Posterior Hypothalamic Astrocytoma Mimicking Hamartoma, Causing Precocious Puberty.

Kenji Fujieda, Nozumi Shinohara, Jun Nakae, and Toshihiro Tajima.

Department of Pediatrics, Hokkaido University School of Medicine, Sapporo, Japan

Abstract: We describe the case of a girl with precocious puberty caused by a posterior hypothalamic astrocytoma. She showed precocious puberty and laughing-crying episodes at one year of age without other neurological signs. CT depicted an isodense mass $2 \times 2.5 \times 2.5$ cm with calcification in the suprasellar region. This was not enhanced with contrast medium. MRI also disclosed that the mass originated from the posterior hypothalamus and compressed the midbrain and thalamus. T1 image showed isointensity, but the T2 image was high intensity with the homogeneous mass and was not enhanced with Gd-DTPA. These clinical and radiological findings were similar to those of a hypothalamic hamartoma, but histological examination verified an astrocytoma. If the configuration of an intracerebral mass is not typical of hamartoma, biopsy is recommended.

Key words: Precocious puberty, hypothalamic astrocytoma, hamartoma.

Introduction

True isosexual precocious puberty occurs as a result of the premature activation of the hypothalamic-pituitary-gonadal axis that leads to increased circulating levels of gonadotropins and sex steroids. The differential diagnosis includes cerebral and idiopathic categories. This differentiation, which cannot be made endocrinologically due to similarities in pituitary and sex steroid levels, may be facilitated by high-resolution CT and MRI (1-4). Cerebral causes of precocious puberty

include hamartoma, glioma, astrocytomas of the hypothalamic region, tumors of the pineal region, dysgerminoma, optic glioma and neurofibromatosis. These tumors have specific characteristics on CT and MR imaging so that biopsy is not required (4-6). Of these tumors, hypothalamic hamartoma is the most common and is being diagnosed more frequently. It is benign and maybe treated conservatively (7,8). Therefore, the differentiation of hamartomas from other tumors is important.

We describe the case of a one year old girl with precocious puberty who had a large mass in the posterior hypothalamus. The clinical and radiological findings were compatible with a hypothalamic hamartoma except for the size of the mass and the presence of calcification. However, histological examination verified the diagnosis of astrocytoma. The

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Correspondence: Kenji Fujieda, Department of Pediatrics, Hokkaido University School of Medicine, N-15, W-7, Kita-Ku, Sapporo, Japan 060

clinical, endocrinological and CT/MRI findings of this case are discussed in relation to hypothalamic hamartoma.

Case report

The patient was a girl born after a normal pregnancy by spontaneous delivery. At birth her length was 45cm and weight was 2280gr. There was a clear vaginal discharge. At the age of 50 days when she had an operation for an inguinal hernia, cystic changes of the ovaries were noted. From seven months of age she had a recurrent bloody vaginal discharge. Breast development was recognized from one year of age when her height and weight increased noticeably. There were several laughing-crying episodes of short duration. At the age of 2 years she attended the pediatric endocrine clinic of Hokkaido University Hospital because of precocious sexual development. At the time of admission, her height was 92cm (+2SD for Japanese), weight was 13.7kg and head circumference was 48.5cm. The breasts were Tanner stage III and pubic hair was stage I. Bone age was estimated to be 5 years by the G-P atlas. No neurological or ophthalmological abnormalities were noted. Hematological and biochemical examinations showed no abnormalities. Tumor markers (β hCG, CEA, AFP) were negative. Endocrine examination showed the basal LH level was 4.1mIU/ml and the LHRH stimulated LH level was 79.2mIU/ml at 60 minutes. The basal FSH level was 7.9mIU/ml and the LHRH-stimulated FSH level at 60 minutes was 39.1mIU/ml. The prolactin response to TRH stimulation was exaggerated. GH, TSH and ACTH did not show abnormal responses. Serum estradiol was 32pg/ml. The plasma IGF- I level was 3.64mIU/ml.

Imaging

Brain CT showed an isodense mass 2×2.5×2.5cm with calcification in the suprasellar

region. This mass was not enhanced with contrast medium. MRI showed that the mass originated in the tuber cinereum, and that the mammillary body was slightly compressing the midbrain and thalamus. The pituitary stalk and optic nerve were identified in the anterior portion of the mass. Coronal imaging of the MRI showed that the mass originated in the left hypothalamic area, decompressing the tuber cinereum. The T1 image was isointense, but the T2 image was high intensity with the homogeneous mass. This image was also not enhanced by Gd-DTPA (Fig. 1).

