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CLINICAL AND PATHOLOGICAL STUDIES ON PINEAL TUMORS

BY

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ABSTRACT

We presented four cases of pineal tumors with autopsy findings. Our pathohistological studies demonstrated that the tumor of cases 1 and 2 was of the two-cell pattern, case 3 was teratoma with foci of the two-cell pattern, and case 4 was a mixed tumor of immature teratoma, embryonal carcinoma, choriocarcinoma and two-cell pattern. Cases 1 and 2 were histologically similar to a part of the tumor of cases 3 and 4.

The histological appearance of "pinealoma" had been discussed since 1923. In considering the results of our studies, we agree with the theory that the pineal tumor of the two-cell pattern arises from the germ cells migrating into the pineal region. The so-called "pinealoma" has to be discussed in more detail from this point of view, and we wish to emphasize that the correct diagnosis of pineal tumor should be based on the examination of all the elements of the tumor.

INTRODUCTION

Pineal tumors present various interesting symptoms and many pathological problems arise in respect to histogenesis, metastasis and classification. This report on our four autopsy cases of pineal tumor is concerned with the clinical and pathological studies, especially on their nature and origin.

CASE REPORT

CASE 1

This 25-year old man was admitted on June 23, 1966, in a lethargic state with nausea and vomiting. Six months previously, he had complained of diplopia and was operated on for strabismus without effect.

Examination. He was lethargic with urinary incontinence. The pupils were nonreactive to light and accommodation. Anisocoria and blurred disc of the left eye were present, the deep tendon reflex was hyper-

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active and the nuchal rigidity was marked. Examination of cerebro-spinal fluid (CSF) revealed a cell count of 58/3, 80.5 mg/dl of protein, 62 mg/dl of glucose and 123 mEg/l of Cl. The electroencephalogram (EEG) demonstrated a deep sleep pattern with a low voltage, irregular alpha waves and 1.5–2.0 c/s delta waves of high voltage. The skull films showed a 7×4 mm calcification in the pineal region.

Clinical Course. Five days after admission, he suddenly had a high fever (40.4°C) with hypersecretion of tear and sweat, and the muscle rigidity of the four extremities increased markedly. At that time, lumbar puncture in a recumbent position showed bloody CSF and an initial pressure of 460 mm. He was treated conservatively. Gradually he improved being able to eat in the bed and walk without help. On October 16, 1966, he was discharged, but three days later he became lethargic again with tinnitus and hearing loss on the left side and was readmitted on October 31. Plain craniograms revealed the sella turcica being destroyed considerably. In February, 1967, his condition deteriorated with decerebrate rigidity. He died on April 5, 1967.

Pathological Findings. Brain was edematous, 1650 g in weighMt. The pons and medulla oblongata were partially necrotic. The tumor was of the size of a small hen egg and situated to the quadrigeminal plate. Moreover, the papillary and/or infiltrative growths were noted along the surface of the wall of dilated right and left ventricles, third ventricle, aqueduct and arachnoid membrane of the pons (Figs. 1 and 2). Bleeding and necrosis were found in the tumor and its surrounding tissue. Microscopically, the tumor showed basically a mosaic pattern consisting of spheroidal cells and small lymphoid cells (Fig. 3). Large cells had a clear ovoid nucleus with distinct eosinophilic nucleoli and a cytoplasm without the blepharoplast. The small cells crowded along the connective tissue among the large

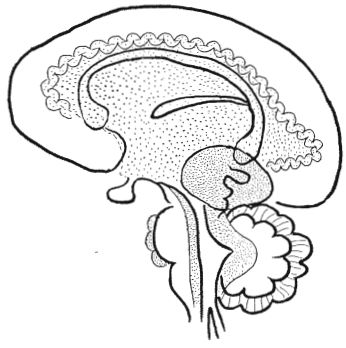


Fig. 1. Case 1.

