Pubertas praecox in craniopharyngioma

Case report

JOSÉ M. CABEZUDO, M.D., CARMELO PEREZ, M.D., JESÚS VAQUERO, M.D., RAFAEL GARCÍA-DE-SOLA, M.D., AND GONZALO BRAVO, M.D.

Department of Neurosurgery and Endocrinology Service, Clinica Puerta de Hierro, Faculty of Medicine, Autonomous University, Madrid, Spain

According to Zülch, craniopharyngiomas are dysontogenetic tumors. They are predominantly suprasellar and account for 2% to 4% of all intracranial tumors at any age. This incidence rises in children from 8.2% to 13%. When only suprasellar tumors are taken into account, the figures for children and adults are 54% and 20%, respectively. The clinical picture is dominated by four main syndromes: increased intracranial pressure, hypothalamic pituitary dysfunction, visual deficits, and cerebral deficits. Hypothalamic pituitary function is affected in 50% to 66% of children, and consists of a variable degree of hypopituitarism with or without accompanying diabetes insipidus. The deficit of gonadotrophic hormones results in a retarded or absent sexual development.

Although Koos and Miller state that precocious puberty can occur in patients with craniopharyngiomas, they do not mention any specific case. Balgura, et al., have recently reviewed the subject of precocious puberty of cerebral origin; they found only one case associated with craniopharyngioma (Case 89 of Bailey, et al.). We have been able to find only two additional cases of precocious puberty associated with craniopharyngioma.

This paper presents a case of craniopharyngioma in which the salient feature was the presence of precocious puberty that developed after subtotal removal of the tumor. It is the second reported case in which appropriate endocrinological evaluation was undertaken.

Case Report

This girl, aged 2 years 8 months, was referred to us in January, 1974, for treatment of a suprasellar tumor. She had been in good health until nearly 1 year before admission, when, according to her parents, she started to complain of headaches. One month before coming under our care, she was admitted to another hospital where a pneumoencephalogram showed a large suprasellar mass filling the suprasellar cistern and pushing the third ventricle upward and forward from underneath. There was no significant hydrocephalus (Fig. 1).

Examination. On admission, her height was 90.2 cm
FIG. 1. Preoperative pneumoencephalogram, lateral view. The suprasellar tumor can be seen filling the third ventricle from below.

FIG. 2. Preoperative air ventriculogram, lateral view. The third ventricle fills only in its anterior part due to the tumor impinging upon it from below.

(15th to 25th percentile), she weighed 12 kg (25th percentile), and her bone age was 2.5 years according to the Greulich tables. The only abnormal neurological finding was an atrophic left optic disc. Visual acuity was decreased on the left. Campimetry was not performed due to the patient's lack of cooperation. On air ventriculography, the third ventricle did not fill in its posterior-inferior portion (Fig. 2).

Operation. On January 22, 1974, the tumor was subtotally removed via a right subfrontal approach. The tumor was predominantly cystic and was located under the optic chiasm and third ventricle; a lateral extension toward the left temporal fossa compressed the left optic nerve. Upon completion of the procedure, the nerve was totally decompressed. On pathological examination, the specimen was found to be a typical craniopharyngioma (Fig. 3).

Subsequent Course. Except for transient diabetes insipidus, the postoperative course was uneventful and the patient's clinical condition improved. Four

FIG. 3. Photomicrograph of the surgical specimen showing the typical epithelial pattern of craniopharyngioma. H & E, X 175.
Pubertas praecox in craniopharyngioma

months later, a discrete increase in breast tissue was noted but not much attention was paid to it. In November, 1974, 10 months after operation, when she was aged 3.5 years, her height was 100.7 cm (97th percentile), she weighed 26 kg (more than 97th percentile), and her bone age was 3 years 9 months. Development of the breasts was Stage 2 and pubic hair Stage 1 in the Tanner scale. Neurological examination was normal. Basal values of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were 2.5 ng/ml and 2 ng/ml, respectively (normal values are less than 1.5 ng/ml for both; biological potency of 1 ng/ml of FSH and LH is 4 mIU/ml MRC 69/104 and 3.7 ± 0.3 mIU/ml MRC 68/40). Thyroid hormones, cortisol, 17-ketosteroids, and growth hormone (GH) were normal.

In November, 1975, at age 4.5 years, the patient's height was 112 cm (90th percentile), her weight was 30 kg (more than 97th percentile), and her bone age was 7 years 10 months. On neurological examination, there was a sixth nerve paresis involving the right eye. Development of the breasts was Stage 3 and pubic hair Stage 2. Skull radiograms showed a suprasellar calcification. Pneumoencephalography revealed a suprasellar mass occluding the infundibular recess, but the suprasellar cistern was free (Fig. 4). Thyroid hormones, cortisol, prolactin (PRL), and GH were normal. Basal FSH was 27 mIU/ml (normal, less than 5 mIU/ml), and basal LH was 9.3 mIU/ml (normal, less than 5 mIU/ml). After LH-releasing hormone (LHRH) stimulation, the values of FSH and LH after 30 and 60 minutes were 35, and more than 60 mIU/ml for FSH and 41 and 29 mIU/ml for LH, a response of a postpuberal girl. Estradiol was 40 pg/ml (normal, less than 40 pg/ml), progesterone was 0.5 ng/ml (normal, 0.1 to 0.5 ng/ml) and 17-ketosteroids in urine 4.5 mg/24 hours (normal, less than 3 mg/24 hours). The diagnosis of precocious puberty was made. Surgical treatment was not undertaken, and the patient was started on medroxyprogesterone in order to arrest sexual maturation.

