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Primary Intracranial Germ Cell Tumours*

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Summary. A histological study has been made of a retrospective series of 17 primary intracranial germ cell tumours found in a collection of 3550 intracranial neoplasms (incidence of 0.48%). All, except for two differentiated teratomas (one extracerebral in a neonate and another in the lateral ventricle), were situated in the midline in persons aged 5 to 37 years (13 males, 4 females). 12 tumours were located in or originated from the (para)pineal region, two of them also invaded the hypothalamus, while three germinomas occupied the retrochiasmal (supra/intrasellar) region without pineal involvement. There were 11 rather pure tumours (7 germinomas, 4 teratomas of various differentiation) and six "mixed" neoplasms (2 germinomas with teratoid areas, 3 embryonal carcinomas containing elements of endodermal sinus tumour, choriocarcinoma and germinoma, and one teratocarcinoma with endodermal sinuses). Only one case showed prominent features of endodermal sinus tumour, but characteristic elements of this type were present in four other "mixed" tumours. All germinomas and germinomatous parts of mixed neoplasms showed an inflammatory reaction of varying intensity, in 6 cases associated with multinucleated giant cells, which may be related to the prognosis of these tumours (one patient with hypothalamic germinoma is alive 6 years after radiotherapy). The close structural similarities between the various types of intracranial and gonadal dysgerminomas and their frequent combination within the same tumour support the concept of a common histogenesis of germ cell tumours regardless of their site of origin. Difficulties of classification may arise from the rather frequent occurrence of "mixed" germ cell neoplasms.

Key words: Germ Cell Tumours — Dysgerminomas — Germinoma — Embryonal Carcinoma — Endodermal Sinus Tumour — Teratoma — "Mixed" Neoplasms.

Introduction

Germ cell tumours of presumably intracranial origin are rare. However, since Russell [32] postulated that many of the so-called pinealomas were in fact atypical teratomas, or more correctly, germinomas, there has been a considerable number of reports on germ cell neoplasms arising within the cranial vault. The majority of these tumours are germinomas and teratomas of varying degrees of differentiation with much less frequent occurrence of embryonal carcinoma, choriocarcinoma and endodermal sinus tumours. All these types may occur in pure forms or in various admixtures [1,4—6,10,17,27,28,33]. The definition and taxonomy of these tumours, which are almost exclusively situated in the midline with the pineal or parapineal regions and hypothalamus as the most frequent sites, have been commented upon by various authors who emphasized that the current—somewhat deviating—classifications of dysgerminomas of the gonads can be readily applied to all germ cell tumours regardless of the site of origin [5,11,12,28,29,37]. The structural and ultrastructural resemblance or even identity of intracranial germ cell tumours to those of the gonads is now well established [1,10—12,27—30,35,36].

* Dedicated to E. Frauchiger, on the occasion of his 70th anniversary.

The incidence of intracranial germ cell tumours ranges from 0.4% [9] to over 3.4% [1a]. While teratomas are known to form 0.2 to 0.5% of all intracranial growths [31,40], there is little information on the actual incidence and distribution of the other types of dysgerminomas. This is due to the fact that in most brain tumour series the pineal neoplasms composing from 0.4% [40] to 4.5% [1a] of the total have not been differentiated according to modern classification schemes.

In order to obtain further information on the incidence, localization and types of intracranial dysgerminomas we reviewed this group of neoplasms in the material of a neuropathological laboratory.

Material and Methods

From a total of about 3550 intracranial tumours listed on the files of the Neurological Institute of Vienna University—including autopsy material received from various sources in 1939—1943 and 1950—1972 and neurosurgical biopsies predominantly received from the Dept. Neurosurg., Univ. Vienna in 1939—1943 and 1964—1972—all neoplasms classifiable as germ cell tumours, in accordance with the current definitions [11,26,29,37], have been reviewed. Metastases from recognized primary tumours in the gonads or elsewhere have been rejected.

In three cases both biopsy and autopsy material was available, in eleven cases only autopsy material, and in three only biopsy material. No tumour was found in the gonads or other extracranial regions of any of the patients who came to autopsy.

The material was fixed in formalin. Paraffin sections were stained with haematoxylin-eosin, cresylviolet, Gomori's reticulin and van Gieson's elastic methods, some with PAS and Sudanblack B. Frozen sections were stained with Sudan III or IV, Sudanblack B, Oilred 0 and Giemsa. Frozen sections from two cases (Nr. 9 and 10) were examined by thin layer histochromatography according to a modified method of Curri *et al.* [8,15].

Results

A total of 17 germ cell tumours of probably primary intracranial origin has been found. The pertinent clinical and pathological features are summarized in Table 1.

The patients included 13 males and 4 females ranging in age from 13 days to 37 years, but the majority was in the second decade. All tumours except for two differentiated teratomas (case 1 and 2) were situated in the midline, six of them in the pineal region (Fig. 6A) and four in the third ventricle, probably originating from the (para)pineal area. Two growths occupied both the pineal and hypothalamus, while three were located in the retrochiasmal (supra/intrasellar) region and hypothalamus without affecting the pineal (Fig. 6B). Metastatic spread from a small pineal tumour was excluded by examination of serial sections of the pineal. The retrochiasmal neoplasms invaded the floor and walls of the third ventricle and infundibulum with almost complete replacement of the neurohypophysis and both infiltration and compression of the adenohypophysis (Fig. 5A). One endodermal sinus tumour (case 8) occupying the pineal and thalamus metastasized to the caudate nucleus (Fig. 4B).

