

Case Report and Ultrastructural Study of Intracranial Embryonal Carcinoma

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SUMMARY: *A case of a primary intracranial embryonal carcinoma, the first with ultrastructural study, is reported. The tumor was associated with precocious puberty in a 6½-year-old female. Characteristic embryoid bodies were present. At the ultrastructural level three cell types were noted: undifferentiated, differentiated, and intermediate types. The undifferentiated showed scanty cytoplasmic organelles and numerous free polysomes, while the differentiated cells contained*

well-developed mitochondria, Golgi apparatus, rough endoplasmic reticulum, and some contained secretory granules. The intermediate cells possessed dilated and irregularly-shaped mitochondria but still retained large numbers of free polysomes. The authors suggest that intracranial germ cell tumors be named in conformity with germ cell tumors in other sites, and that terms such as "ectopic pinealoma" and "atypical teratoma of the pineal" be used no longer.

RÉSUMÉ: *Nous rapportons le premier cas étudié au microscope électronique de carcinome embryonnaire primaire intracrânien. La tumeur était associée à une puberté précoce chez une fille de 6½ ans. Les corps embryoides caractéristiques étaient présents. Au niveau ultramicroscopique on nota trois types de cellules: non différenciées, différenciées et intermédiaires. Les cellules non différenciées montraient peu d'organelles cytoplasmiques mais beaucoup de polysomes libres alors que les cellules différenciées con-*

tenaient des mitochondries, appareils de Golgi, reticulum endoplasmiques bien développés et parfois même des granules sécrétoires. Les cellules intermédiaires possédaient des mitochondries dilatées et de forme irrégulière, mais contenaient cependant de nombreux polysomes libres. Les auteurs suggèrent de nommer les tumeurs germinales intracrâniennes selon le code employé pour les mêmes tumeurs ailleurs et de ne plus utiliser des termes tels "pinéalome ectopique" ou "tératome atypique de la pinéale".

INTRODUCTION

Primary intracranial germ cell tumors are rare. A subtype, embryonal carcinoma, occurs rarely in its natural location, testis and ovaries, but is even rarer within the cranium. Borit (1969) reported the first case occurring in the pineal region. Since then, other cases have been reported (Jellinger et al, 1970; Albrechtsen et al, 1972; Russell and Rubinstein, 1977), but ultrastructural studies were not included.

The purpose of this article is to report for the first time the ultrastructure of primary intracranial embryonal carcinoma.

CASE REPORT

A 6½-year-old female was admitted thirteen days prior to death for investiga-

tion of a six-week history of headache, vomiting, polyuria, polydipsia, and personality change and a seven-month history of precocious puberty. She had been mentally retarded since birth and attended a special school.

Physical examination showed an odd facies, with broadbridged nose, widening and bossing of forehead, and low-set flattened ears. Her fundi were normal. There was no vision in the left eye; a temporal hemianopic defect was noted on the right. She had suprapubic hair, pubertal fat distribution and a Tanner I breast development.

Skull roentgenograms showed suprasellar calcification. A skeletal survey showed advanced bone age. Electroencephalogram disclosed mild diffuse slow activity abnormalities without focal changes. An EMI scan showed a sellar and suprasellar solid tumor mass extending towards the left side along the optic nerve. It protruded towards the left clinoid process and was round without evidence of a cystic component. The ventricles were normal. (Fig. 1). Bilateral carotid angiogram showed a highly vascular intra- and suprasellar tumor.

Chromosome studies showed female karyotype. Serum cortisol was 0.8 mcg/dl (normal 6-20), 17 ketosteroids 0.54 mg (normal 3mg), FSH 4.2 mIU/dl (normal 2-12), T₄ 4.6 mcg/dl (normal 4.5-11.5), T₃ 31.6% (normal 35-45). Other laboratory tests were normal.

Ten days after admission, a bifrontal craniotomy was done and a suprasellar tumor was found extending under and flattening the optic nerve on the left side. The tumor was adherent to the optic nerve and extended inside the sella. The tumor was vascular and, because of the adhesions and invasion of the optic nerve, radical removal did not seem possible. Through a fenestration of the tumor capsule, partial intracapsular resection was done to obtain tissue for histological examination. The patient tolerated the procedure well, but postoperatively signs of progressive cerebral edema developed. The edema did not respond to dexamethasone and mannitol.

