EYE SIGNS IN PINEAL TUMORS

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Tumors of the pineal body are rare. According to Cushing's figures, 0.7 per cent of his 2,000 intracranial tumors were pineal in origin. In spite of their rarity, however, certain clinical manifestations of growths in this region are of more than usual interest. Among these features are the disturbances concerned with pupillary activity, movements of the eyeballs and other ocular disorders. The paper here presented is devoted chiefly to a clinical study of these oculomotor and other related disturbances.

The material from which this information has been gathered consisted of 16 cases in which a diagnosis of pineal tumor was made at the Lahey Clinic during the years 1933 to 1944 inclusive. In 11 of the 16 patients the lesion was verified histologically either from tissue removed at operation or at autopsy. In the other 5 patients a presumed and almost certain diagnosis was made on the basis of the clinical evidence together with the finding of the characteristic filling defect in the posterior portion of the third ventricle as seen in the ventriculogram. These diagnostic features were supported by the demonstration of internal hydrocephalus and the complete relief of symptoms and signs following a decompression and roentgen therapy. In spite of the fact that it was not possible to verify the tumor histologically in these 5 patients, we feel that the clinical picture, the ventriculogram and the course following decompression and radiation therapy all support the diagnosis of pineal tumor with sufficient certainty to include them in this survey.

The surgical removal of a pineal tumor is an extremely difficult task and entails considerable risk. On the other hand, as Horrax and Daniels have pointed out, subtemporal decompression followed by radiation therapy offers a comparatively safe method of treatment which has proved highly satisfactory in several cases. For this reason it is highly important to obtain all available evidence bearing upon the diagnosis of a growth in the pineal region. The oculomotor and pupillary disturbances furnish considerable information along these lines.

Before taking up in detail the various ocular disorders that may occur with pineal tumors, it may be well to note briefly certain general features shown by patients harboring these lesions. By recalling the strategic position of the epiphysis just above the corpora quadrigemina (Fig. 1), one can predict with a good deal of accuracy the most frequent signs and symptoms resulting from a tumor of this structure:

1. Increased intracranial pressure, often acute, producing headache,
nausea, vomiting and papilledema. Mechanism: compression and obstruction of the aqueduct of Sylvius with resulting internal hydrocephalus.

2. Pressure on the corpora quadrigemina, giving rise to:
   (a) Eye signs.
       (1) Impaired pupillary reactions.
       (2) Limitations of extra-ocular movements, especially conjugate movements upward.
       (3) Nystagmus.
       (4) Strabismus.
   (b) Central deafness. This is now believed to be due not entirely to pressure on the inferior colliculi but also to involvement of the lateral lemnisci.

3. Cerebellar signs, by transmitted pressure downward against the tentorium.

In addition to the foregoing features, certain other general disturbances of function may be present. These are:

1. Possible endocrine dysfunction in the form of macrogenitosomia praecox. This is a relatively infrequent condition and, when present, has been observed only in males under the age of puberty. Of the 6 patients under the age of fifteen in this series, only one (C.C.) showed this syndrome. In Russell and Sachs's review of the literature there were 17 patients under fifteen years of age with the diagnosis of a pineal tumor. Of this number, 3 presented the clinical picture of macrogenitosomia praecox.
2. Diabetes insipidus. Five of our 16 patients (31 per cent) presented this picture, while it was present in 15 of the 58 cases (26 per cent) reviewed by Russell and Sachs.

3. Dystrophia adiposogenitalis. The symptoms suggested by this descriptive term are infrequently seen in patients with tumors of the pineal body. Inasmuch as a rare case has presented this syndrome, we are including it here for the sake of completeness. In our series there was but one patient (M. J. K.) who was even questionably obese. The remaining patients presented no evidence of a Fröhlich-like syndrome. Marburg\(^6\) believed that the adiposity sometimes seen in patients with pineal tumors was the result of an overfunctioning pineal body. Other investigators have concluded it was due to a hypofunctioning pineal body. Cushing accounted for the adiposity by attributing it to changes in the hypophysis as a result of increased intracranial pressure from the usually marked internal hydrocephalus. The last explanation seems the most logical in view of the fact that it is based on pressure changes, which are known to take place intracranially with these tumors, and in no way dependent on the questionable hormonal influences of the pineal. That the pineal body is capable of any secretion has been seriously doubted by many investigators, and this is still a debated issue. The experimental investigations of Horrax\(^3\) and others, notably Foà,\(^2\) supported by clinical evidence would seem to suggest that the organ might have some endocrine function up to the time of puberty. If present, this function would appear to be concerned with inhibiting physical and mental maturity. A tumor of the pineal body in a patient who has not yet reached the age of puberty has been assumed to have destroyed this inhibiting influence and to have allowed the precipitation of precocious maturity. The pros and cons of this question were considered at some length by Horrax and Bailey.\(^4\)

Returning now to the specific ocular disturbances which form the main theme of this paper, the incidence and types of these disorders in our 16 patients are presented in Table 1 and they are summarized in Table 2. From these tables it can be seen that a comprehensive examination of the eye is likely to prove highly important in patients suspected of harboring pineal tumors. However, it should be stressed that the routine study of the eye that is included as a part of every thorough neurologic examination is sufficient to discover these signs.

