DOUBLE MIDLINE INTRACRANIAL ATYPICAL TERATOMAS*
A RECOGNIZABLE NEUROENDOCRINOLOGIC SYNDROME

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THE simultaneous occurrence of 2 midline intracranial atypical teratomas and their attending neuroendocrinologic syndrome is not widely appreciated. However, the typical clinicoroentgenographic findings virtually assure the diagnosis, and indeed, allow treatment without surgical exploration or histologic confirmation of the tumor.

Four patients with remarkably similar clinical and roentgenographic findings, and a review of the literature are presented in this report.

REPORT OF CASES

CASE 1. R.D. A 13 year old male noticed increased thirst for 2 months and nausea and vomiting for 2 weeks prior to his admission to our hospital in September, 1969. He also had nocturia (3 to 4 times a night) and had noticed that his urine was pale. Physical examination, including neurologic and ophthalmologic examinations, were negative. Laboratory studies revealed neurogenic diabetes insipidus and panhypopituitarism.

An electroencephalogram (EEG) and brain scan were normal, but plain skull roentgenograms showed a small, midline calcification in the area of the pineal gland (Fig. 1). A positive contrast ventriculogram revealed a mass deforming the anterior third ventricle (Fig. 2). The appearance and location of this lesion led to a presumptive diagnosis of craniopharyngioma. A smaller mass surrounding the pineal calcification was also noted (Fig. 2), but the possibility that it represented a second lesion was not universally entertained. Consequently an anterior craniotomy was performed and as much as possible of the anterior lesion was removed. It was encapsulated and located posterior and inferior to the optic chiasm and below the hypothalamus. Histologic diagnosis was craniopharyngioma.

Following surgery the patient was maintained on pitressin and other replacement therapy for his panhypopituitarism. One year after surgery, however, he developed blurred vision, and physical examination revealed paralysis of upward gaze (Parinaud's syndrome), pupils nonreactive to light, and a right upper outer quadrant field defect. A brain scan showed an area of increased tracer activity in the region of the pineal gland, and a ventriculogram demonstrated a large mass in this area (Fig. 3). The third ventricle was grossly deformed and the aqueduct obstructed. A presumptive diagnosis of pinealoma was made and the tumor was treated with radiation therapy (5,000 r). After treatment the patient improved and his visual findings returned to normal.

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nation of the cerebrospinal fluid showed neoplastic cells. These were judged to be of epithelial origin, and because of this, tissue from the original anterior third ventricular lesion was re-examined. The tumor was then reclassified as "atypical teratoma" and the abnormal cells in the spinal fluid were believed to be seedlings from it.

The patient expired within a few days, but no postmortem examination was permitted.

CASE II. J.V. A 12 year old male had a 2 year history of increased water consumption and nocturia (3 to 4 times a night), and a 3 month history of lethargy, ataxia, blurred vision, and headache. Physical examination revealed loss of upward gaze (Parinaud's syndrome) and dilated pupils, slowly reactive to light. Papilledema was also present and laboratory tests led to a diagnosis of neurogenic diabetes insipidus, but not panhypopituitarism.

The brain scan was normal, but plain skull roentgenograms showed a midline calcification in the region of the pineal gland (Fig. 4). A carotid angiogram showed mild dilatation (hydrocephalus) of the lateral ventricles, while a positive contrast ventriculogram demonstrated a mass deforming the anterior third ventricle and a second, separate mass in the region of the pineal gland (Fig. 5).

An anterior craniotomy was performed and the anterior tumor was found to extend around the optic chiasm and to invade the adjacent

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Fig. 2. Case 1. Positive contrast ventriculogram demonstrates the larger anterior tumor (1) and the small, almost inconspicuous, posterior tumor (2). Both tumors protrude into the third ventricle. Note that the anterior lesion is suprasellar, but also somewhat posterior in position.

The patient did well for approximately another year but then returned with weakness and paresthesias of his lower extremities. Eventually, this progressed to involve his trunk and upper extremities. A lumbar puncture demonstrated a cerebrospinal fluid protein content of 206 gm. per cent, and cytologic exami-

Fig. 3. Case 1. Note how large the posterior lesion has become 1 year after initial treatment and how it completely deforms the posterior third ventricle and lateral ventricles. The aqueduct is also deformed and obstructed and hydrocephalus is present. Note that the anterior lesion, although still present, is smaller.

Fig. 4. Case II. Note calcification in the region of the pineal gland (arrow). This calcification was midline. The pituitary fossa is generous in size.
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Fig. 5. Case II. Positive contrast ventriculogram demonstrates the anterior (1) and posterior (2) lesions. The concave truncated deformity of the anterior third ventricle is similar to that seen in Case I. The calcification in the center of the posterior lesion is seen again, and the posterior tumor is producing deformity and truncation of the posterior third ventricle and aqueduct.

Brain stem. Histologic diagnosis was atypical teratoma (Fig. 6). The patient was shunted and treated with radiation therapy (5,000 r) to both tumor sites. The entire neural axis was not prophylactically irradiated.