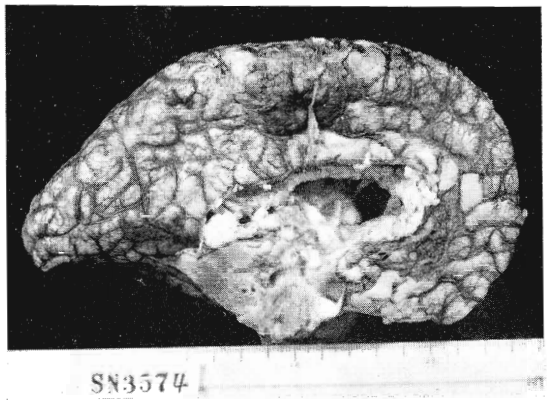


Fig. 2. Case 1.

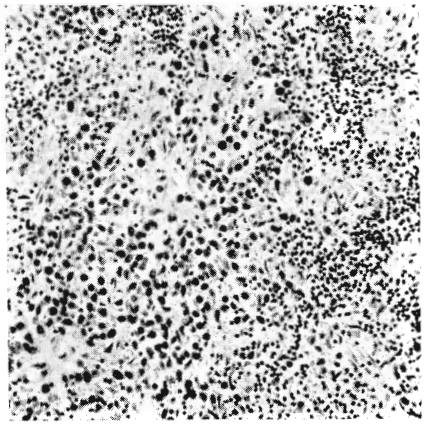


Fig. 3. Case 1. H.E. ×100

cells were poor in cytoplasm and had a round, strongly basophilic nucleus, and mitoses were observed frequently. Such a histological picture was seen in not only the quadrigeminal region but also in the pineal region, as well as in the right and left ventricles, aqueduct and the arachnoid membrane of the pons.

CASE 2

This 19-year old man was admitted to our clinic on March 24, 1966, complaining of nausea, vomiting, headache, diplopia, bilateral tinnitus and ataxic gait.

Examination. Consciousness was clear. He had nuchal rigidity, bilateral sluggish light reflex, right abducens paresis, Parinaud's sign, left facial paresis and left hearing loss. The deep tendon reflex was markedly increased, especially in the right extremities, with pathological reflexes bilaterally. The CSF initial pressure was 410 mm H_2O by lumbar puncture. Plain craniogram demonstrated an 8×5 mm calcification in the pineal region. Angiogram showed an upward displacement of the internal cerebral vein. Pneumoventriclography revealed a large defect in the third ventricle and a moderate ventricular dilatation. As mentioned above, we diagnosed this as the tumor in the quadrigeminal region developing into the third ventricle.

Clinical Course. Five days after admission, a ventricular drainage was performed. The V-A shunt was carried out on May 18, 1966. He improved being able to walk without help and was discharged on June 10. But he was readmitted in a comatose condition, which occurred after a clonic convulsion. At that time both pupils were mydriatic and nonreactive to light. The deep tendon reflex was exaggerated and his posture

showed decerebrate rigidity. Then nasal tube feeding was begun, but his condition became worse with hiccup and hyperperspiration. On August 15, 1966, craniotomy and partial intracapsular removal were performed, but he expired seven days after the operation.

Pathological Findings. The tumor lay on the midline from the pineal region to the interthalamic adhesion, attached to the fornix and the floor of the third ventricle. It was encapsulated and of the size of pigeon egg. A yellowish growth of 5 mm in diameter was found in the infundibulum. The pineal body was intact (Figs. 4 and 5). The histological appearance was of the two-cell pattern as seen in case 1. Areas of large cells were lobulated by the connective tissues including the small lymphoid cells. Mitosis was moderately frequent (Fig. 6). A relatively high vascularity

Fig. 4. Case 2.