In March, 1977, when the patient was aged 5 years 11 months, her height was 124 cm (97th percentile), weight 39.5 kg (97th percentile), and bone age 8 years 10 months. Her FSH and LH levels were 6.6 mIU/ml and 1.7 mIU/ml, respectively. Estradiol was 65 pg/ml and progesterone 0.42 ng/ml. Development of the breasts was Stage 4 and pubic hair Stage 3. Cyproterone acetate was begun to stop sexual maturation and to slow bone maturation. In May, 1978, she began to complain of decreased visual acuity in the right eye, and a left temporal hemianopsia was detected. Computerized tomography (CT) showed a cystic, partially calcified, contrast-enhancing suprasellar tumor, associated with very slight hydrocephalus (Fig. 5), and in June, 1978, the recurrent tumor was subtotally removed by the previous approach. Pathological diagnosis was craniopharyngioma. The postoperative course was uneventful, and she regained visual acuity. Subsequently, she received a radiotherapy course of 5000 rads.

In June, 1980, when last seen, the patient was aged 9 years 1 month; her height was 136 cm (more than 97th percentile), weight was 49 kg (more than 97th percentile), and bone age 13 years 8 months. Devel-

![Fig. 4. Pneumoencephalogram showing recurrence of the tumor. The suprasellar cistern is free, but the anterior recesses of the third ventricle do not fill due to tumoral impingement upon them.](image)

![Fig. 5. Computerized tomographic scan in May, 1978, showing cystic and calcified recurrent tumor.](image)
development of the breasts was Stage 4 and pubic hair Stage 3. Her FSH and LH were both 1.5 mIU/ml, estradiol was 100 pg/ml, and progesterone 0.49 ng/ml. Cortisol, thyroid hormones, PRL, and GH were normal. She is neurologically asymptomatic and attending normal school; a CT scan did not show growth of the residual tumor.

Discussion

Precocious puberty is a pathologically accelerated puberty, which without therapy leads to sexual maturity before 10 years of age in boys and 8 years in girls. For girls reaching puberty early, who have still not experienced menarche, the term “precocious puberty” is used if they show symptoms of sexual maturity before they reach 6 years of age. Precocious puberty can be due to cerebral or noncerebral causes. Among the former are entities such as hypothalamic hamartomas, gliomas of the hypothalamochiasmatic region, pineal region tumors, suprasellar cysts, hydrocephalus, postinfective states, and neurofibromatosis. Puberty can be due to cerebral or noncerebral causes. Among the former are entities such as hypothalamic hamartomas, gliomas of the hypothalamochiasmatic region, pineal region tumors, suprasellar cysts, hydrocephalus, postinfective states, and neurofibromatosis. The pathophysiology of precocious puberty is not fully understood, although the basic mechanisms involved may be the secretion by the lesion of a gonadotrophin-releasing hormone, or the destruction of the areas that are tonically inhibiting the hypothalamus. The final result is hyperactivity of a hypothetical sexual area in the inferior hypothalamus. The early accelerated somatic growth ultimately leads to low stature due to premature epiphyseal closure.

Among the 82 cases of precocious puberty of cerebral origin collected by Balagura, et al., only one was associated with craniopharyngioma. This case was reported by Bailey, et al., in a 9-year-old girl who showed secondary sexual characteristics when she was 7 years of age, although she did not experience menarche. We have been able to collect only two other cases in the literature: the first is reported by Banna, et al., and the second case was reported by Zachmann and Illig that the fast rate of growth must be attributed to the high levels of sexual hormones. The same applies to breast development. It could be argued that precocious puberty in our patient could be due to hydrocephalus, but this was not the case. Another possible cause could be the surgical manipulation of the diencephalic area, but to our knowledge this consequence has not been reported in clinical practice; indeed, the opposite occurs in most instances.

Although we have no preoperative gonadotrophic hormone assays in our patient, her history is surprisingly similar to that of Zachmann’s patient in whom precocious puberty was also diagnosed after operation, but in whom preoperative endocrinological work-up showed an abnormally high response of FSH to LHRH stimulation. It is possible that precocious puberty may have already started in our patient prior to operation.

We conclude that, once the diagnosis of precocious puberty had been sustained in our patient, and hydrocephalus and surgical manipulation of the diencephalic area had been ruled out as the etiological factors, the causative factor leading to precocious puberty in our patient was likely the presence of the craniopharyngioma. Thus, the possibility of a craniopharyngioma should be considered in the differential diagnosis of precocious puberty of cerebral origin.

Acknowledgment

The authors express their appreciation to Mrs. Ana Maria Artero for typing the manuscript.

References

5. Cushing H: Intracranial Tumours. Notes Upon a Series of Two-Thousand Verified Cases with Surgical-Mortal-
Pubertas praecox in craniopharyngioma


Received November 5, 1980.
Accepted in final form January 30, 1981.
Address reprint requests to: José M. Cabezudo, M.D., Servicio de Neurocirugía, Clínica Puerta de Hierro, San Martín de Porres 4, Madrid 35, Spain.