Two years after the initial diagnosis the patient, on pitressin therapy, is doing well.

Case III. S.L. A 12 year old male presented with vomiting in April, 1972. He was seen by

his family physician, who also noted that his urine specific gravity was low. In September, 1972, because of persistent difficulties, he was referred to our hospital, and at this time, in addition to the problem of vomiting, he also related a history of nocturia (2 to 3 times a night). Physical examination was normal, but laboratory tests led to a diagnosis of neurogenic diabetes insipidus and mild panhypopituitarism. A brain scan was normal.

Plain skull roentgenograms showed a calcification in the region of the pineal gland (Fig. 7, A and B), and a pneumoencephalogram demonstrated 2 tumors, one in the region of the

Fig. 6. Case II. Histologic section: atypical teratoma. Note that the tumor is composed of cells with fairly abundant cytoplasm. Vacuolated cells suggest early degenerative changes. Also note the elongated fibrous trabeculae containing small lymphocytes. The findings are consistent with those of atypical teratoma. (H and E X 100.)

Fig. 7. Case III. (A) Note small calcification in the region of the pineal gland (arrow). The sella is normal. (B) Towne's projection shows the calcification to be just to the right of the midline (arrow).
anterior third ventricle and another in the area of the pineal gland (Fig. 8). A presumptive diagnosis of atypical teratoma was made, and no operative procedure was attempted.

The patient was treated with radiation therapy (5,000 r) to both lesions, and was subsequently discharged on pitressin and other appropriate replacement hormonal therapy for his hypopituitarism.

One year after treatment the patient is doing well.

Case iv. J.R. This case was discovered in our autopsy files some time after the first 3 were studied. This 13 year old white male presented in August, 1962, with a 1 year history of nocturia (3 to 6 times a night), sleeplessness, and weight loss. Vomiting and polydipsia were present for 6 months, and dizziness and stumbling for 2 or 3 months. Physical examination demonstrated generalized weakness, pupils which were dilated and not reactive to light, and a lack of upward gaze (Parinaud's syndrome).

Roentgenograms of the skull revealed 2 intracranial calcifications (Fig. 9). One was located in the region of the pineal gland, and the other in the suprasellar region. Unfortunately, the suprasellar calcification was missed on initial inspection in 1962, and on later inspections was felt to represent an area of superimposed normal inner table sclerosis. A brain scan was also obtained at this time and was interpreted as normal, but in retrospect it is felt that an area of increased tracer activity was probably present in the suprasellar region.

A pneumoencephalogram showed a small tumor mass around the pineal gland area, protruding into the third ventricle and obliterating the pineal and suprapineal recesses (Fig. 10). The area of the anterior third ventricle was not adequately visualized, but in retrospect the anterior recesses were felt to be somewhat truncated. However, at the time of the study the area of the anterior third ventricle was considered normal and a provisional diagnosis of pinealoma was made. Radiation therapy (6,000 r over 6 weeks) was administered and the boy was discharged on replacement therapy for his endocrinologic deficits.

He returned some 9 months later with weakness of the right arm and leg, hyperactive deep tendon reflexes, and bilaterally positive Babinski responses. At this time the brain scan revealed an area of increased uptake in the frontal region, just slightly to the left of midline (Fig. 11, A and B). Radiation therapy was administered to this lesion, but improvement was only temporary. Within 4 months the patient expired.
At postmortem examination a 5 mm. pineal tumor, with central calcification, was identified. No specific comment was made regarding the anterior tumor site, except that the posterior lobe of the pituitary gland was atrophic. Even at this time the presence of the anterior tumor seemed to elude all concerned, and yet on the basis of the clinical findings, plain film calcification, and brain scan it was clearly present. Radiation therapy probably contributed to some decrease in its size, but it is also possible that the tumor was more infiltrative than mass-like.

In the brain stem and upper cervical spinal cord a large tumor mass, measuring 5 cm., was identified. It was somewhat cystic in appearance, and on histologic examination was an atypical teratoma (Fig. 12). It was believed to be metastatic. The diagnosis was corroborated by the Armed Forces Institute of Pathology.

DISCUSSION

Atypical teratomas of the central nervous system most frequently occur as single lesions and most are located in the suprasellar or pineal areas. The occurrence of these tumors at both sites simultaneously is less well appreciated. Furthermore, the fact that they might represent a definite neuroendocrinologic syndrome has not been overly stressed, and indeed, when such a case is cited, it is usually done in passing only.

Typically these tumors occur in males between the ages of 5 and 25 years, and symptoms referable to either the anterior or posterior lesion may cause the patient to seek medical attention. However, most often it is the insidious, but progressive, onset of diabetes insipidus that heralds the syndrome. Some patients may also show signs of decreased anterior pituitary lobe function, but these changes are often subtle. Most often it is the gonads that are involved first, but the adrenal and thyroid glands can also be involved, and indeed hypoadrenalism may lead to adrenal

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FIG. 10. Case IV. Pneumoencephalogram demonstrates the posterior lesion (2) to be producing truncation and a concave deformity of the posterior third ventricle. The pineal and suprapineal recesses are obliterated. The anterior calcification is just vaguely identified on this study (1), but a discrete tumor is not seen. The anterior third ventricle is poorly visualized.

