Neurochirurgia 27 (1984) 120–124

Atypical pineal teratoma: clinical and computer tomographic features of two patients with disseminated ependymal lesions

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Summary

Two cases of atypical pineal teratoma (APT) with massive ventricular dissemination are reported; the diagnosis was based on CT appearances and characteristic neurological and endocrinological abnormalities. Both patients responded well to radiotherapy. The CT features and the management of these patients are discussed.

Atypisches Pinealis-Teratom mit ependymaler Dissemination

Es werden 2 Patienten mit einem atypischen pinealen Teratom und massiver ventriculärer Dissemination mitgeteilt. Die Diagnose wurde auf Grund der computertomographischen Konfiguration sowie typischer neurologischer und endokrinologischer Befunde erstellt. Bei beiden Patienten kam es unter Strahlentherapie zu einer völligen Remission. Die computertomographischen, neurologischen und endokrinologischen Befunde sowie das therapeutische Management werden besprochen.

Key-Words: Atypical pineal teratoma – Pineal teratoma – CT scan – Radiotherapy

Introduction

The classification of the tumours of the pineal and suprasellar regions was controversial until *Rubinstein* introduced a new system in 1972 (1). This system classifies all midline CNS tumours of germ cell origin in one group, regardless of whether they arise in the pineal body itself or within the region of the pineal body or in the suprasellar region. Tumours thought to arise from the pineal parenchymal cells are classified as a different group (Tab. 1). Germinomas have been variously called pinealoma, supra- and intrasellar germinoma, dysgerminoma, ectopic pinealoma, atypical pineal teratoma and "anisomorphic pinealoma" (2–7).

There are many earlier reports based on air-studies and isotope scans (8–13), but to our knowledge the computertomographical appearances of patients with atypical pineal teratomas and with disseminated ependymal lesions have not yet been described in detail. The purpose of this paper is to report on the computer tomographical and clinical findings and the management of two patients with ependymal dissemination of atypical pineal teratoma.

Tab. 1 Classification of tumours of the pineal region

Tumours of germ cell origin

Typical Teratoma (Synonyms and releated terms):
1. Choriocarcinoma, Chorioepithelioma, Chorionic gonadotropin secreting tumour
2. Embryonal carcinoma, Teratocarcinoma, Endodermal Sinus Tumour

Atypical Teratoma (Synonyms and releated terms):
Germinoma, Pinealoma, Ectopic Pinealoma, Anisomorphic Pinealoma, Atypical Pineal Teratoma

Tumours of pineal parenchymal cells
(Synonyms and releated terms):
1. Pineoblastoma, Pinealoblastoma, Medulloblastoma pinealis
2. Pineocytoma, Pinealcytoma, Isomorphic Pinealoma

Tumours of glial cells and other forms

Cysts

Patients

Case 1, a 15-year-old boy had been in good health until the age of 13, when his appetite became poor and he developed episodes of intensive thirst and polyuria. In the subsequent months he complained of fatigue, nausea and vomiting and lost weight rapidly. His mental state deteriorated. A suspected diagnosis of diabetes mellitus and thyrotoxicosis could not be confirmed. Seven months prior to admission to our hospital, a neurological examination was done and the only abnormality found was absence of the pupillary reaction to light. At his time pupillotonia was considered to be the most likely explanation.

In view of the negative results of various examinations, the patient was thought to be suffering from anorexia nervosa and psychiatric therapy was instituted. However, the condition of the patient deteriorated further. There were episodes of confusion and he became incontinent. At last his weight was 30 kg and he had to be tube-fed. He was admitted for the first time to this hospital in a lethargic state on November 18th, 1981.