To understand more fully the eye signs in cases of pineal tumor it may be helpful to review briefly the location of some of the structures involved. It can be seen from Fig. 2 how compression of the corpora quadrigemina by a pineal tumor could upset the function of the third and fourth cranial nuclei. The nucleus of the sixth nerve has less chance of suffering any direct damage by a growing pineal tumor, but inasmuch as greatly increased intracranial pressure is a prominent feature in these patients, sixth nerve palsies are frequently encountered (25 per cent of our cases).

Since certain clinical features of pineal tumors concern the pupillary and
TABLE 1
Incidence and types of eye signs in 16 cases of pineal tumor

<table>
<thead>
<tr>
<th>Patients</th>
<th>Appearance</th>
<th>Pupils</th>
<th>Reaction</th>
<th>Diplopia</th>
<th>Nystagmus</th>
<th>Limitation of</th>
<th>VI Nerve</th>
<th>Papilledema</th>
<th>Visual Fields</th>
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<tbody>
<tr>
<td></td>
<td>Light</td>
<td>Accommodation</td>
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</tr>
<tr>
<td>1. M.H.</td>
<td>Dilated L&gt;R</td>
<td>Poor</td>
<td>Good</td>
<td>None</td>
<td>None</td>
<td>Upward</td>
<td>Left, occasional</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>2. Y.N.</td>
<td>Normal</td>
<td>Poor</td>
<td>Good</td>
<td>None</td>
<td>Occasional to left</td>
<td>None</td>
<td>Right</td>
<td>5-6 D. bilateral</td>
<td>Normal</td>
</tr>
<tr>
<td>3. C.B.</td>
<td>Dilated</td>
<td>Poor</td>
<td>Poor</td>
<td>None</td>
<td>None</td>
<td>Upward</td>
<td>None</td>
<td>? Early</td>
<td>Normal</td>
</tr>
<tr>
<td>4. G.B.</td>
<td>Dilated</td>
<td>Poor</td>
<td>Good</td>
<td>None</td>
<td>On lateral gaze</td>
<td>Upward</td>
<td>None</td>
<td>None</td>
<td>Slightly constricted</td>
</tr>
<tr>
<td>5. B.S.H.</td>
<td>Normal</td>
<td>Good</td>
<td>Good</td>
<td>On left lateral gaze</td>
<td>On lateral gaze bilateral</td>
<td>None</td>
<td>Slight left</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>6. M.P.</td>
<td>Dilated</td>
<td>Poor</td>
<td>Poor</td>
<td>None</td>
<td>None</td>
<td>? Upward + Lateral</td>
<td>None</td>
<td>4 D. bilateral</td>
<td>Normal</td>
</tr>
<tr>
<td>7. M.J.K.</td>
<td>Normal</td>
<td>Good</td>
<td>Good</td>
<td>None</td>
<td>Slight on lateral gaze</td>
<td>None</td>
<td>None</td>
<td>4-5 D. bilateral</td>
<td>Normal</td>
</tr>
<tr>
<td>8. R.M.</td>
<td>Normal</td>
<td>Fair</td>
<td>Good</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Sec. optic atrophy</td>
<td>Normal</td>
</tr>
<tr>
<td>9. E.P.</td>
<td>Dilated</td>
<td>Good</td>
<td>Good</td>
<td>Occasional</td>
<td>On lateral gaze</td>
<td>None</td>
<td>None</td>
<td>4 D. bilateral</td>
<td>Normal</td>
</tr>
<tr>
<td>10. C.C.</td>
<td>Normal</td>
<td>Poor</td>
<td>Good</td>
<td>Frequent</td>
<td>On lateral gaze</td>
<td>None</td>
<td>Right</td>
<td>3-4 D. bilateral</td>
<td>Normal</td>
</tr>
<tr>
<td>11. J.H.</td>
<td>Normal</td>
<td>Good</td>
<td>Good</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>5 D. bilateral</td>
<td>Left temporal defect</td>
</tr>
<tr>
<td>12. B.N.</td>
<td>Normal</td>
<td>Good</td>
<td>Good</td>
<td>None</td>
<td>None</td>
<td>Upward</td>
<td>None</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>13. B.P.</td>
<td>Normal</td>
<td>Good</td>
<td>Good</td>
<td>Frequent</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>4-5 D. bilateral</td>
<td>Normal</td>
</tr>
<tr>
<td>14. S.F.</td>
<td>Normal</td>
<td>Good</td>
<td>Good</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Bitemporal hemianopsia</td>
</tr>
<tr>
<td>15. P.D.</td>
<td>Normal</td>
<td>Absent</td>
<td>None</td>
<td>None</td>
<td>Upward and lateral</td>
<td>None</td>
<td>None</td>
<td>Bilateral</td>
<td>Normal</td>
</tr>
<tr>
<td>16. P.A.P.</td>
<td>Normal</td>
<td>Good</td>
<td>Good</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Normal</td>
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Oculomotor apparatus, a brief review of the neurologic mechanism involved during normal and impaired function of this apparatus may serve a useful purpose. The nucleus of the third nerve has several parts (Fig. 3). The lateral nuclei are concerned with the function of the extrinsic muscles of the eye, while the Edinger-Westphal nucleus controls accommodation and innervation of the constrictor pupillae. Winkler9 believes the Edinger-Westphal nucleus has to do with synergic movements of the eye, especially
upward associated movements, in addition to its pupillary action. The afferent arm of the pupillary light reflex is shown in Fig. 4. After the long afferent fibers from the retina reach the pretectal region a synapse occurs and impulses continue to the Edinger-Westphal nucleus, then along the efferent arc to the ciliary ganglion and from there to the constrictor pupillae muscle. Interference with this arc by a lesion anywhere on the afferent side up to the synapse at the third nerve nuclei can cause an Argyll-Robertson pupil, that is, failure of the constrictor action of the pupil to light with preservation of pupillary constriction on accommodation convergence.