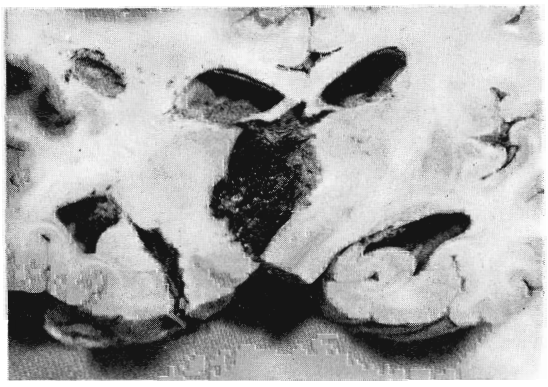
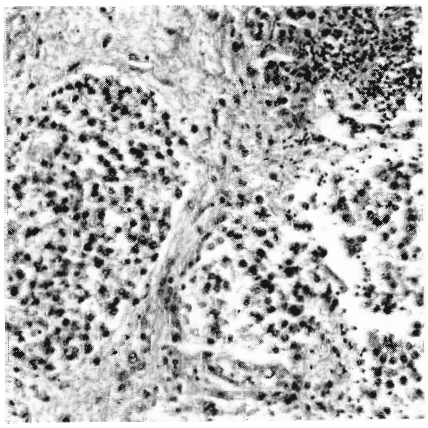
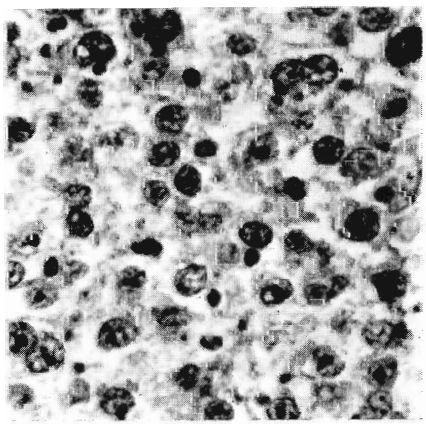


Fig. 5. Case 2.



a. H.E. ×100



b. H.E. ×400

Fig. 6. Case 2.

and bleeding were seen in the tumor. The tumor in the infundibulum showed histologically the same pattern.

CASE 3

A 6-year old boy was hospitalized on March 1, 1967, with a chief complaint of vomiting. He was expressionless and with poor nutrition, and the skin was slightly dry.

Examination. Bradylalia was noted, but his answer to the questions was correct. Light reaction was sluggish bilaterally and a left abducens paresis was seen. The abdominal reflex was depressed especially on the left. The CSF protein was 30 mg/dl. The EEG was of abnormal pattern with a high voltage, irregular delta waves and mixed spikes. Plain craniogram showed digital markings and dilatation of the sella turcica. By the angiogram, the anterior cerebral artery was markedly unrolled, and the distance between the posterior cerebral arteries was widened in the P-1 portion by the A-P view of the vertebral angiogram.

Clinical Course. The V-A shunt was performed on March 13, 1967. Subsequently he was relieved from headache and vomiting. But on April 16 he became lethargic and suffered from hearing loss, left hemiparesis and Parinaud's sign. Nasal tube feeding was begun from May 9, but afterward his condition alternated between remission and exacerbation. On December 15, with a diagnosis of a cystic tumor, evacuation of the cyst was performed. A yellowish clear fluid of about 150 cc was aspirated and ventricular drainage was performed. But he died, two days later, of postoperative intraventricular hemorrhage.

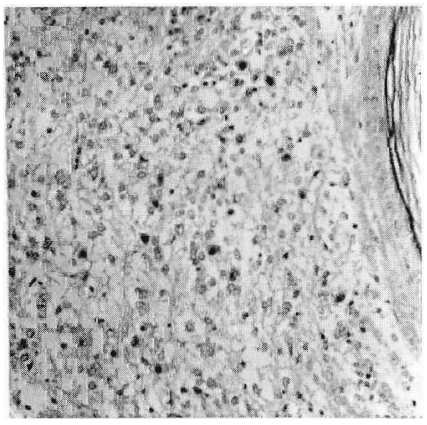
Pathological Findings. Brain edema and congestion were striking. Excessive bleeding, which was responsible for the death, was found in the right and third ventricles. A fist-sized cystic tumor occupied the entire third ventricle. The cyst was devided into several parts by a membranous wall, along which three massive tumors were seen. They were of the size of a pea or the tip of the small finger and contained a few hairs. The pineal body could not be found (Figs. 7 and 8). Microscopically, the tumor was a teratoma arising from the three germinal plates and consisting of the bronchus, epidermis, sweat gland, sebaceous gland, cartilage and nerve tissue. Between the well-differentiated organs or tissues. there was a two-cell pattern tumor consisting of large spheroidal cells and small lymphoid cells (Fig. 9). The pineal body could not be found histologically, too. The pituitary gland was intact.