On examination, he was intermittently stuporose. When awake, he was oriented; articulation and comprehension of speech were normal. A slight bilateral papilloedema was noted, but no visual field defect could be detected. The pupils were dilated and fixed to light. A complete paralysis of conjugate upward gaze was present (fig. 1), but the cranial nerves otherwise were normal. Diffuse muscle wasting was present with rigid muscle tone but with good strength. The tendon reflexes were symmetrical and the plantar responses were flexor. Sensation appeared intact as far as it could be tested. Cerebellar functions were normal. Grasp and suck responses were present bilaterally. Myoclonic twitches of the face, tongue, neck and arms were seen at times. Physical examination revealed absence of pubic and axillary hair, and small testes. His growth was retarded (height 152 cm).

The lumbar puncture yielded clear, colourless cerebrospinal fluid (CSF). The CSF cell count was 30 lymphocytes/cmm; the CSF protein was

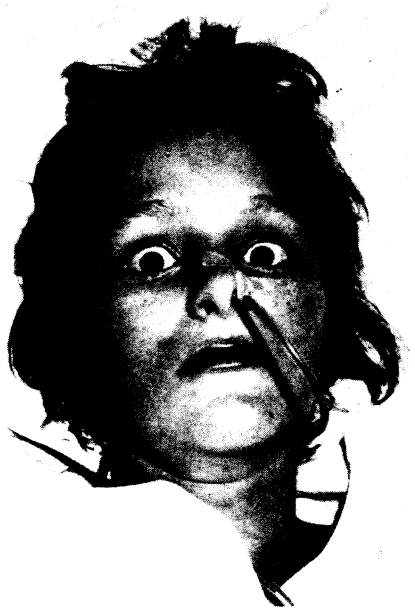

Fig. 1 "Sunset phenomenon" (A marked sickle of sclera between the eyelid and the upper margin of the iris).

40 mg%. Cytologic examination revealed one tissue fragment consisting of about 25 atypical cells with slight polymorphism of the nuclei and rather abundant light blue cytoplasm. These cells were suspected to be tumour cells.

An electroencephalogram showed continuous slowing over both hemispheres with frequent paroxysmal delta activity. Abnormal pineal calcification was seen on the skull X-rays. The bone age was delayed about three years.

The CT appearances of case 1 are shown in fig. 2. The density of the tumour masses within the floor of the third ventricle, the pineal region and the walls of the lateral ventricles varied between 29 and 61 *Hounsfield* Units (H. U.). There was marked enhancement after intravenous administration of meglumine iothalamate, density values now ranging between 57 and 78 H. U.

The endocrine data are summarized in table 2. Pituitary function tests revealed partial anterior pituitary insuffiency including the corticotropic, gonadotropic and somatotropic systems with a concomitant hyperprolactinaemia and diabetes insipidus.

The following laboratory tests gave normal results: ESR, RBC, WBC, Hc, Hb, platelet count, serum electrolytes, SGOT, SGPT, alkaline phosphatase, electrophoresis, chest X-ray, BUN, serum creatinine. The Tuberculin-Tine test was negative. A clinical diagnosis of APT was made, based on the CT appearances, neurological and endocrinological abnormalities.

A Rickham reservoir was implanted and radiation therapy was begun. A dose of 30.0 Gy of ^{60}Co was given in 20 fractions to both hemispheres over a period of four weeks. Parallel opposed 20 × 13.5 cm fields were employed in order to encompass the entire cranial contents. After having given 15.0 Gy a CT scan was repeated: surprisingly, the lesion had already disappeared by that time. The ventricular size returned to normal without any ventriculo-cardiac shunt having been implanted. Therefore, the irradiation of the brain was discontinued after a dose of 30.0 Gy had been reached. In view of the transventricular dissemination of the lesion and the CSF cytology findings, a prophylactic irradiation with a dose of 30.0 Gy of ^{60}Co was subsequently delivered to the entire neural axis within a period of four weeks, employing two posterior fields of 20 × 4 cm with a moving gap.

Replacement therapy for the endocrine deficits was administered including hydrocortisone, arginine-vasopressin and human growth hormone.