The *clinical symptoms* of the cases of midline tumours were non-specific signs of increased intracranial pressure (case 4, 6, 8) or were those of a mass in the pineal region with visual symptoms, ataxia and obstructive hydrocephalus (case 7, 13, 14, 16 and 17) or were indicative of hypothalamic involvement including diabetes insipidus, small stature, hypogenitalism, optic atrophy and other pituitary dysfunctions (case 5, 9, 11, 12, 15, 27) or hyponatraemia and

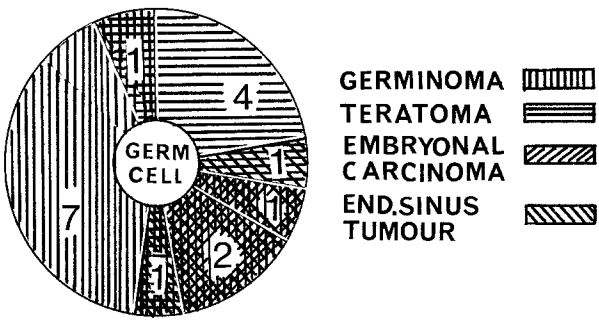

Fig. 1. Types of 17 intracranial germ cell tumours in the present material. The numbers within the areas of single or double hatching indicate the number of pure and mixed tumours of each type

abnormalities of plasma and urine osmolarity (case 10) attributable to hypothalamic lesions [10,22], while pubertas praecox was never observed. Radiology in the cases of supra/intrasellar germinoma disclosed no or only slight sellar enlargement [13]. The clinical duration before surgery or death in cases of germinoma, teratocarcinoma and embryonal carcinoma ranged from 2 to 18 months, but only in four exceeded 1 year (case 9—11, 14), while the others had symptoms for less than 6 months. Among six patients who underwent neurosurgical intervention, three died in the postoperative period, while two are still alive and well 6 years after surgery. These are a male with early infantile hemiparesis in whom at the age of 20 years a large cystic teratoma was removed from the right lateral ventricle (case 2), and a girl with suprasellar germinoma who, 6 years after surgery and deep irradiation therapy, shows no other clinical abnormalities than a short stature and hypogenitalism (case 12).

For the classification of the various types of dysgerminomas a scheme modified from that of Dixon and Moore [11] and in accordance with Teilum [37] was used and comparison was made with the British classification of testicular tumours [7]. The various types are shown diagramatically in Fig. 1 which indicates the proportions of "pure" and mixed tumours in the present material.

Among the 11 rather "pure" germ cell neoplasms there were seven germinomas and four teratomas of varying degrees of differentiation. The six "mixed" tumours (35.3%) included two germinomas with small teratoid areas and three "embryonal carcinomas", one consisting mainly of endodermal sinus tumour with small teratoid and germinomatous areas, while the two others showed combinations of undifferentiated embryonal carcinoma with endodermal sinus tumour and germinoma or choriocarcinoma.

Of the five *teratomas* only one was cystic, the others were solid. Two contained mainly differentiated and organoid elements of any of the three germ layers including cartilage, respiratory and squamous epithelium, exocrine glands, lobules of liver tissue, neuroepithelial rosettes or retina-anlage like areas (Figs. 2 A and B), and thus were classified as differentiated teratomas (case 1 and 2). Three other tumours in the third ventricle were considered as teratocarcinomas or malignant teratomas intermediate A [7]. In addition to some mature tissue they consisted mainly of undifferentiated solid or tubular areas, one with elements of endodermal sinus tumour (case 3), another (case 5) with bands and tubules of columnar epithelium resembling primitive medullary epithelium (Fig. 2 C and D) as observed in medulloepitheliomas [16,31].

Table 1. Clinico-pathological features of 17 cases of intracranial germ cell tumours

Case	Age Sex	Abstract clinical history	Macroscopic findings	Histologic findings	Classification
1 62-69[a]	13 days M	Prenatal hydrocephalus Caes. section, IIC PEG: large left tumour	A: Solid tumour (300 g) left cran. fossa excavating hydrocephalic brain	Mature or organoid tissue of any of the 3 germ layers	(Tri)teratoma differentiated (TD)
2 N139-67	20 years M	Early infantile left hemiparesis; IIC. Lives 6 years after surgery	B: Cystic tumour 10:8:6 cm right lateral ventricle	Similar	Teratoma differentiated (TD)
3 316-72	5 years F	5 mos a.e. mental changes hypotonia, facial paresis Scan: tumour basal ganglia. Died after shunt	A: solid tumour 8:6:5 cm occupying 3rd ventr. and right lateral ventr., expanding interped. fossa	Mature tissue mixed with undifferent. areas (primitive germ cells + endodermal sinuses)	Teratocarcinoma = Malignant teratoma intermediate A (MTIA) with endodermal sinuses
4 212-70	17 years M	Age 4: measles encephalitis? mental retardation, 2 mos a.e. left hemiparesis, IIC	A: solid hemorrhagic tumour 4:4:3 cm 3rd ventricle and pineal region	Mature tissue mixed with undifferentiated (solid + tubular) areas	Teratocarcinoma/MTIA without endodermal sinuses
5 37-44	12 years M	Hypogenitalism, short stature. Acute IIC	A: solid tumour 3:3:3 cm 3rd ventricle and pineal region	Mature tissue mixed with undifferentiated areas (columnar bands)	Teratocarcinoma/MTIA with medulloepitheliomatous areas
6 234-69[b]	13 years M	4 mos a.e. IIC, hemiparesis PEG: tumour pineal region, shunt, surgery, radiation	B: solid tumour 5:4:4 cm A: pineal region	Solid undifferentiated embryonal carcinoma + endodermal sinus + embryoid bodies + germinoma	Embryonal carcinoma = Malignant teratoma intermediate B/MTIB with endodermal sinus tumour and germinoma
7 45-56	19 years M	3 mos a.e. visual disorder, left hemiparesis, Parinaud syndrome, IIC, coma after PEG (internal hydrocephalus)	A: solid tumour 4:4:4 cm pineal region and right thalamus	Solid undifferentiated embryonal carcinoma + endodermal sinus + choriocarcinoma + germinoma	Embryonal carcinoma + endodermal sinus tumour + choriocarcinoma and germinoma
8 6-55	15 years F	Several mos a.e. somnolence, seizures, paresis, IIC	A: solid tumour 3:2:2 cm 3rd ventr. + pineal reg. + left thalamus; pea-sized metastasis right caudate nucleus	Endodermal sinus structures in myxoid stroma & glandular structures and rare germinomatous areas (pineal region)	Endodermal sinus tumour ("embryonal carcinoma") with teratoid areas and germinoma