CASE 4

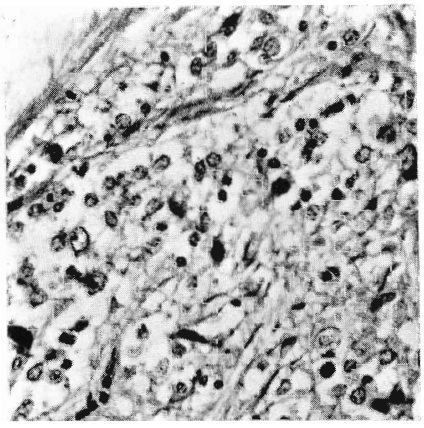
This 19-year old man had suffered from polydipsia and polyuria since high school days. At the beginning of November 1967, he had a sudden

Fig. 7. Case 3.

Fig. 8. Case 3.



a. H.E. ×100



b. H.E. ×200

Fig. 9. Case 3.

onset of vomiting and headache. He was admitted to our clinic with brain tumor being suspected.

Examination. He was expressionless but occasionally fell into agony. He was not conscious of the disease and became delirious due to severe thirst. The cranial nerves were intact except for choked discs. The CSF pressure was 260 mm H_2O with a positive Queckenstedt's sign. The plain films demonstrated a calcification (6×4 mm) in the pineal region. The angiograms indicated an arterial displacement suggesting internal hydrocephalus.

Clinical Course. Two days after admission, the amount of urine was 7,000 cc. On that night he fell into coma with mydriasis and absence of light reflex. Tracheotomy was done immediately and a V-A shunt was performed subsequently. The postoperative condition was unchanged ex-

cept for a slight improvement in consciousness. But on January 1, 1968, he went into coma again and died three days later.

Pathological Findings. The brain weight was 1370 g. An encapsulated massive tumor was seen occupying the anterior two thirds of the third ventricle, adhering to the fornix. The tumor of walnut size occluded Monro's foramen and the right and left ventricles were dilated. In the infundibulum a small distinct tumor was present (Figs. 10 and 11). Microscopically the walnut-size tumor was an immature teratoma in which were seen various foci of embryonal carcinoma, choriocarcinoma, cartilages, tubular structure, epidermoid cyst and chorioepithelial tissue (Figs. 12 a, b, c). In the teratoma, the two-cell pattern and mosaic appearance similar to those of cases 1, 2 and 3 were detected (Fig. 12 d). The pineal body became a two-cell pattern tumor. The infundibulum and the posterior

Fig. 10. Case 4.

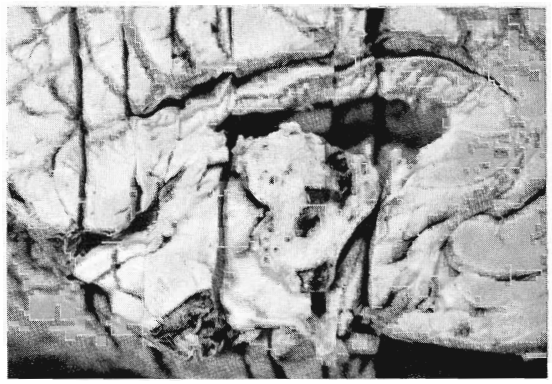


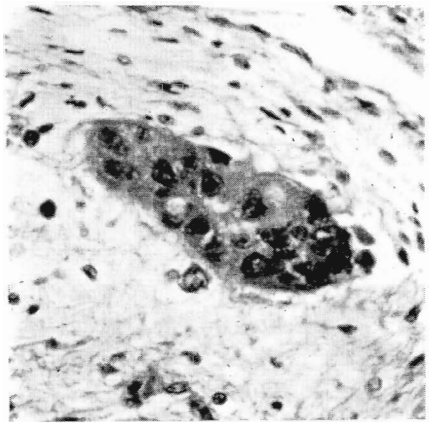
Fig. 11. Case 4.

lobe of the pituitary as well as the pineal body were infiltrated by the two-cell pattern tumor. Especially the posterior lobe of the pituitary was occupied by the tumor completely, which seemed to cause diabetes insipidus, though the anterior lobe was intact.