Biopsy findings

Because of the size of tumor and the presence of the calcification, biopsy was performed by a right fronto-temporal craniotomy. The surface of the tumor looked like brain itself and its internal structure consisted of grey matter. On histological examina-

Figure 1 (a) CT with contrast medium

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Figure 1 (b) MRI with Gd-DTPA; sagittal image

Figure 1 (c) MRI with Gd-DTPA; coronal image

Figure 1. CT with contrast medium (a), MRI with Gd-DTPA (b): sagittal image and (c): coronal image. CT showing isodense mass $2 \times 2.5 \times 2.5$ cm with calcification in the suprasellar region, not enhanced with contrast medium. In MRI with Gd-DTPA the sagittal image shows that the mass originates from the tuber cinereum, with the mammillary body slightly compressing the midbrain and thalamus. Coronal image shows the mass originates from the left hypothalamic area, compressing the tuber cinereum. T1 image is isointensity, but T2 image is high intensity with the homogeneous mass. This image is also not enhanced by Gd-DTPA.

Figure 2. Histology of the biopsied specimen. No ganglion cells are recognized. Glial cells show atypia of nuclei and increased cellularity. This indicates that the astrocytoma is grade II by Kernohan classification.

tion no ganglion cells were recognized. Glial cells showed slight atypia of the nuclei and increased cellularity. These findings indicated that the mass was an astrocytoma grade II by Kernohan classification (Fig. 2).

Clinical course

Because most of the tumor was resected at the time of biopsy, we did not perform a further operation for total resection. The tumor was observed for 4 years by biannual MRI scans and no regrowth was seen. The precocious puberty was treated with LHRH analogue and has been well controlled.

Discussion

Idiopathic precocious puberty is common in girls and is likely to be due to intra-cerebral lesions even in the girls presenting earlier than the age of 3 years (3,9). Of such tumors hypothalamic hamartoma is the most common and is being diagnosed more frequently. Hypothalamic astrocytoma also occurs but is less common than optic nerve glioma (10,11). Precocious puberty due to optic nerve glioma is usually associated with the diencephalic syndrome. Hamartoma of the CNS is a congenital malformation characterized by heterotopic hyperplastic tissue that is usually encountered at the base of the brain, the interpeduncular cistern or within the hypothalamus in proximity to the tuber cinereum and mamillary bodies. These tumors cannot be treated by surgical or radiological means (7,8). In assessing precocious puberty associated with CNS tumors, it is first necessary to exclude these hamartomas. Precocious puberty caused by hamartomas tends to occur early (2.8 years on average), contrasting with the much later onset in astrocytoma. Other clinical findings are gelastic seizures, absence seizures, behavioral disturbances and mental retardation (7). The earlier onset of puberty and the presence of the laughing-crying episodes in the present case are also characteristic of the hamartomas. It is rare for a hypothalamic astrocytoma to be associated with precocious puberty before one year of age. It appears that the astrocytoma in this patient might be congenital, because of the earlier onset of puberty (12).

The characteristic image of a hypothalamic hamartoma on CT scan is reported as isodense to the grey matter with and without injection of contrast medium (4,5). Furthermore MR imaging, which is diagnostically superior to CT, usually depicts hamartomas as normal to low-intensity by T1 images and a high signal intensity area on T2-weighted images (5,6). In the present case CT scan showed isodense and MRI scan depicted the

lesion as isointensity by T1 image and high intensity by T2 image. This mass was not enhanced with contrast medium on CT scan or with Gd-DTPA on MRI scan. In hypothalamic astrocytoma, contrast enhancement around areas of low attenuation is usually observed. The location of the mass in this case was in the posterior hypothalamus, originating from the tuber cinereum and mamillary body. These findings are compatible with those of a hamartoma. Hamartomas range in size from several millimeters to several centimeters, but are usually smaller than 2cm. Rarely, calcifications may be found within hamartomas (4). These unusual features of the large size of the tumor and calcification led us to perform biopsy of the mass to confirm its nature.

The association of precocious puberty and CNS tumors, together with their propensity to involve the hypothalamic-pituitary axis, suggests a causal relationship. It has previously been reported that hypothalamic hamartomas contain GnRH secretory granules (13), but they are not found in all cases. Some other mechanism, such as dysinhibition of the inhibitory signals of the hypothalamus, might operate in the manifestation of precocious puberty. The location of the tumor and the similarity of the clinical findings observed in this astrocytoma, suggest that hamartomas and astrocytomas arising from the posterior hypothalamus share the same pathophysiological mechanism for inducing precocious puberty.

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