

Precocious Puberty due to Human Chorionic Gonadotropin-Secreting Pineal Tumor

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We present a 9-year-old boy with central precocious puberty and hydrocephalus caused by a human chorionic gonadotropin (β -hCG) secreting pineal tumor. High levels of β -hCG in the serum and cerebrospinal fluid were observed in this patient. The patient received radiotherapy and chemotherapy without surgical intervention. Subsequently, significant tumor regression was observed and the serum β -hCG level normalized. There was no evidence of tumor recurrence at follow-up one year after treatment. The role of tissue biopsy to establish a diagnosis in pineal germ cell tumors remains controversial because it can be a difficult procedure and may be dangerous, causing severe complications. In this patient, the elevated β -hCG level indicated the presence of a tumor and was considered sufficient evidence to warrant initiating treatment. (*Chang Gung Med J* 2006;29:198-202)

Key words: β -human chorionic gonadotropin, pineal tumor, precocious puberty, parinaud syndrome.

INTRODUCTION

Tumors of the pineal region account for 0.4% to 1% of all primary tumors of the central nervous system; pineal tumors account for about 3% to 8% of brain tumors in the pediatric age group.⁽¹⁾ Most pineal tumors are germ cell tumors, pineal parenchymal tumors or astrocytomas, with germ cell tumors being the most common. In a Japanese series of 153 cases of intracranial germ cell tumors, 41% were germinomas, 20% teratomas, 32% mixed germ cell tumors, 3% embryonal carcinomas, 2% yolk sac tumors and 2% choriocarcinomas.⁽²⁾ An elevated tumor marker has been used to indicate the tumor component of pineal tumors, either non-germinomatous germ cell tumors (NGGCTs) or malignant mixed germ cell tumors.⁽¹⁻⁴⁾

We report our experience in treating a 9-year-old boy who had a beta human chorionic gonadotropin (β -hCG) secreting pineal region tumor and central precocious puberty (PP). He was treated with chemotherapy and radiotherapy without surgical intervention.

CASE REPORT

This 9-year-old boy was brought to our hospital because of an enlarged penis and testes, appearance of pubic hair, low-pitched voice and acneiform eruption on his face and anterior chest for about three months. Tracing back his history, he was taken to a local hospital because of severe headache and diplopia. A computed tomographic scan showed hydrocephalus and a lesion in the pineal region; a

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ventriculo-peritoneal (VP) shunt was inserted. Three days later, he was transferred to our hospital because of recurrent headache. On admission, he had clear consciousness but was irritable. Many acne lesions were present on his face and chest. His height was 140 cm (90-97th percentile) and body weight was 40 kg (> 97th percentile). He had an enlarged penis (4-5 cm in length) and testes (6 ml in volume) with an amount of pubic hair (Tanner stage III). Blood pressure was 140/67 mmHg and heart rate was 92 beat per minute. On neurological examination, he was unable to gaze upward and his pupils reacted poorly, indicating Parinaud syndrome. His headache immediately subsided after VP shunt revision. The laboratory data showed high β -hCG levels in both the cerebrospinal fluid (1041 mIU/ml) and serum (187 mIU/ml). The cerebrospinal fluid was red and turbid with white blood cells $2/\text{mm}^3$, red blood cells $84010/\text{mm}^3$, glucose 52 mg/dL, total protein 319.5 mg/dL, lactate 13.8 mg/dL and chloride 52 mEq/L. The serum levels of testosterone and cortisol were 5.17 mIU/ml and 3.78 mIU/ml. Serum levels of follicle stimulating hormone (FSH) = 7.13 mIU/ml, luteinizing hormone (LH) = 2.92 mIU/ml, alpha fetoprotein (α -FP) = 1.84 mIU/ml and adrenocorticotrophic hormone (ACTH) = 12.7 mIU/ml. Bone age was increased and estimated as 13.5 years. The Magnetic Resonance Imaging (MRI) studies showed an infiltrating mass in the pineal region, about 32 x 16 mm in diameter (Figs. 1 and 2). With this evidence of a β -hCG secreting germ cell tumor, chemotherapy was begun. JEB regimen (carboplatin 500 mg/m²/day on day 1, bleomycin 15 IU/m²/day on day 2, etoposide 120 mg/m²/day on days 1-3) was administered without undergoing tumor excision or biopsy. After two courses of chemotherapy, the serum β -hCG levels fell to within normal range, and the follow-up MRI showed tumor regression to about 8 mm in diameter (Fig. 3). The patient received two further courses of chemotherapy and subsequent radiotherapy, with a total dose of 5400 cGy to the pineal tumor site. The tumor disappeared completely six months after initiation of chemotherapy (Figs. 4 and 5). The patient received a total of six courses of chemotherapy. On follow-up examinations, his mental status was normal and Parinaud syndrome had disappeared. The signs of PP were stationary. At follow-up one year later, there was no evidence of tumor recurrence.