Discussion

In 1923 Krabbe[1] stated that the pineal tumors of the two-cell pattern were similar to the pineal body histologically and named them pinealoma.

In 1925 Horrax and Bailey[2] distinguished the spongioblastic type consisting of the embryonic cells of neuroglia from the pinealoma of the adult type originating from the pineal parenchymatous cells. To the contrary, in 1931 Globus and Silbert[3] advocated that the pineal tumors were put into a single group excluding from their classification the spongioblastic or neuroblastic form of pinealoma.



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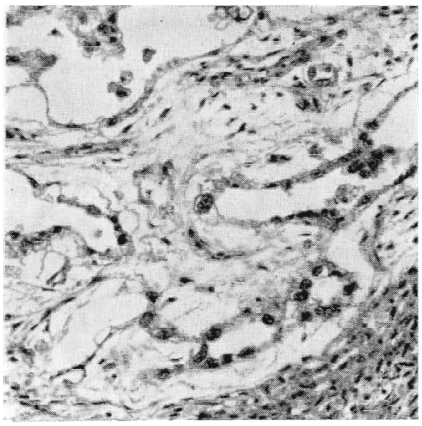

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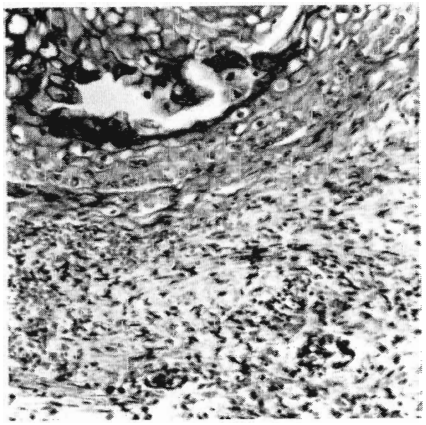
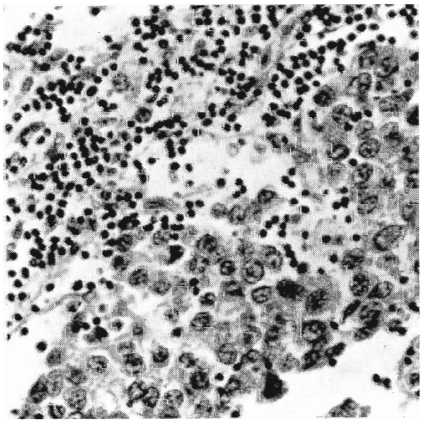


c. H.E. ×100



d. H.E. ×200

Fig. 12. Case 4.

In 1939 Baggenstoss and Love[4] added a new type of "pineal epedymoma" to the two types described by Horrax and Bailey. In the same year Mackey[5] also reported on the pineal tumor which seemed to arise from the anlages in the ependyma. These theories are based on the fact that the pineal parenchymal cells were derived from the same origin as th ependymal cells. Embryologically it is surmised that the ependyma may be the origin of a certain pineal tumor just as the pineal body.

In 1943 Russell and Sachs[6] mentioned that the term "pinealoma" should be reserved exclusively for those primary tumors of the pineal body, which contain the two types of cells and have the characteristic arrangement of a mosaic pattern, just like the pineal body is at the time of birth.