9 241-72	12 years F	15 mos a.e. diabet. insip, short stature, opt. atrophy, Xray: slight excavation of sella; PEG: suprasellar tum.	B: Solid tumour 3:2:2 cm A: pineal region + hypothalamus invading neurohypophysis	Germinoma with endodermal sinus, glands, epithelial cysts, ependym. rosettes, giant cells	Germinoma with teratoid areas
10 259-72	17 years M	1,5 yr a.e. adynamia, diab. insip., hypernatremia, CSF: tumour cells. Xray: normal sella; PEG: suprasell. tumour	A: solid tumour 3:2.5:2 cm hypothalamus-neurohypophysis, aqueduct. Pineal region free !	Germinoma with occasional glands + tubules; severe IR with giant cells	Germinoma with some teratoid parts
11 966-71	27 years M	1 year a.e. diab. insipidus, Cushingoid, gynaecomastia, genital hypoplasia; PEG: suprasellar tumour	A: solid tumour 2.5:2:2 cm B: hypothalamus, supra-intrasellar-neurohypophysis; Pineal free!	Germinoma with severe IR and some giant cells	Germinoma
12 19-69	20 years M	5 months a.e. diabet. insip., visual disorders, optic atrophy; PEG: pineal tumour	A: cherry-sized solid tumour pineal region and post. hypothalamus, seeding into ventricular walls	Germinoma with severe IR and some giant cells	Germinoma
14 50-54	37 years M	Age 27 years seizures, optic atrophy, confusion, IIC. Died after PEG (hydroceph.)	A: cherry-sized tumour pineal region and Sylvian aqueduct	Germinoma with severe IR; some giant cells	Germinoma
15 N87-66	12 years F	Short stature, diabetes insip., Xray: normal sella. Living 6 years after surgery and irradiation!	B: gray solid cherry sized suprasellar tumour	Germinoma with polymorphous cells and severe IR	Germinoma
16 12-41	17 years M	2 months a.e. ataxia, diplopia, IIC. PEG: int. hydroceph., shunt	A: solid 3:2:2 cm tumour pineal area and roof 3rd ventricle	Germinoma with moderate IR	Germinoma
17 N279-66	12 years M	2 months a.e. diplopia, IIC. PEG: tumour 3rd ventr. Course unknown	B: gray 3:2:2 cm tumour pineal area and roof 3rd ventricle	Germinoma with polymorphous cells, with little IR	Germinoma

A = autopsy; B = biopsy
a.e. = ante exitum
IIC = increased intracranial pressure
IR = inflammatory reaction
PEG = pneumoencephalography.

[a] Published Lachmann *et al.* [20].
[b] Published Jellinger *et al.* [17].

