Suprasellar germinoma in association with Klinefelter's syndrome

Case report

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A case is presented of suprasellar germinoma in a 20-year-old man with Klinefelter's syndrome. Hypogonadism is known to be a characteristic of Klinefelter's syndrome, and has often been described in cases of suprasellar germinoma. Thus, both pathological entities may mimic one another. It is emphasized that a chromosomal karyotype should be determined in every case of intracranial germ-cell tumor associated with hypogonadism.

KEY WORDS • Klinefelter's syndrome • suprasellar germinoma • hypogonadism

KLINEFELTER'S syndrome is characterized by hypogonadism, azoospermia, an elevated gonadotropin level, and an extra X chromosome in a phenotypic male patient. Various neoplasms have been described in association with Klinefelter's syndrome, and there seems to be a clear affinity of this disease with breast cancer. Some authors have suggested the increased risk of development of an extragonadal germ-cell tumor in cases of Klinefelter's syndrome; however, most of these germ-cell tumors were seen in the mediastinum, and only one case has been reported in the central nervous system. A case is presented here in which a patient with Klinefelter's syndrome also had a suprasellar germinoma.

Case Report

This 20-year-old Japanese man was admitted to St. Marianna University Hospital because of the gradual onset of polyuria, polydipsia, and visual disturbance. He had previously been diagnosed elsewhere, on the basis of clinical findings and chromosomal karyotype, as having Klinefelter's syndrome.

Examination. Physical examination revealed a eu- nuchoid body habitus with small testicles (Fig. 1) but no apparent gynecomastia. Visual field examination showed a lower temporal quadrant defect in the left eye and enlargement of the physiological blind spot in the right eye. Chest x-ray film was normal. Cranial computerized tomography (CT) demonstrated a suprasellar mass of slightly increased density with peripheral calcification, and a posteriorly located area of low density (Fig. 2A). The high-density region enhanced evenly after an intravenous infusion of contrast medium (Fig. 2B). The pineal region seemed to be normal. Angiography revealed vascular displacement indicating a suprasellar mass without abnormal vascularity. Chromosomal karyotype was confirmed to be 47, XXY (Fig. 3). Urinary levels of estrogen (3.1 μg/day) and testosterone (16 μg/day) were low. Serum concentrations of follicle-stimulating hormone (2.3 mIU/ml) and luteinizing hormone (6.2 mIU/ml) were normal, in contrast with the usual findings in uncomplicated cases of Klinefelter's syndrome. The thyroxine level (2.2 μg%) was low, and there was an exaggerated and delayed response to the thyrotropin-releasing hormone test. Prolactin concentration was slightly high (53.1 ng/ml), with no response to the chlorpromazine test and an appropriate fall on the L-dopa test. Urinary output was 3000 to 4000 ml/day (specific gravity 1.010 to 1.020). On a water deprivation test, serum and urine osmolarity remained, respectively, greater than 291 mOsm/liter and less than
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75 mOsm/liter. Serum levels of both alpha-fetoprotein (below 0.33 mg/ml) and human chorionic gonadotropin (below 6.6 mIU/ml) were normal.

Operation. At surgery, performed through a right frontotemporal approach, apparent bulging of the lamina terminalis and thickening of the optic nerves were observed. The suprasellar cistern was patent and the diaphragma sellae looked intact. Since frozen section of a biopsy specimen strongly suggested a germinoma, no further extirpation was carried out. Permanent sections showed the typical microscopic appearance of germinoma characterized by large spheroid cells with vesicular nuclei, and small darkly stained cells with scanty cytoplasm (Fig. 4). After radiotherapy with a dose of 3000 rads to the suprasellar region and 2000 rads to the whole brain, the suprasellar mass almost disappeared on the follow-up CT scan.

Discussion

The CT appearance of peripheral calcification, and the low-density area suggesting a cyst formation, misled us to the preoperative diagnosis of a craniopharyngioma. However, an anterior third ventricular tumor, such as suprasellar germinoma, was suspected...
because of the relatively early manifestation of diabetes insipidus which was confirmed on water deprivation testing.\textsuperscript{2,21} Since operative attack was thought to carry little risk, surgical exploration was chosen as the first therapeutic procedure. The final diagnosis was suprasellar germinoma. Naidich, et al.,\textsuperscript{15} denied the calcification of a suprasellar germinoma, but some authors have described calcification\textsuperscript{3,22} and cyst formation\textsuperscript{22} associated with this tumor.

Although in Klinefelter's syndrome the serum gonadotropin level should be elevated,\textsuperscript{11} it was normal in the present case. This could be attributed to hypothalamic-pituitary hypofunction due to the suprasellar germinoma.

Susceptibility to tumor formation in Klinefelter's syndrome has been suggested previously,\textsuperscript{16} and it has been noted that the XXY cells were transformed three to 10 times more frequently by virus in patients so afflicted than in a normal control population.\textsuperscript{14} Actually, various kinds of neoplasms have been reported in patients with this disease, although most of them were isolated occurrences, except for cases of breast cancer\textsuperscript{5,6,10,18} and, less often, leukemia.\textsuperscript{1,7,12} Recently, several cases of Klinefelter's syndrome in association with mediastinal germ-cell tumors have been documented.\textsuperscript{5,13,19,20} Sogge, et al.,\textsuperscript{19} found two patients with Klinefelter's syndrome in a review of 24 reported cases of primary mediastinal germ-cell tumors.

Since the incidence of Klinefelter's syndrome has been estimated at approximately 0.06% of the control population,\textsuperscript{8} it was concluded that patients of Klinefelter's syndrome may be predisposed to development of germ-cell tumors, particularly those of extragonadal origin.\textsuperscript{19} Up to this time, however, there has been only one report of an intracranial germ-cell tumor in association with Klinefelter's syndrome.\textsuperscript{17} Hypogonadism is a frequent feature in cases of intracranial germ-cell tumors.\textsuperscript{9,21} In this respect, germ-cell tumors may resemble Klinefelter's syndrome. Only chromosomal karyotyping can confirm the latter. If hypogonadism is attributed solely to the germ-cell tumors and karyotype is not determined, Klinefelter's syndrome may be overlooked. We believe that cases of suprasellar germinoma with Klinefelter's syndrome will be encountered more frequently if karyotyping is performed in every case of germ-cell tumor with hypogonadism.

References


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