The morphologic resemblance of certain neoplasms to the seminoma of testis was already pointed out by Harris and Cairns[7]. In 1944 Russell[8] reported that a pure pinealoma was rare and that the large spheroidal cells of the "pinealoma" were different from the pineal cells, because the former had one or more conspicuous eosinophilic nucleoli, little affinity for silver carbonate and lack of the processes. Russell noted that the mosaic structure of the fetal pineal body consisted of pineal cells and their immature forms (smaller cells), while the mosaic appearance of the tumor consisted of large spheroidal cells and small lymphoid cells. So she pointed out that many cases of "pinealoma" resembled histologically the seminoma and had to be classified as an atypical teratoma. In fact, she said, the neoplasms described as "pinealoma" had parts resembling teratomatous changes and the teratoma included the pinealomatous foci, these foci being observed sometimes in the same specimen. With regard to the so-called ectopic pinealoma, she stated that this was nothing but an atypical teratoma. Russell's theory, being different from the classical argument, meant that the two-cell pattern tumors of the pineal region originated neither from the mature form nor from the immature form of the pineal cells and the neuroglias. So it was an epoch-making theory in all respects.

In 1947, in reviewing the literature, Friedman[9] found ten cases of atypical teratomas identical to the seminoma described by Russell. "Pinealoma" and seminoma showed the similar granulomatous reaction and sensitivity to irradiation. And the recent electron microscopic studies[17,18] revealed that the fine structures of both tumors showed the same appearance.

Then Friedman suggested that such a growth should be called germinoma because it arised from the primordial germ cells[9]. In regard to the germ cells, Witschi[19] reported that the germ cells originated from the yolk sac endoderm and migrated widely throughout the embryo before localizing in the gonadal ridges. The extragonadal germ cells sequestered gradually with normal morphogenesis[21], but the germ cells being sequestered in the midline structure[22] remained to become the origin of the germ cell tumors. So the germinomas were found not only in the testis and ovarium but also in the pineal body, third ventricle, suprasellar region and mediastinum. Moreover, in the retroperitoneum and the sacrococcygeal region, neoplasms originating from the germ cells are seen frequently[10,22].

On the other hand, Dixon and Moore[11] stated that, in the diagnosis of the germinal tumor, what is important is not to decide if the tumor is seminoma, embryonal carcinoma, teratoma or choriocarcinoma, but to detect what tumors compose the neoplasm. And they gave five classifications as follows:

I. Seminoma, pure.

II. Embryonal carcinoma with or without seminoma.
III. Teratoma with or without seminoma.
IV. Teratoma with embryonal carcinoma and/or choriocarcinoma with or without seminoma.
V. Choriocarcinoma pure or with either seminoma or embryonal carcinoma, or both.

In accordance with this criteria, Nishiyama[12] and his coworkers classified the germinal neoplasms of the central nervous system.

As mentioned above, the theories about the origin of the pineal tumor were reviewed, but the other authors published various other theories[13,14], making further studies necessary for a satisfactory explanation of the pineal tumors[15]. Nevertheless, it is reasonable to think that the pineal tumors of the two-cell pattern (including the so-called ectopic pinealoma) were classified into seminoma (germinoma), because of their resemblance to the latter in histological appearance, the localization and the sensitivity to irradiation.

Case 1 was the tumor of the two-cell pattern, which diffusely infiltrated the surface of the ventricular system. Such a case was reported as a pinealoma of the ependymal origin by Mackey and Kawabuchi[16], but in case 1, the large cells did not have blepharoplasts or rosette formation. From the clinical course, case 1 was typical of a germinoma which occurred primarily in the pineal region and disseminated all over the ventricular system.

In case 2, the tumor was of pigeon-size in the posterior part of the ventricle. But the pineal body was not affected. The same tumor was seen distinctly in the infundibulum. The large cells of the tumor were uniform and eosinophilic and had one or two nucleoli but no blepharoplast. These cellular features were similar to those of case 1. Case 1 and 2 were germinomas as described by Friedman, and according to the criteria of Dixon and Moore were classified as Dixon-Moore.I. (D-M.I.).

Case 3 was a teratoma with the foci of the two-cell pattern that resembled case 2, and consequently was typical of D-M.III.

Case 4 was a mixed tumor composed of immature teratoma in the anterior part of the third ventricle and the foci of the two-cell pattern in the pineal body, the infundibulum and in the posterior lobe of the pituitary. Moreover, it was interesting that the immature part of the mixed tumor included the foci of the embryonal carcinoma, choriocarcinoma and two-cell pattern, being typical of D-M.IV.

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