmental defects. J Pediatr 1953; 43: 301-307.
13. Balagura S, Shulman K, Sobel EH. Precocious puberty of cerebral origin. Surg Neurol 1979; 111: 315-326.
14. Culler FL, James HE, Simon ML, Jones KL. Identification of gonadotropin-releasing hormone in neurons of a hypothalamic hamartoma in a boy with precocious puberty. Neurosurgery 1985; 17: 408-412.
15. Gascon GG, Lombroso CT. Epileptic (gelastic) laughter. Epilepsia 1971; 12: 63-76.