While in no instance in this series was there a true Argyll-Robertson pupil, it should be noted that in 50 per cent of the cases there was definite impairment of pupillary constriction to light with normal reaction on accommodation. In one patient (P. D.) there was no reaction of the pupils to light. The patient was a three-year-old baby and no mention was made of the reaction of the pupil on accommodation. Pressure of the pineal tumor and edema in the region between the lateral geniculate body and the pretectal area could cause this Argyll-Robertson-like reaction. Interference with the efferent parasympathetic pupilloconstrictor impulses from the Edinger-Westphal nucleus to the ciliary ganglion could explain the presence of dilated pupils. Such dilatation of the pupils was present in 31 per cent of our 16 cases.

Let us now turn to some of the mechanisms that are concerned with control of the extra-ocular movements. The cortical centers that control conjugate movements of the eyes have been identified in the posterior one-third of the second frontal convolution and near the visual center in the occipital lobe. The upward movement of the eyeballs is accomplished by the simultaneous action of the superior recti and inferior oblique muscles, both of which are innervated by branches of the third cranial nerve.

Table 2 summarizes the incidence of the chief eye signs noted in our series of 16 patients with tumors of the pineal body. In 56 per cent of the cases papilledema was noted, with an average of 4 diopters swelling of the

<table>
<thead>
<tr>
<th>Table 2: Summary of eye signs</th>
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<tr>
<td>Total Cases</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>16</td>
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</table>


disks. A high degree of increased intracranial pressure is a frequent finding in these patients and is easily explained by the location of the pineal body astride the aqueduct of Sylvius. Any tumor of this organ can blockade the aqueduct and thereby produce acute internal hydrocephalus. Although 9 of our patients (56 per cent) showed marked papilledema, in 5 of these the swelling of the optic disks and other general complaints associated with increased intracranial pressure were the only definite signs and symptoms to present themselves. A frequent clinical diagnosis in these cases was cerebel-
lar tumor, and in 5 instances exploration of the posterior fossa was carried out, as illustrated by the following case report.

M.J.K. A 25-year-old white, single, female teacher was seen on Jan. 20, 1944, having been referred by Dr. Katherine S. Andrews, of Boston, Massachusetts. The patient complained of unsteadiness in walking, headaches, nausea and vomiting for the past year. Her menstrual periods for the past two years had been definitely irregular and about two years ago she rapidly gained 15 pounds in a few months. During the month before her examination here the patient noted while reading that she would often be unable to see the next word. The history was otherwise negative. She had been seen at another clinic where a diagnosis of probable pituitary adenoma was made.

On examination here, the pupils were normal in size and reacted normally to light and in accommodation. Ocular movements were normal in all spheres. There were a few slow, nystagmoid jerks to the right and to the left. Examination of the fundi revealed 4 to 5 diopters of choking bilaterally, with marked venous engorgement. Romberg's test was markedly posi-
tive, with a tendency to fall to the right. The gait was ataxic, with a list to the right. There was marked hypotonia of the right arm. The remainder of the examination was negative. The clinical impression favored cerebellar neoplasm in the median line, with involvement of the right hemisphere as well. A ventriculogram was performed on Jan. 27, 1944. This revealed a defect in the posterior part of the third ventricle, with marked dilatation of the lateral and anterior third ventricles (Fig. 5).