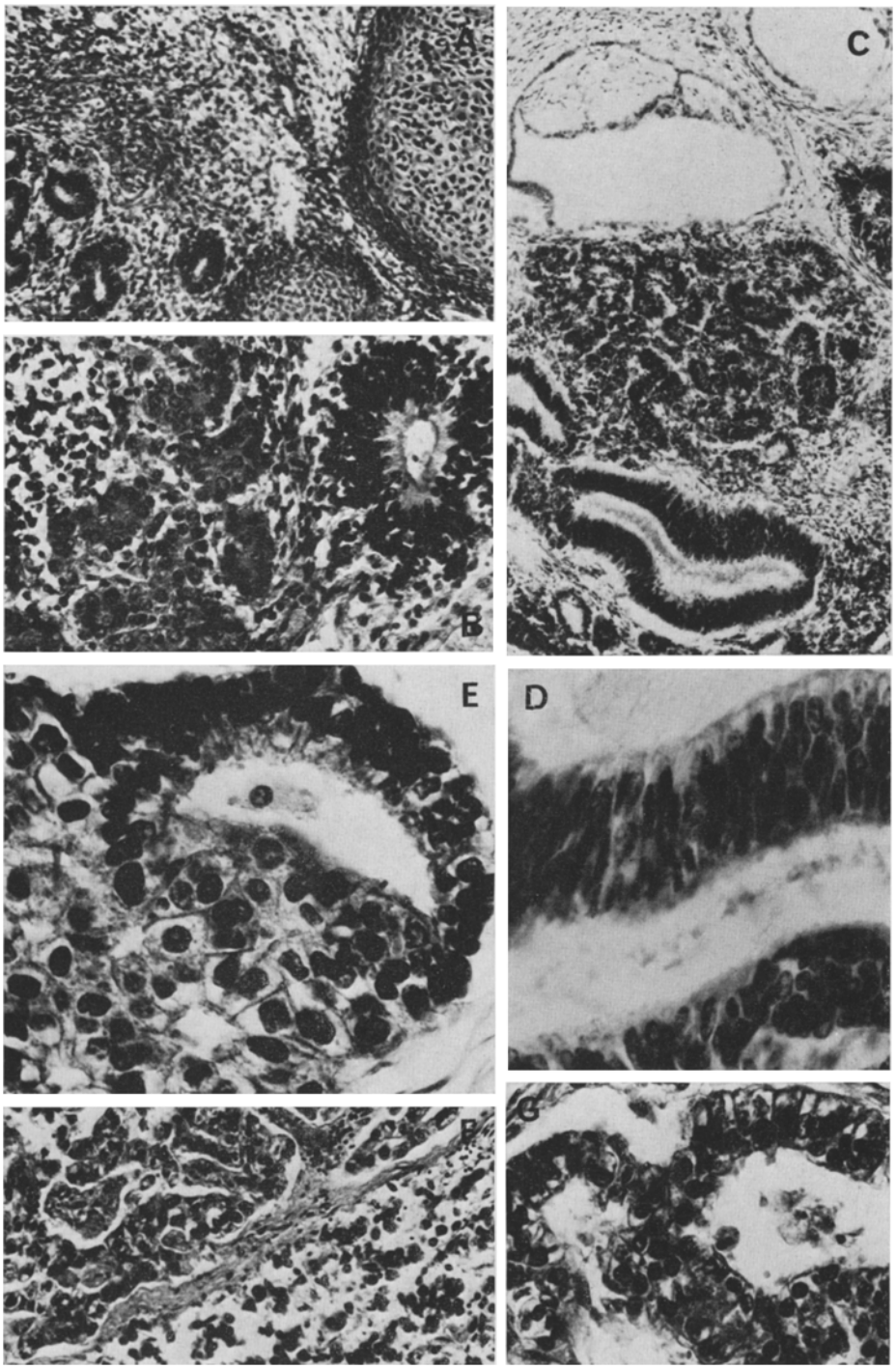

Fig. 2 A–G

Of the three growths classified as "*embryonal carcinoma*" of the pineal, only one consisted mainly of solid undifferentiated tissue with bands, glandular or papillary formations of tall vacuolated columnar cells, but also contained embryoid bodies and some areas of endodermal sinus tumour and germinoma (Figs. 2E—G). Another pineal tumour showed an admixture of embryonal carcinoma with PAS-positive and hyaline globules (Fig. 3C), embryonal adenocarcinoma (Fig. 3A), endodermal sinus tumour (Fig. 3E), embryoid bodies, choriocarcinoma with cytotrophoblasts and syncytiotrophoblasts (Figs. 3D and F), and germinoma (Fig. 3B). Only one case, a girl aged 13 years, showed a solid pineal growth with the prominent histological pattern of endodermal sinus tumour [37], characterized by endodermal sinus structures with mantling of vessels of yolk sac endoderm (Figs. 4A, D and E) within a myxoid reticular stroma resembling the "magma reticulare" (Fig. 4A). This tumour contained additional glandular structures (Figs. 4C and E) and small amounts of germinoma with calcified concrements (Fig. 4D).

Of the nine *germinomas* one contained additional endodermal sinus tumour elements, epithelial cysts and ependymal rosettes, presumably not derived from invaded ventricular walls or subependymal areas (Figs. 5B—G), while another retrochiasmal tumour showed small teratoid areas with tubular and glandular structures (Figs. 6D and E). All germinomas and the germinomatous areas in "mixed" tumours consisted of two distinct cell types: large spherical cells with acidophilic cytoplasm and central, vacuolated nuclei, frequently with large, prominent, PAS-positive nucleoli, and varying amounts of dark small lymphocytes in the stroma and around the tumour (Figs. 5B and D, Fig. 6F), while plasma cells were rare. The large cells showed varying degrees of pleomorphism and mitotic figures were frequently found. Six tumours showed a granulomatous inflammatory reaction with multinucleated foreign body type giant cells (Figs. 5B and F, Fig. 6C). Large hypertrophic astrocytes were present in the marginal zones of germinomas and were mixed with large tumour cells and lymphocytes in the surrounding regions. Occasional perivascular lymphocytic cuffings outside the tumour and neoplastic seeding into the leptomeninges and ventricular walls were observed.

In some germinomas, particularly in those with a strong inflammatory reaction and the occurrence of epithelioid or giant cells, there was a variable number of histiocytes, not infrequently showing considerable cytoplasmic deposits of easily soluble, sudanophilic and partly birefringent lipid material or with occasional lymphocytophagia. Histochromatographic examination of frozen sections of two germinomas stained with Sudan IV and Oilred 0 gave

Fig. 2A and B. Sections from solid, differentiated intracranial teratoma (300 g) excavating the left cerebral hemisphere in boy aged 13 days (case 1). A Islands of cartilage, glands and mesenchyma. H. & E. ×110. B Lobules of liver tissue and neuroepithelial rosette. H. & E. ×280

Fig. 2C—D. Sections from large teratoma of third ventricle in male aged 12 years (case 5). C Large epithelial-lined cysts, renal-like tissue, glands and papillary structures with columnar epithelium. C.V. ×65. D Bands of columnar epithelium with defined limiting membranes. C.V. ×500

Fig. 2E—G. Sections from embryonal carcinoma of pineal region in male aged 13 years (case 6). E Solid part with occasional tubules and gland-like structure composed of tall columnar epithelium. H. & E. ×500. F Endodermal sinus-like epithelial bands adjacent to germinomatous area. H. & E. ×120. G Bands of tall vacuolated columnar cells. H. &. E. ×270