FIG. 11. Case IV. (A and B) Brain scans obtained 5 months after initial examination show a large area of increased tracer activity (arrows) in the suprasellar region. In B this area of increased activity is noted to lie just to the left of midline (arrows).
crisis during pneumoencephalography or surgical exploration.

Neurologic deficit is usually limited to findings in the eyes, and is not always present from the onset. Field deficits from the anterior lesion may be noted in some patients, while the posterior lesion may produce Parinaud’s syndrome and loss of the pupillary light reflex. If the aqueduct is obstructed, hydrocephalus with headaches, lethargy, and vomiting may be noted.

Electroencephalograms and brain scans are usually normal in the early stages. Calcification in the region of the pineal gland, however, is almost always present and is a most important roentgenographic finding. Indeed, in the presence of the proper clinical setting, such a calcification, especially in a child, should lead to the proper diagnosis. Calcification in the anterior lesion occurs less frequently and can be confused with that of craniopharyngioma. Sellar changes are usually absent or minimal.

Just why these patients tend to present with symptoms referable to the anterior lesion first is not definitely known. Perhaps it is due to the large size of the tumor in some of these children. But it may also be that the anterior lesion tends to encroach upon more critical areas sooner (i.e., the various hypothalamic-pituitary tracts and the hypothalamus itself). Direct extension or pressure upon the pituitary gland itself is less likely, as most of these tumors do not extend into the pituitary fossa.

Ventriculography or pneumoencephalography usually demonstrate these tumors best. The anterior lesion appears as a rounded mass projecting into the anterior third ventricle, while the posterior lesion obliterates the pineal and suprapineal recesses, and if large enough, displaces and obstructs the aqueduct.

The histologic identification and classification of these tumors is often controversial and one may be presented with a multiplicity of terms for the same lesion (i.e., germ cell tumors, germinoma, dysgerminoma, testicular dysgerminoma, seminoma, etc.). However, most authorities consider these lesions to be atypical teratomas and concur with Russell’s initial impressions in 1944. Atypical teratomas have long been known to metastasize, especially within the confines of the subarachnoid space, and reported metastatic sites include the cerebellum, lateral ventricles, fourth ventricle, cerebral hemispheres, and spinal cord. However, when two intracranial lesions are seen from the beginning, one might justifiably ask, whether they need necessarily be considered metastatic. Indeed, there is the possibility that both tumors might be separate, that is, autochthonous in origin. This question is of more than academic interest, for the postulated origin of these tumors is important in prescribing treatment. Unfortunately, the problem is not completely resolved, although most would favor a metastatic origin.

Radiation therapy is the treatment of choice, and good results can often be obtained. In fact, these tumors can be considered radiocurable. Because of this, and because of the fact that the anterior or posterior lesion may be roentgenographically elusive in the initial stages, treatment to both sites is advisable. Our Cases 1 and 4 speak to this
point, but the real problem is whether to prophylactically treat the entire neural axis or to simply treat both areas of the third ventricle. If one favors the concept that the 2 tumors are autochthonous, radiation of the third ventricle alone would probably suffice. If, on the other hand, a metastatic process is invoked to explain the 2 tumors, it would be reasonable and desirable to irradiate the entire neural axis. However, even with this orientation, there are some who feel that such extensive radiation therapy is not always necessary, especially when there is a negative millipore filter examination of the cerebrospinal fluid.

In terms of differential diagnosis, we know of no other lesion which characteristically and simultaneously occurs at these 2 sites, and it is for this reason that we feel a presumptive diagnosis of atypical teratoma can be made without surgical exploration or biopsy. Although craniopharyngiomas, gliomas, adenomas, sarcoidosis, etc. can occur at either site individually, it is unusual to encounter any of these lesions at the 2 sites simultaneously.

CONCLUSIONS AND SUMMARY

Although we report only 4 cases, the striking similarity of clinical presentation and roentgenographic findings in these cases, and those reported by others, causes us to strongly consider this entity a distinct neuroendocrinologic and roentgenographic syndrome.

These patients suffer from double, possibly simultaneously arising, atypical teratomas and may present with symptoms referable to one or other of the lesions. However, the anterior lesion usually produces symptoms first and characteristically there is insidious, but progressive, onset of diabetes insipidus and hypopituitarism. The posterior lesion characteristically leads to abnormal eye signs consisting of loss of pupillary light reflex and loss of upward gaze (Parinaud's syndrome).

In addition, if the lesion is large enough, aqueduct obstruction and hydrocephalus occur. The anterior lesion, if large enough, may encroach upon the optic nerves and produce visual field deficits.

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