Within ten days after starting the therapy a significant improvement was noted in the patient's mental status. However, the Parinaud syndrome

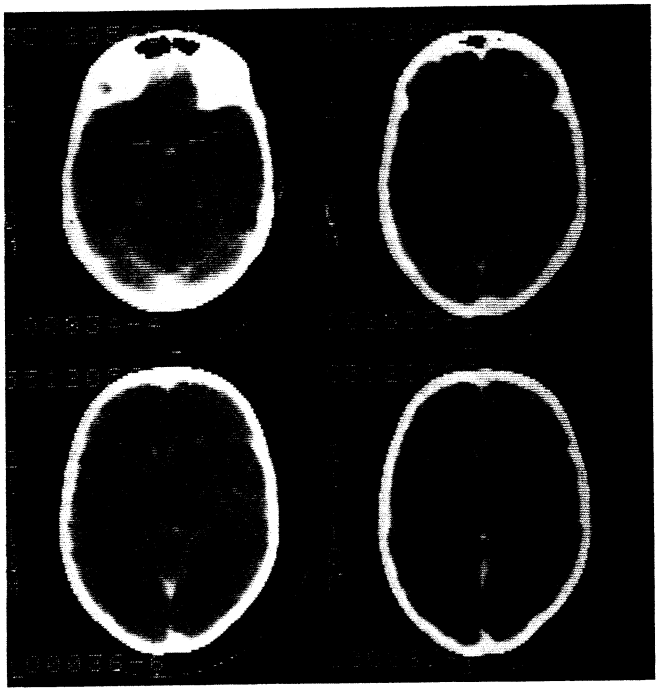

Fig. 2 Case 1, CT scan with enhancement. There is a mass within the floor of the third ventricle extending into the suprasellar cisterns. A remarkably small mass can be seen in the pineal region with involvement of the quadrigeminal plate. Several enhancing lesions within the wall of the lateral ventricles indicate transventricular spread of the neoplastic process. A mild obstructive hydrocephalus is present.

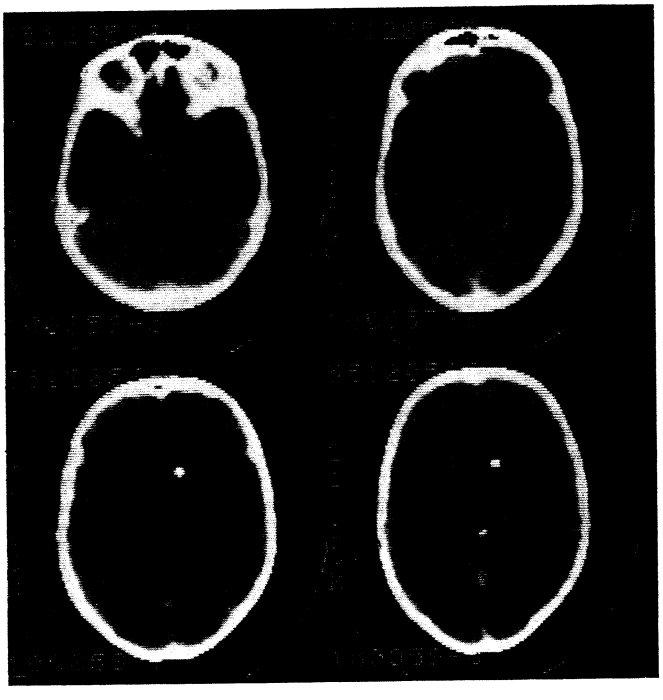

Fig. 3 Case 1, post-irradiation CT scan with enhancement. All the enhancing lesions are gone. A mild widening of the ventricles is still present and the tip of a ventricular catheter is seen in the right frontal horn.

remained unchanged. Hormonal substitution is being continued and he is now doing well under outpatient care.