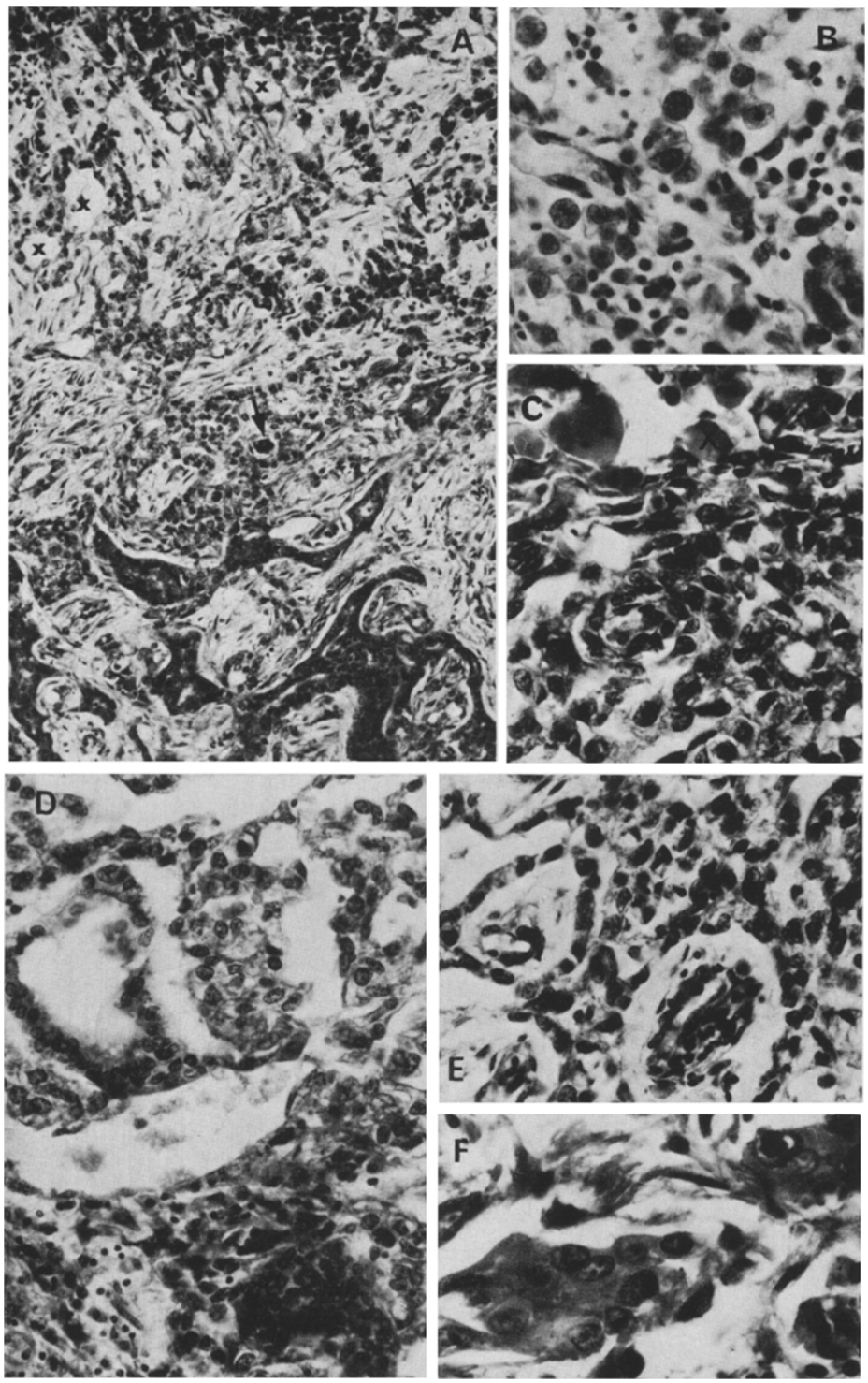

Fig. 3 A—F

similar results, indicating the presence of large amounts of cholesterol and esterified cholesterol, varying amounts of triglycerids and fatty acids, and traces of phosphatides. Loss of sudanophilia after chromatographic elimination of neutral lipids in the cytoplasm of histiocytes indicated that they were the favoured sites for lipids. From the available data, however, could not be concluded whether these lipid deposits in germinomas were primarily due to regressive changes or also resulted from active storage phenomena in histiocytes or other cells.

Discussion

A retrospective study of primary intracranial germ cell tumours, made in a series of about 3550 intracranial neoplasms, revealed a total of 17 such tumours, their incidence being 0.48%. This is in accordance with a recent survey of similar material in which dysgerminomas accounted for 0.5% of all intracranial growths [1], while in an other brain tumour series their incidence was considered to range from 0.39% [9] to 1.75% [19].

All our patients, except for two cases of germinoma, died or came to operation before the age of 20 years, and 76.5% were males, which is in keeping with the known age distribution and marked preponderance of males over females with ratios of 4—5:1 [1,10,28]. All tumours, except for two teratomas, were located in the midline, all but three of them in the pineal or parapineal region. Two pineal germinomas also invaded the hypothalamus, while three were situated in the supra and intrasellar region without affecting the pineal. This corresponds to the usual site of "ectopic pinealomas" [18,22a] or suprasellar germinomas [13,33,38]. Sixty to eighty percent of intracranial germ cell tumours are known to be situated in the pineal and parapineal region, while about 20% or more affect other areas with preponderance for the hypothalamus [1,10,28,31]. The lateral ventricle is a rare, but well documented site of intracerebral teratoma [14].

Germinomas, known to be the most common type of germ cell tumours [1,10, 11,26,28,31], accounted for more than half of the cases in the present series. Teratomas constituted less than one-third, but germ cell neoplasms of *mixed* type represented *35.3*%. The usual ratio of intracranial germinomas to teratomas of about 3:1 with an incidence of about 20% of "mixed" tumours [1,10,19,28] is considered to be similar to that of gonadal dysgerminomas. The combination within the same tumour of easily distinguishable and often well demarcated elements of two or more types of germ cell neoplasm has been repeatedly observed (see Introduction). A thorough histological review of the material of intracranial dysgermi-

Fig. 3 A—F. Mixed embryonal carcinoma (endodermal sinus tumour with choriocarcinoma) and germinoma in pineal region in male aged 19 years (case 7). A Mixture of germinomatous areas (top) with compact aggregates of undifferentiated cells, tubules and acini lined by cuboidal cells (*x*), endodermal sinuses (arrow) and areas resembling embryonal adenocarcinoma with papillary structures (bottom). H. & E. ×100. B Germinomatous part with large, polymorphic cells and lymphocytes. H. & E. ×380. C Aggregate of undifferentiated cells with PAS-positive hyaline globules (*x*) in stroma. PAS ×250. D Double-layered epithelial structure forming blastocyst-like embryoid body and adjacent darkly staining multinuclear syncytial cell resembling syncytiotrophoblast. H. & E. ×270. E Endoneural sinus structures with central blood vessel surrounded by layer of cuboid cells. H. & E. ×250. F Polyhedral multinuclear cells with clear cytoplasm and distinct cell borders resembling cytotrophoblasts. H. & E. ×380