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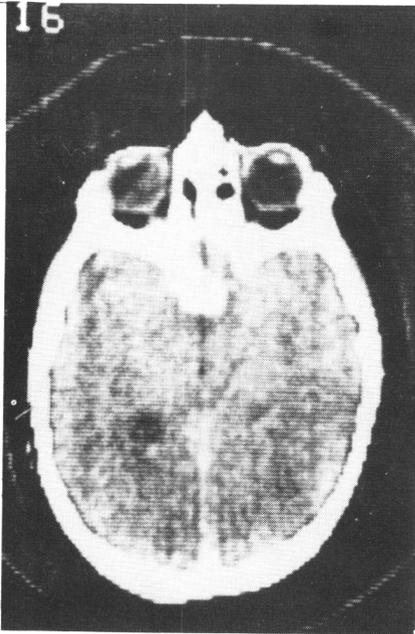


Figure 1—Computerized axial tomography scan without contrast enhancement shows a round mass in the anterior portion of the sella with extension to the left optic foramen.

Because of the malignant and inoperable nature of the tumor, it was decided not to resort to further measures. After evidence of tentorial and foraminal coning, respiratory arrest developed and the child died four days after surgery. Consent for necropsy was refused, but the possibility that the intracranial tumor was a metastases from a primary gonadal tumor was considered most unlikely.

PATHOLOGY

Method

Tissues for light microscopy were fixed in 10% buffered formaldehyde, processed to paraffin, cut at 5 micra, and stained with hematoxylin and eosin. Fresh minced tissue for electron microscopy was fixed in 2% cacodylate—buffered glutaraldehyde (pH 7.2 at 4°C), washed in 0.1M cacodylate buffer, and post fixed in 1% osmium tetroxide in 0.1M phosphate buffer. Tissues were then dehydrated in graded alcohol and embedded in Spurr's low viscosity medium. Sections were cut on Reichert OMU3 Ultramicrotome, stained with 25% methanolic uranyl acetate and Reynolds lead citrate, and examined with Philip's 201 electron microscope.

Microscopic

Sections examined by light microscopy showed large pleomorphic tumor cells and fragments of cortex. The tumor cells were arranged in various patterns; in some areas they were syncytial, in others there were sheets of well-defined cells, and in still others a perivascular and pseudoglandular pattern predominated. Well formed embryoid bodies were present (Fig. 2). The cytoplasm of tumor cells was abundant, eosinophilic with ill-defined margins. Some tumor cells showed well-defined distinct cytoplasmic borders. Cytoplasmic vacuoles were present in some cells. The nuclei were large, pleomorphic, vesicular, and basophilic. Bizarre large cells, some with single or multiple nuclei were interposed amidst other tumor cells. Most nuclei contained more than one irregular eosinophilic large nucleolus. Mitotic figures were abundant, including several abnormal forms. Cleft-like spaces were present between tumor cells and some amorphous eosinophilic material was noted in the scanty stroma.

Ultrastructurally, three types of tumor cells were seen: undifferentiated,

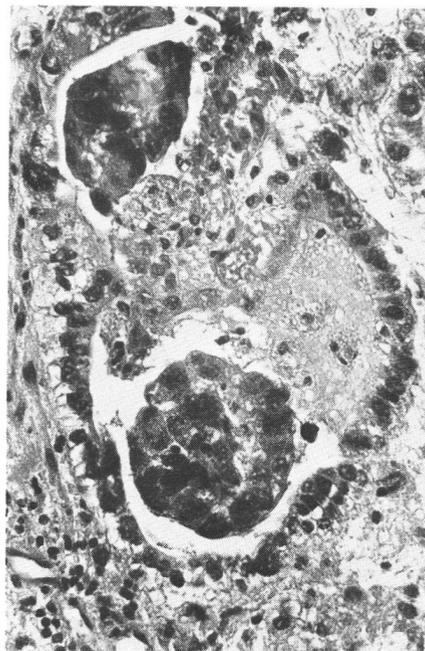


Figure 2—Section shows embryoid bodies. This is characteristically seen in embryonal carcinoma. Hematoxylin and Eosin x 290.