Because of the marked cerebellar symptomatology and the absence of eye signs it was thought that the shadow in the posterior portion of the third ventricle represented the protrusion of a cerebellar tumor upward rather than a growth in the pineal region. Accordingly, a posterior fossa exploration was performed, but nothing abnormal was found. Consequently, at the same session, a right occipital bone flap was turned down and the region of the posterior third ventricle was explored after dividing the posterior part of the corpus callosum. A large pineal tumor was disclosed in this location, verified by frozen section, and a grossly complete removal of the tumor was achieved.

After a somewhat stormy convalescence, the patient made an excellent recovery, and has remained very well until the present time, 1½ years after operation.

Comment. This case illustrates how easily a pineal tumor can imitate a cerebellar tumor. It is representative of the 69 per cent of the cases in this series in which extra-ocular movements were well done and without limitation of gaze upward or in any other direction. Parinaud, in 1879, noted the difficulty that patients with lesions in the midbrain, especially near the colliculi, had in upward convergence. Certainly, the finding of paralysis in conjugate movement of the eyeballs above the horizontal is a most signifi-
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cant observation and often may be the deciding factor in the localization of a lesion. It should be remembered, however, that many tumors occur in the pineal region without impairment of extra-ocular movements (two-thirds of the patients in our series), and also that tumors in other situations may impair these movements by transmitted pressure.* In their review of 58 verified pineal tumors, 36 per cent of the patients were reported by Russell and Sachs to have had impairment of conjugate movement of the eyes upward. It should also be noted that the pupillary reactions in the case reported above were normal despite the fact that a large tumor was demonstrated in the pineal region. In retrospect, the only clue to the diagnosis of pineal tumor as against cerebellar tumor in this case was the misinterpreted defect in the posterior part of the third ventricle, as shown in the ventriculogram.

DISCUSSION

It is well to note once again that a comprehensive study of the eyes is an especially worthy portion of the general examination in any patient suspected of having a pineal tumor. Conscientious observation of the fundi, the extra-ocular movements and the pupillary reactions in these patients is likely to furnish invaluable information. This, when added to the history, the other physical signs and the ventriculogram, may be of the utmost assistance in formulating the diagnosis.

As has been stated above, the clinical manifestations of pineal tumors may closely resemble those of cerebellar neoplasms. During the study of these patients the differential diagnosis between the relatively frequent cerebellar tumor or the rare pinealoma may be quite uncertain. The cerebellar growth can readily be dealt with directly by exploration of the posterior fossa; the patient with a pineal tumor can usually be offered a better prognosis by subtemporal decompression and radiation therapy. The decision as to the location of the growth, therefore, is not an academic subject. Rather, it is vital to the question as to what type of operation and at what site it is to be undertaken.

The characteristic defect in the posterior part of the third ventricle seen in the ventriculograms of patients with pineal neoplasms must certainly be considered a very significant observation. In a number of cases this finding will prove to be decisive. But there will also be occasions in which even the ventriculogram will not be infallible. The information, however convincing, gained from any diagnostic procedure must be interpreted with due perspective and with due regard to the history and physical findings. A study of the eyes, as an integral part of the general and neurologic examinations in patients in whom a pineal tumor is suspected, can provide useful clues to the correct diagnosis.

* Not infrequently, patients with acoustic neuromas have considerable limitation of conjugate eye movements upward, and this impairment likewise occurs at times with tumors in the cerebral hemispheres.
SUMMARY

As a result of the study of this series of pineal tumors, the following data may be summarized:

1. The eye signs in 16 cases of pineal tumors are tabulated.
2. Dilated pupils were present in 31 per cent of the cases, and in 50 per cent there was impaired reaction to light. Reaction of the pupils on accommodation was impaired in only 12 per cent of the cases.
3. Papilledema was present in 56 per cent of the cases, with an average of 4 diopters elevation.
4. Upward gaze was limited in 31 per cent of the cases.
5. These tumors often present a clinical picture closely resembling that of cerebellar tumors.

CONCLUSIONS

Tumors of the pineal body can be diagnosed by clinical study and ventriculogram. An accurate diagnosis of these growths may save the patient the risk of an exhausting, perhaps fatal craniotomy undertaken at a different site on the basis of a mistaken diagnosis. By recognizing these neoplasms preoperatively one can offer the patient a less hazardous procedure, usually with an encouraging prognosis, by means of a subtemporal decompression and roentgen therapy. Appreciation of the eye signs produced by tumors of the pineal body will contribute to the earlier diagnosis of these growths.

REFERENCES