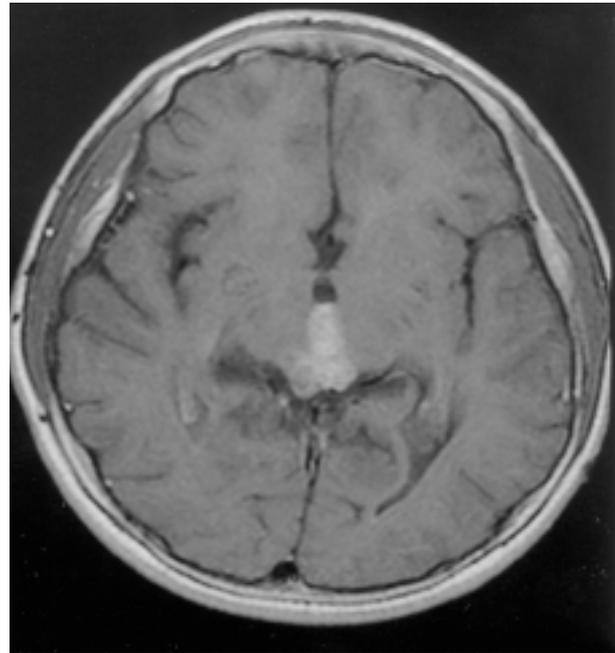


Fig. 1 Pretreatment MRI axial view (T1 with contrast) shows infiltrating mass in the pineal region, 32 x 16 mm in size.

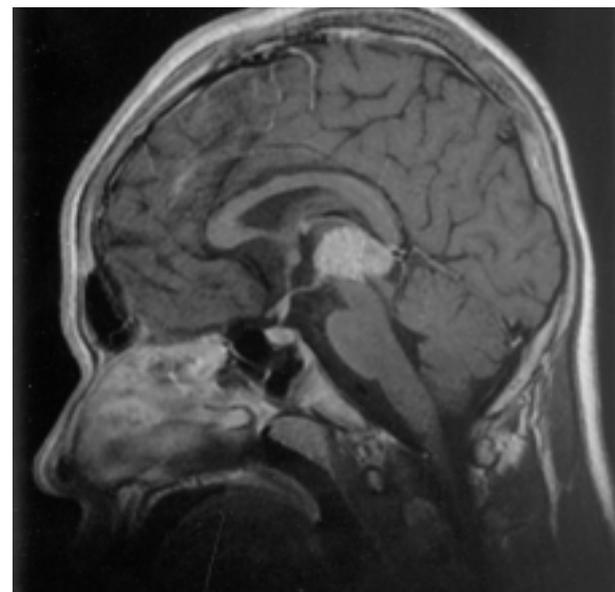


Fig. 2 Pretreatment MRI sagittal view (T1 with contrast) shows infiltrating mass in the pineal region.

DISCUSSION

PP can be caused by inhibitory or stimulatory factors involving the hypothalamic-pituitary axis.

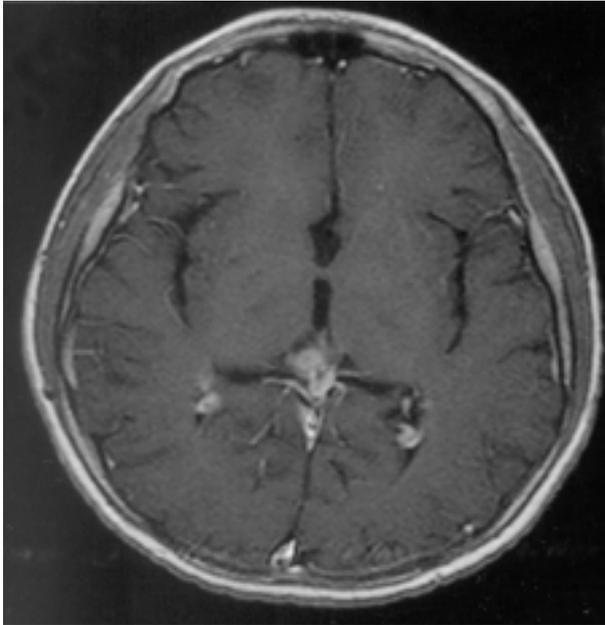


Fig. 3 MRI axial view (T1 with contrast) shows regression of tumor size after two courses of chemotherapy (36 days).