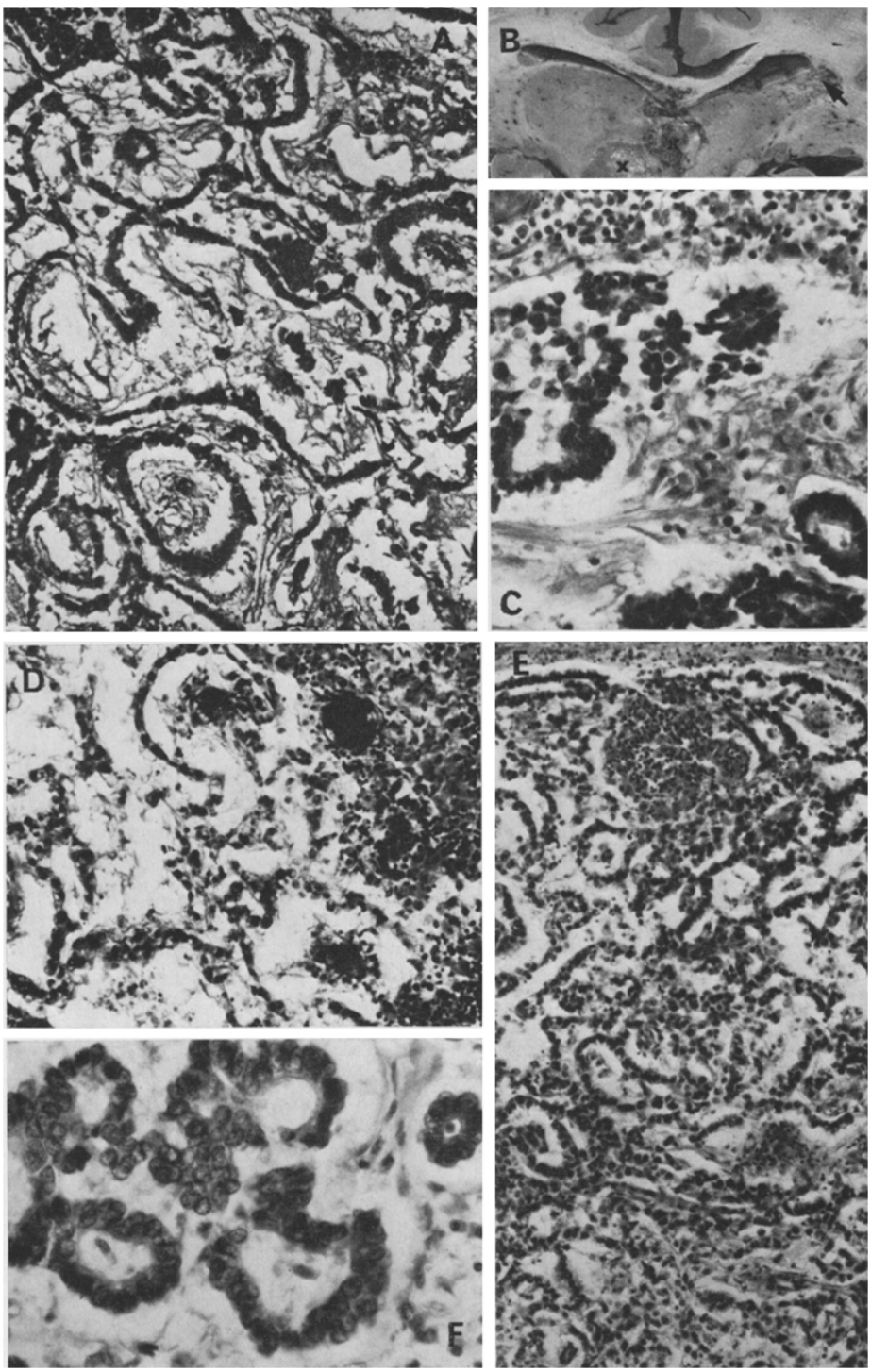

Fig. 4 A—F

nomas collected in this laboratory, however, has brought to light a considerable incidence of such "mixed" tumours which, on the other hand, increases the difficulties in their classification.

Areas of classical germinoma were observed in all but three cases, teratomas of varying degree of differentiation (case 1, 2 and 4). Although some of the germ cell tumours found in the pineal region almost completely replaced the pineal gland, small areas of pineal parenchyma diffusely invaded by tumour and containing acervulus were occasionally observed (Fig. 4D). However, none of the pineal dysgerminomas contained areas or cells resembling those seen in true pinealocytomas [10,31], and, indeed, no such combination has been reported in the recent literature [1,31].

Areas with the characteristic histological pattern of endodermal sinus tumour [37,38], considered as a specific ovarian growth of germ cell origin and as a counterpart to certain types of "juvenile embryonal carcinoma" [26] or yolk sac carcinoma of the infantile testis [29,37], have been observed in rare cases of intracranial dysgerminoma [4,5]. These elements were found to be present in five tumours or almost 30% of the present series, including one teratocarcinoma (case 3), one germinoma (case 9) and three "embryonal carcinomas" (cases 6, 7 and 8), one of which has been previously reported [17]. Although only one pineal tumour in a girl aged 15 years consisted mainly of this type of neoplasm (case 8), these findings agree with recent data reported by Albrechtsen *et al.* [1] who argued that growths with areas characteristic of endodermal sinus tumour may account for 0.1% of all intracranial neoplasms and about 10% of the midline tumours in the pineal and hypothalamus.

"Embryoid bodies", considered as rare features in both malignant gonadal teratomas [3,11,26,29,37] and intracranial germ cell tumours [1,5,27], were noted in two embryonal carcinomas of the pineal (case 6 and 7). One of them also showed trophoblastic differentiation with syncytial giant cells resembling syncytiotrophoblasts or cytotrophoblasts typical for choriocarcinoma which is a rare but well known form of pineal or hypothalamic dysgerminoma [6,18,27]. It is usually mixed with other types [5], while pure intracranial forms are rare [34].