Case 2, a 19-year-old boy was referred to our hospital on March 3, 1982. He had been in good health and his growth and development were normal. Polyuria and polydipsia had begun suddenly about nine months prior to admission and gradually increased. He noted a loss of facial, axillary and pubic hair and he felt a lack of libido. Since november 1982 he had experienced progressive fatigue and lethargy and his weight dropped 15 kg within a few weeks. His main complaint was of diplopia on distant vision which had been present for two months prior to admission. An ophthalmological examination revealed a complete palsy of upward gaze and bilaterally dilated pupils non-reactive to light.

On examination, he was underweight (height 50 kg). Facial, axillary and pubic hair were sparse and breaking of the voice had not yet occurred. There was a gross vertical gaze palsy and the pupils were dilated and fixed to light with an intact accommodation reaction. The visual field and the fundoscopic findings were normal. The other cranial nerves were also normal. Hyperreflexia was present in the lower extremities and there were bilateral extensor plantar responses. Primitive reflexes as the palmomental and snout reflex as well as head retraction could be elicited.

The EEG was reported as moderately abnormal showing generalized slow wave activity. The CSF could not be examined, because the patient refused lumbar puncture. Plain skull X-rays showed an enlarged calcification in the pineal region. The CT findings of case 2 are shown in figura 4. The density of the tumour masses ranged between 39 and 46 H. U., and after contrast enhancement from 53–57 H. U.

The endocrine data are listed in table 2. In view of the normal bone age, there was no evidence of a somatotropic failure. Diabetes insipidus and a partial anterior pituitary dysfunction were present with deficiency of the corticotropic and gonadotropic systems.

The diagnosis of APT was made. The tumour was irradiated with ^{60}Co at a total dose of 55.5 Gy. Initially a dose of 30.0 Gy was given to both hemispheres over a period of four weeks, employing parallel opposed 14 × 20 cm fields. Then a follow-up CT scan was done which demonstrated a very small residual tumour mass of 12 × 18 mm adjacent to the pineal calcification (fig. 5). For this, arc therapy was planned using a computer. The field measured 4 × 4 cm over an arc of −90° to +90° and the dose was 25.5 Gy in 17 fractions over a period of three and a half weeks. Later, the patient was lost for lollow-up and the irradiation of his spinal subarachnoid space could not be done. Hormonal replacement therapy with hydrocortisone and arginine-vasopressin was given. The patient recovered quickly within a few weeks and his neurological findings returned to normal, his eye movements were full and his pupillary reaction became normal. A follow-up CT scan after completion of irradiation showed no pathological findings apart from the large pineal calcification which had remained unchanged.

Discussion

In our cases of APT the diagnosis was made on the basis of a typical constellation of endocrinological, neurological and CT findings. In the differential diagnosis craniopharyngiomas, gliomas, adenomas, lymphomas, tuberculomas, sarcoidosis etc. (9) were considered. In both cases the first manifestation of the tumour was diabetes insipidus which remained undiagnosed for about two years in case one and nine months in case two. Endocrine disturbances thus appeared long before other neurological deficits occurred (8, 9, 14–18, 19). Both patients presented with diabetes insipidus and partial anterior pituitary insuffiency.

The leading neurological manifestations consisting of palsy of vertical gaze associated with dilated and fixed pupils appeared rather late in the course of the disease as in other patients reported in the literature (2, 3, 8, 9). Visual field defects were not observed in our patients. Case one developed pyramidal signs, urinary incontinence and somnolence indicative of hydrocephalus. In both patients we did not find any signs of meningeal irritation. The course in both patients indicates that the primary lesion should be sought in the hypothalamus or in the pituitary gland.