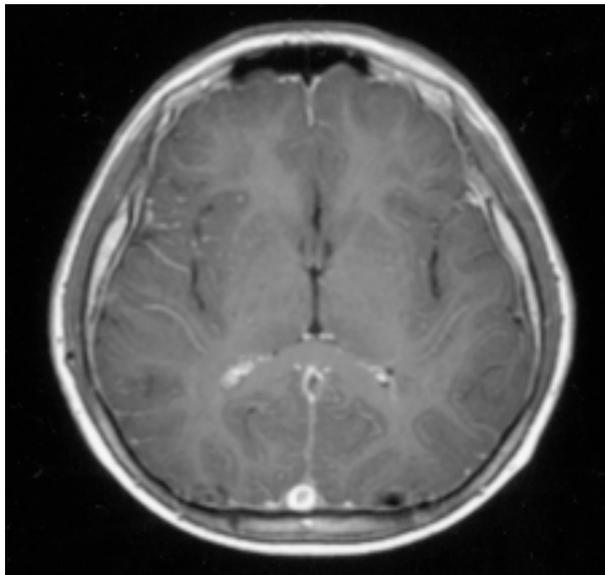


Fig. 4 MRI axial view (T1 with contrast) shows no evidence of tumor in the pineal region six months after initial treatment of chemotherapy.

The causes of PP include hypothalamic hamartoma, brain tumors, hydrocephalus, severe head trauma, myelomeningocele and idiopathic etiology. Lesions causing PP are often located in the posterior hypo-



Fig. 5 MRI sagittal view (T1 with contrast) shows no evidence of tumor in the pineal region six months after initial treatment of chemotherapy.

thalamic or pineal region. Most cases occur in boys with high levels of serum β -hCG.⁽¹⁻⁴⁾

The management of pineal area tumors remains controversial because of tumor heterogeneities. Benign tumors, which comprise one-third of all pineal tumors, can be treated by surgery alone. The remaining two thirds are malignant tumors with a propensity to seeding.⁽⁵⁾ Most of these cases are treated by aggressive surgical resection followed by irradiation. The five-year survival rate for germinomas approaches 90% but NGGCTs have only about a 25% five-year survival rate. Recently, the treatment outcome of NGGCTs has improved after the addition of adjuvant chemotherapy.⁽⁵⁻⁸⁾

The tumor marker plays an important role in diagnosis and monitoring treatment response. A pineal region tumor often has mixed histology, so diagnosis using tumor biopsy may be misleading due to the small specimen available for examination. Many doctors prefer exploration and tumor resection.^(7,8) Even with improved neurosurgical techniques and supportive treatment, few pineal region tumors are amenable to complete resection and there is no evidence to indicate the advantage of subtotal resec-

tion.⁽⁷⁾ In our case, the β -hCG value was extremely high in both the serum and cerebrospinal fluid, indicating the existence of specific malignant components within the tumor such as choriocarcinoma, embryonal carcinoma and malignant mixed germ cell tumors.^(1,5) In view of the infiltrative nature of the mass and the risk of tumor spillage causing remote metastases, chemotherapy was initiated without obtaining tissue for histological confirmation. The serum β -hCG levels became normal after two courses of chemotherapy, indicating significant regression of the tumor. The persistence of elevated tumor markers after surgical or adjuvant treatment is known to be associated with a poor prognosis.^(5,7)

Radiotherapy plays an important role in the management of malignant pineal tumors. For patients with central nerve system germinomas, chemotherapy could reduce the required dose of radiotherapy.⁽⁹⁻¹¹⁾ Our experience suggests that the combination of chemotherapy and radiotherapy without surgical intervention may be adequate in the treatment of selected cases of intracranial malignant germ cell tumor containing non-germinomatous elements.

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分泌乙型人類絨毛膜性腺激素之松果體腫瘤，合併中樞性早熟

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我們報告一個案經驗：一個9歲大的男孩罹患分泌乙型人類絨毛膜性腺激素之松果體腫瘤，合併中樞性早熟及水腦，這男孩在沒有經過外科手術及病理組織切片即接受化學治療和放射線治療，經治療後腫瘤消失，追蹤一年沒有復發的跡象。目前對松果體腫瘤尚無固定的治療模式，主要在於其組織成分之異質性及對放射線治療和化學治療的反應不一。雖然病理組織的取得對腫瘤的治療相當重要，但對顱內的腫瘤而言，病理組織的取得確有其困難之處，且易造成嚴重之後遺症；若血液及腦脊髓液中之乙型人類絨毛膜性腺激素值上升，則病理檢查變的較不必要，因為治療上是相似的。(長庚醫誌2006;29:198-202)

關鍵字：松果體腫瘤，性早熟，乙型人類絨毛膜性腺激素。

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