Rare giant cells within dysgerminomas, indicating trophoblastic differentiation, are to be separated from multinucleated giant cells of the foreign body or Langhans- or Touton(?)-type which are not infrequently observed in germinomas. They were present in two-thirds of our small sample. They are usually associated with accumulation of small cells which do not differ ultrastructurally from lymphocytes

Fig. 4A—F. Pineal endodermal sinus tumour with germinoma in girl aged 15 years (case 8). A Areas showing perivascular structures of endodermal sinuses with loose vacuolated network and wide mashes lined by mantles and bands of epithelial cells in loose myxoid reticulum resembling "magna reticulare". H. & E. ×100. B Tumour occupying third ventricle and left midbrain (*x*) with metastasis in right lateral ventricle (arrow). C Glandular structures within loose mesenchymal stroma adjacent to germinomatous areas (top.). H. & E. ×250. D Area of endothelial sinus tumor adjacent to solid germinomatous areas with calcified concretions in pineal region. H. & E. ×100. E Oral pole of tumour showing complicated labyrinth of communicating cavities and channels with numerous endodermal sinuses. H. & E. ×100. F Glandular structures in other part of tumour. H. & E. ×400

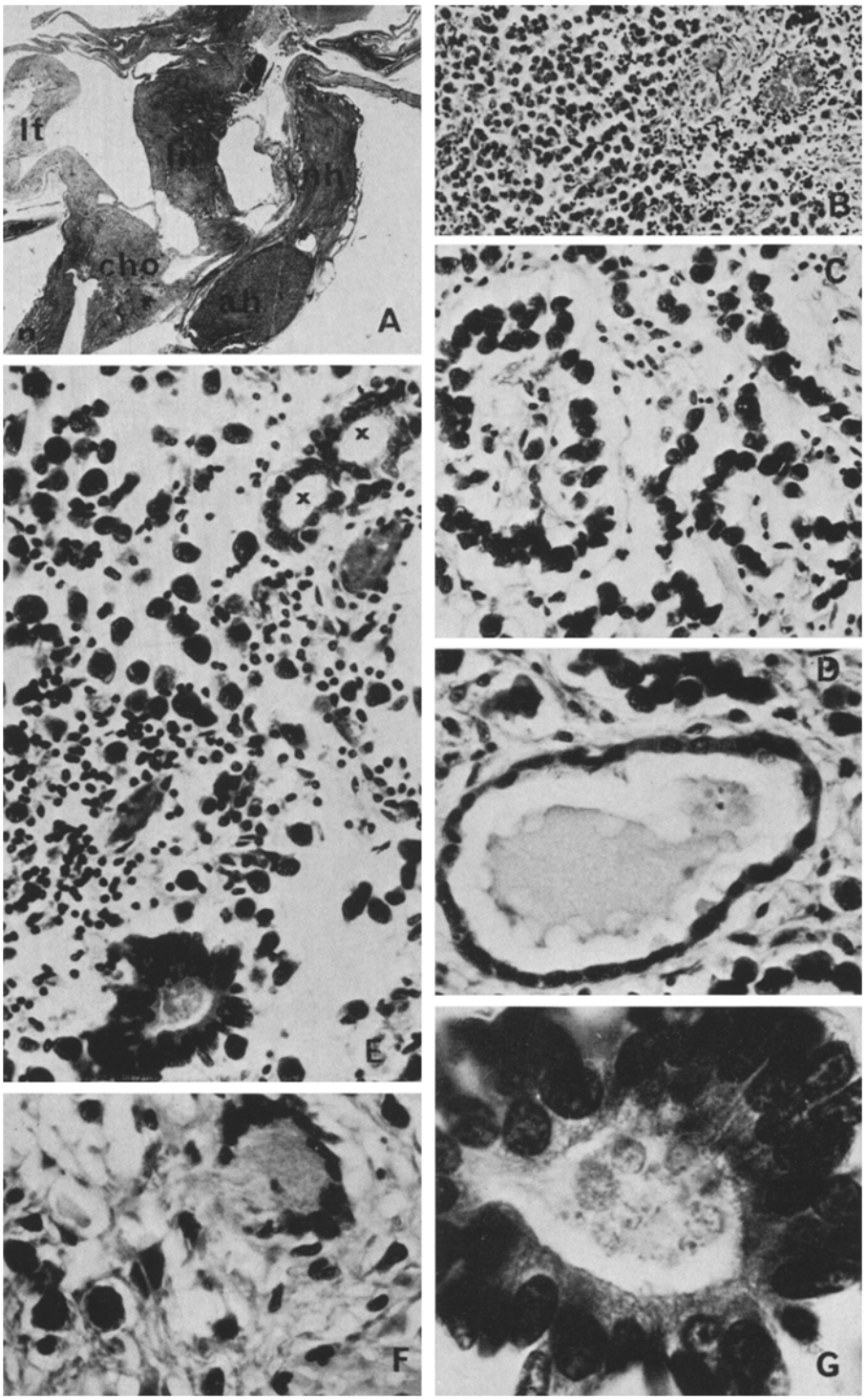

Fig. 5 A–G

[35] and, together with rare plasmocytes, are considered to be derived from blood cells [35]. Intermediate forms between the large seminoma-like tumour cells and the lymphocytes [18a] have not been confirmed. The lymphocytic infiltration is thought to be an inflammatory reaction probably due to some specific immune activity [11,23]. Its intensity and particularly its combination with a granulomatous (epithelioid and giant cell) reaction is supposedly related to the malignancy of the tumour [28]. Similar positive correlations between the prognosis (duration of survival) and the degree of lymphocytic infiltration have been reported in neuroblastomas [22] and gonadal seminomas [11]. Although no quantitative estimation of lymphocytic infiltration has been performed in the present material and in another small series of intracranial germinomas [28], we gained the impression that there was a different duration of clinical symptoms, before surgery or death, in cases with different degrees of inflammatory reaction. Cases of germinoma with teratoid areas (cases 9 and 10) and those with considerable lymphocytic infiltration and giant cell reaction apparently showed a more prolonged clinical history, up to 18 months, than did the rare instances with a less intensive inflammatory reaction (cases 15—17). The small sample, however, did not allow any statistical evaluation. The fact that one patient with a suprasellar germinoma is alive 6 years after deep radiotherapy (case 15) is consistent with the high radiosensitivity of germinomas [5a,10,22a,31].