intermediate, and differentiated. The undifferentiated cells showed a marked alteration of nucleocytoplasmic ratio in favor of the nucleus. The cells had a single nucleus, some of which had such deep nuclear membrane indentations and infoldings that they appeared bizarre. The nuclear membrane was thick, the chromatin arranged in patchy fashion along the nuclear membrane and in the nucleoplasm. Large irregular multiple nucleoli were present. Cytoplasmic organelles were scarce. The Golgi apparatus and endoplasmic reticulum were scant, and mitochondria, though few, were more noticeable. Numerous free polysomes and ribosomes were present. Although cells appeared to be arranged in a syncytium on light microscopy, at the ultrastructural level all cells had distinct cytoplasmic membranes (Fig. 3), which in some areas were so apposed as to give a lattice-like appearance with few rudimentary microvilli (Fig. 4). The differentiated cells, which were equally numerous, showed similar nuclear pattern as the undifferentiated cells, but the cytoplasm was different. There were abundant mitochondria, Golgi



Figure 3—Embryonal carcinoma, undifferentiated. The cells are characterized by irregular and regular shaped nuclei with nucleoli. Lattice-like pattern of the cytoplasmic membranes is present. Although all organelles could be found after some search, the cytoplasm is typical showing large numbers of ribosomes and polysomes. Uranyl acetate and lead citrate x 3380.

apparatus was easily seen but free polysomes and ribosomes were markedly reduced in quantity. Glycogen granules were present. Some cells contained secretory granules (Fig. 5). Well developed microvilli were seen.

Cells of intermediate forms were recognized by cytoplasmic features



Figure 4—Microvilli. Notice tight junction between cells. Uranyl acetate and lead citrate x 20160.

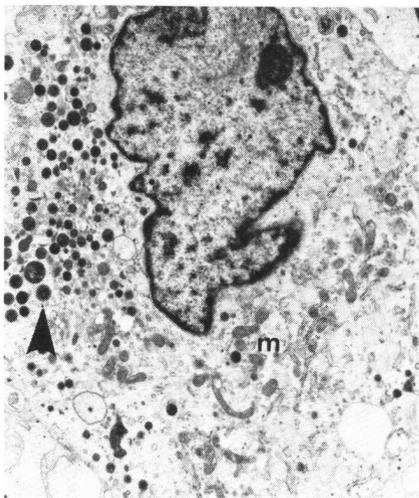


Figure 5—Embryonal carcinoma, differentiated. The cytoplasm contains well-developed mitochondria (M), rough endoplasmic reticulum and Golgi apparatus. Secretory granules (arrowhead) are also present. Uranyl acetate and lead citrate x 5080.

which included moderate number of mitochondria, Golgi apparatus, and endoplasmic reticulum. The mitochondria were large, dilated, and vacuolated. Numerous free polysomes and ribosomes were noted as in undifferentiated cells.

Material for light and electron microscopy was scant; all material submitted for electron microscopy was examined, but the embryoid bodies seen in the light microscope could not be found at the ultrastructural level.

DISCUSSION

Germ cell tumors are malignant neoplasms of the gonads which have been variously classified (Collins and Pugh, 1964; Dixon and Moore, 1953). The occurrence of seminoma, embryonal carcinoma, teratocarcinoma, and choriocarcinoma singly or together has further confused classification. Dixon and Moore (1953) offered the best classification. They regarded seminoma and embryonal carcinoma to be of germ cell origin but otherwise unrelated, with embryonal carcinoma arising from a totipotent cell capable of differentiating to teratocarcinoma and choriocarcinoma. This concept agrees with Teilum's (1965) (Fig. 6) and has received support from experimental

work (Kleinsmith and Pierce, 1964). Germ cell tumors have been described in extra-gonadal sites: within the cranium (Dayan et al, 1966; Russell and Rubinstein, 1977), sacrococcygeal (Friedman, 1951; Thiele et al, 1971), mediastinum (El-Domeiri et al, 1968), peritoneum, vagina and cervix (Allyn et al, 1971).

Primary intracranial germ cell tumors have been reported under a variety of names—atypical teratoma or germinoma when occurring in the pineal region and ectopic pinealoma when occurring in other midline intracranial sites, adding difficulty to understanding their histogenesis. Rubinstein and Russell (1977) classified tumors of the pineal region into four types. The first two are germ cell tumors; teratoma (typical and teratoid) and germinoma. The remainder, pineoblastoma and pineocytoma, glial forms and cysts are of neuroectodermal origin and not relevant to this discussion. We agree with Russell and Rubinstein (1977) who favor the term teratoma and germinoma for germ cell tumors of the pineal region, but would suggest that intracranial germ cell tumors be named according to their individual histologic subtype—teratoma, embryonal carcinoma, choriocarcinoma,