The endocrine data were more consistent with a primary pituitary lesion, for example, the normal prolactin in case two and the absence of LH and FSH response to LHRH stimulation in both cases. The findings were not characteristic of a hypothalamic lesion although such a defect could not be excluded endocrinologically. A further endocrine differentiation could only have been accomplished by measuring the ACTH response to vasopressin and repeated administrations of GnRH and/or a clomiphene test. These were not done because of the critical condition of both patients. In contrast to the endocrine findings, the CT scan showed involvement of the hypothalamus and complete sparing of the pituitary fossa in both cases, this being more in favour of a deficit of hypothalamic-releasing hormones responsible for the various endocrine abnormalities described above.

Tab. 2 Endocrine data obtained from our patients

	Case 1	Case 2	Normal values
basal HGH	1.0	–	0–10 µg/l
after Argininfusion	1.0	–	> 9 µg/l
basal FSH	1.6	1.0	3–15 mU/ml
after LHRH	no response	no response	> 12 mU/ml
basal LH	3.7	1.5	3–15 mU/ml
after LHRH	no response	no response	> 12 mUl/ml
basal ACTH	20	<20	10–100 pg/ml
metapyrone test	–	<20	>200 pg/ml
basal Prolactin	1300	285	170±60, max 280 mU/ml
after TRH	600	941	3 times basal
basal Cortisol	<1	1.5	5–20 µg/dl
after Synacthen	1	4.9	15–40 µg/dl
basal TSH	2.1	1.1	0– 7 mU/ml
after TRH	10.0	9.4	> doubling of basal
T_4 RIA	7.5	3.5	4.6–11.5 µg/dl
FT_4 Index	–	1.1	1.6– 5.2
TBI	–	32.1	25–25%

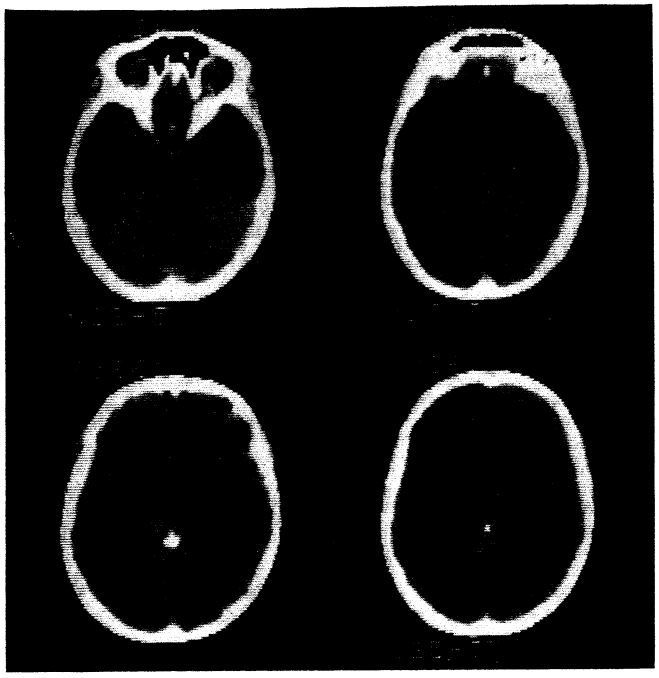

Fig. 4 Case 2, first CT scan with enhancement: A small enhancing mass is present in the suprasellar cistern. A separate, large mass involves the pineal and is associated with an abnormal calcification. Transventricular spread is indicated by enhancement of the walls of both frontal horns. There is a mild obstructive hydrocephalus.