The close structural and ultrastructural relationships between the various types of germ cell tumours of the gonads and of extragonadal sites, including the cranial vault, and their frequent combination within the same tumour, clearly demonstrated in this and other case series, support the concept of 1. the common origin of the various dysgerminomatous and teratoid elements from undifferentiated multipotential ("embryonal carcinoma") cells [11,26,29,37], and 2. a histogenetic relationship or even identity between the germ cell neoplasms of the brain and those in other sites including the gonads. That germ cells originate in the yolk sac endoderm and migrate widely through the embryo before localizing in the gonadal ridges is well established [25,39]. Very occasionally these wandering germ cells have been observed within the developing brain of the embryo [24] which is supporting evidence for the misplaced germ cell hypothesis first suggested by Askanazy [2]. However, further correlative biochemical, cytological and clinicotherapeutic studies are needed for a further confirmation of the suggested uniform histogenesis of gonadal and intracranial germ cell tumours.

Fig. 5A—G. Pineal and hypothalamic germinoma with teratoid structures in girl aged 12 years (case 9). A Sagittal section of supra- and intrasellar region showing replacement by tumour of infundibulum (*In*), neurohypophysis (*nh*) and compression of adenohypophysis (*ah*) and optic chiasm (*cho*). H. & E. ×12. B Germinoma with lymphocytic infiltration and giant cell (arrow) in anterior hypothalamus. H. & E. ×90. C Endodermal sinus-like arrangement of large cells in single cords. H. & E. ×260. D—G Posterior parts of tumour in pineal area. D Cyst lined by uniform layer of cuboid cells and filled with mucoid substance. H. & E. ×300. E Two tubular (glandular) structures (*x*) and isolated ependymal rosette (bottom) within germinoma. H. & E. ×250. F Granulomatous area with foreign body multinucleated giant cell of Langhans Type. H. & E. ×420. G Ependymal rosette with central lumen and occasional blepharoblast-like granules next to internal limiting membrane. H. & E. ×1100

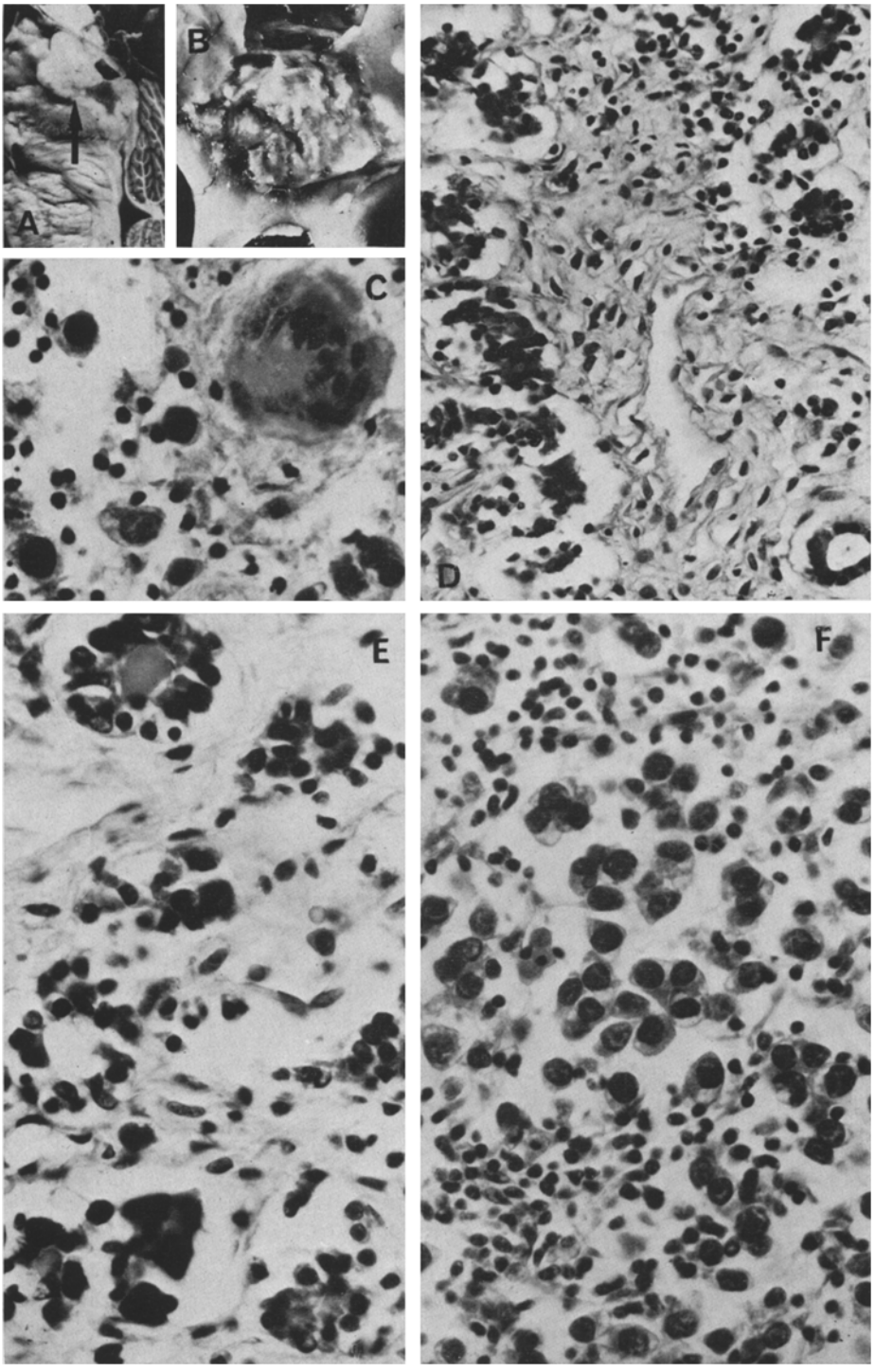

Fig. 6 A—F

Fig. 6A. Pineal germinoma in male aged 20 years invading the Sylvian aqueduct (case 13) Fig. 6B—F. Supra- and intrasellar germinoma with teratoid structures in male aged 20 years (case 10). B Retrochiasmal tumour replacing bottom of third ventricle. C Foreign body multinucleated giant cell. H. & E. ×270. D, E Hypothalamic areas with admixture of germinoma and globules, tubules and glandular structures within loose stroma. H. & E. ×250 and 370. F Characteristic histologic pattern of germinoma with mixture of large epithelial cells and lymphocytes. PAS ×420

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