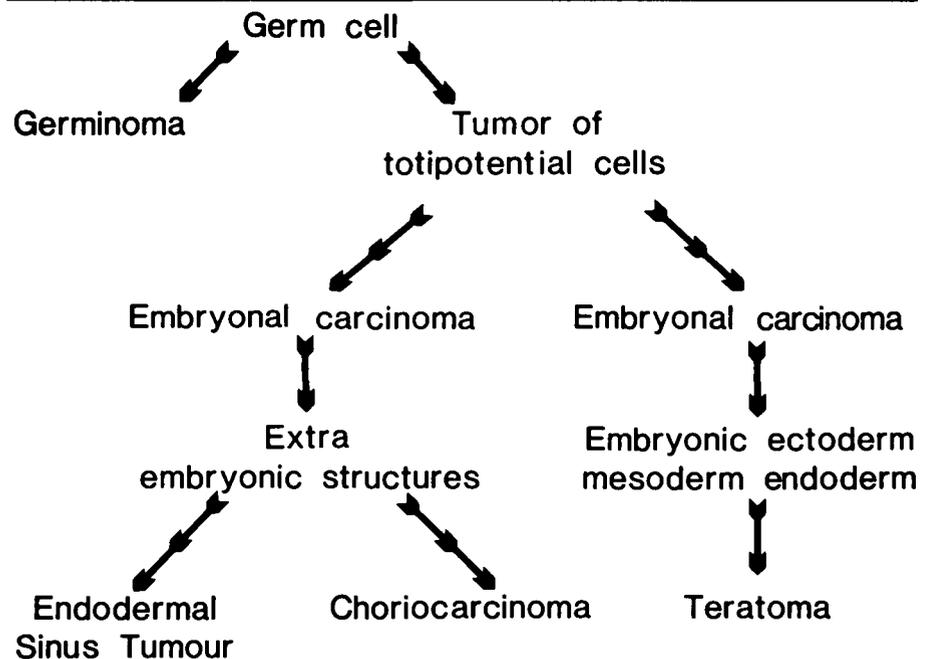


Figure 6—Diagrammatic representation of Teilum's concept of germ cell tumors.

and endodermal sinus tumor, rather than using the all-embracing term teratoma for this group of tumors. This would conform to the classification of Dixon and Moore (1953) and Teilum (1965).

These intracranial germ cell tumors were first recognized in the pineal region. It has become clear that they can arise in other midline intracranial sites, and the view that in these other sites they arise from ectopic pineal tissue or as metastases from a primary pineal tumor has been discounted (Russell and Rubinstein, 1977). Løken's case (1957) provided convincing evidence for the teratomatous nature of these extrapineal tumors. These extrapineal tumors should not be referred to as "ectopic pinealomas", but should be named as are other germ cell tumors. The origin of all intracranial germ cell tumors is speculative, but it may reflect a disturbance in the primitive streak.

Our case had specific histologic features which characterized it as embryonal carcinoma rather than a germinoma or other germ cell tumor. Embryonal bodies were present and the ultrastructure was similar to that of embryonal carcinoma of testis in man and mouse. (Pierce, 1966; Pierce and Beals, 1964).

Precocious puberty is a well recognized phenomenon that occurs with germinoma of the pineal region. Germinomas in any site are non-secreting tumors and the endocrine effects of tumors arising in the pineal gland have been attributed to their anatomic site, which interferes with the hypothalamic-pituitary axis. Other germ cell tumors can be secreting tumors and specific histologic characterization of these tumors may focus attention on their endocrine effects which can then be better studied. Choriocarcinomas can secrete human chorionic gonadotrophin (Ishiguro, 1975), endodermal sinus tumors can secrete alpha fetoprotein (Ballas, 1972; Talaman and Haije, 1974), and embryonal carcinoma can also elaborate alpha fetoprotein and human chorionic gonadotrophin (Kurman and Norris, 1976). Our patient showed precocious puberty but specific endocrine function was not studied during life. The location of

the tumor in this patient was in the parapituitary region, away from the pineal region. The presence, at the ultrastructural level, of secretory granules raises the question of whether this was a secreting tumor. Kurman and Norris (1977) found that precocious puberty was a feature of about half the pre-menarchal girls with ovarian embryonal carcinoma. However, the possibility that the tumor in our patient exerted an endocrine effect by its anatomic position in the hypothalamic-pituitary axis cannot be excluded.

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