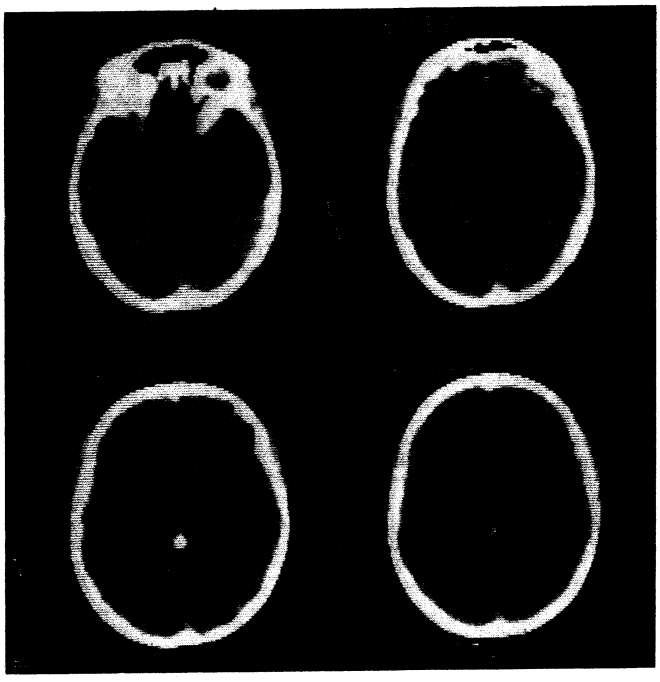

Fig. 5 Case 2, post-irradiation CT scan with enhancement: The pineal calcification is unchanged but the tumour size is reduced considerably. The lesions within the frontal horns and the suprasellar cisterns have vanished.

The special endocrine function of the pineal gland also deserves comment. It has been suggested from animal experiments that melatonin has both anti- and progonadotropic effects (21, 22). In both cases, not only the gonadotrophs but also the adrenocorticotrophes were involved. Therefore a mediation of the hyticotrophes were involved. Therefore a mediation of the hypogonadism by an endocrine substance secreted by the pineal The CT scans showed multiple lesions located on the floor of the third ventricle, in the pineal region and in the walls of the lateral ventricles as well as a mild obstructive hydrocephalus. There was no CT evidence of any pituitary involvement. From the CT features at that time, it was not possible to tell which of the lesions was the primary one. Considering the size of the lesions, one may speculate that in case one the very small pineal lesion was not primary. However, in case two the pineal tumour was by far the largest lesion present and may have been the primary one.
The clinical presentation of our patients suggested the presence of two midline lesions, one in the anterior part of the third ventricle associated with endocrine abnormalities, the other more posteriorly located causing the Parinaud syndrome (19, 20). It is by this very combination of clinical findings, that *Swishuk* et al. (1974) separated such cases from other patients with single tumours of the pineal region and suggested they might represent a definite neuroendocrinological syndrome. As his clinical observations were made on the bases of air studies and isotope scans, the presence of further or multiple lesions may have remained unrecognized. However, *Puschett* et al. (1968) described five such patients with the same clinical presentation but with a single tumour in the pineal region. Again, double or multiple lesions cannot be considered as having been ruled out in those patients, CT not having been available at that time.
Among patients with CT-proven solitary tumours of the pineal region we have not yet encountered a single case with the same clinical presentation and course as these two cases of APT. Our limited experience therefore confirms *Swischuk*'s suggestion that young male patients with anterior pituitary dysfunction and Parinaud syndrome be diagnosed as cases of "double midline atypical teratoma". The term "double" referring to the mode of presentation with two clinically manifest lesions, although CT would show more or multiple lesions in the majority of these patients. There may be cases of APT with a single lesion, when the diagnosis is made early in the course of the disease.
It is generally agreed that radiotherapy is the treatment of choice in such patients (23–27). In cases where there is a good response to radiotherapy the clinical diagnosis of APT is further substantiated. Since most if not all APT can be cured by radiation, surgical removal does not seem to have a place in their initial management (28).
Whether the spinal subarachnoid space should be irradiated prophylactically is still being debated (2, 3, 8, 9, 12, 13). In our opinion, prophylactic irradiation is indicated in cases with massive ventricular dissemination or in the presence of tumour cells in the CSF.
In the presence of hydrocephalus and altered level of consciousness a Rickham reservoir should be implanted as the first step. We recommended that shunt operations be withheld as long as possible after the institution of radiation therapy in order to avoid systemic dissemination.

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