Granular cell myoblastoma of the neurohypophysis
Report of two cases

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Two cases are described in which a granular cell myoblastoma of the pituitary gland presented as a space-occupying lesion, and was successfully removed. Reports of comparable cases are discussed. Important diagnostic criteria include the angiographic demonstration of abnormal circulation and the absence of calcification.

KEY WORDS · pituitary tumors · granular cell myeloblastoma · angiography

The granular cell myoblastoma, one of the least common benign tumors found in the region of the pituitary fossa, was first described under the name "choristoma" by Sternberg in 1921. The name "myoblastoma" derived from the similarity of the lesion on histological and histochemical examination to the myoblastoma of other sites, but it is clear from recent pathological analyses reviewed by Burston, et al., that the lesion in the sellar or parasellar area, though morphologically similar to myoblastomas elsewhere, apparently arises from the pituicytes of the posterior hypophysis. While its occurrence as a small lesion is detectable in careful autopsy examination and is well recorded, its presentation as a space-occupying lesion during life is rare. The present paper records two cases treated in the National Hospital, Queen Square, in the past decade, and reviews current opinions on the origin of this unusual lesion.

Case Reports

Case 1
This 49-year-old man came to the National Hospital, Queen Square, in 1961, with a complaint of failing vision in the right eye for 18 months and some impairment in vision in the left for 8 months. The only other significant feature in the history was some loss of libido over 18 months preceding admission.

Examination. The patient was a well-built man with rather pale, silky skin. Visual acuity was reduced to 6/60 (J.16) on the right, and 6/12 (J.12) on the left (findings corrected for refractive error). The fundi showed bilateral pallor of the nerve heads, and plotting of the visual fields showed bilateral crescentic paracentral scotomata, more obvious on the right than on the left side.

Biochemical investigations showed the level of urinary steroid production to be nor-
Myoblastoma of the neurohypophysis

mal, but the water-loading test produced 61% diuresis in 4 hours, corrected with 75 mg cortisone to 100% diuresis in 4 hours. The basal metabolism rate (BMR) was 77%, and the glucose tolerance test normal. Cerebrospinal fluid (CSF) examination showed no cellular or serological abnormality, but the protein content was 150 mg%, with a positive Pandy test. Skull films showed flattening and tilting forward of the posterior clinoids, typical of the presence of a suprasellar mass. Carotid angiography showed some elevation of the origin of the left anterior cerebral artery and slight unfolding of the carotid siphon on the right side. An air encephalogram (Fig. 1) showed elevation of the anterior end of the third ventricle which remained in the midline; the recesses of the third ventricle were splayed. The clinical investigation seemed typical of a suprasellar tumor, which was thought to be most probably a craniopharyngioma.

Operation. Right frontal craniotomy (Mr. Harvey Jackson) disclosed a solid whitish mass apparently entirely suprasellar with one small cyst containing 2 or 3 ml of fluid. Its relation to the pituitary stalk could not be determined. The tumor, which was hard and vascular, was subtotally removed. The histological analysis of the lesion is detailed below (after Case 2).

Postoperative Course. Recovery was largely uncomplicated, although an episode of neck stiffness some days after surgery was thought to signify a mild reactionary hemorrhage. The patient was found to have developed a complete bitemporal hemianopia, and visual acuity at the time of discharge from the hospital was 6/36 on the right and 6/18 on the left (corrected). He became lethargic with somewhat sluggish reflexes, and the BMR was found to be 75% (compared with the preoperative level of 77%). He was placed on thyroxine, 0.05 mg twice a day, in addition to routine replacement of cortisone, 37.5 mg per day. He had a mild nonparetic diplopia immediately postoperatively, but by the end of a year this had disappeared. Visual acuity by that time had improved to right, 6/12; left, 6/9, although the bitemporal hemianopia remained complete. Because of one fit 12 months postoperatively, he was placed on a small dose of Phenobarbitone and Epanutin. He has been continuously followed since operation, and his condition remains unchanged now, 6 years postoperatively. No deep x-ray therapy was given in this instance.

Case 2

A 56-year-old man came to the National Hospital, Queen Square, in 1969 because of intermittent occipital headache for 2 to 3 years, gradually increasing in severity. The headaches were aggravated by alcohol and changes of posture, and relieved by codeine phosphate. By the time of his admission they had become so severe as to interfere with work and social life, lasting up to 3 hours at a time.

Examination. The patient was a healthy man, with a fine skin. Libido was claimed to be normal, but the patient was infertile and had adopted a family. Visual acuity was 6/24 on the right, correcting to 6/6, and 6/60 on the left, correcting to 6/6. Examination of the fundi showed no abnormality. Visual fields showed a partial left temporal field defect to a red object. The blind spots were not enlarged. Tendon reflexes were uniformly sluggish, and there were scattered patches of eczema on the legs.

Biochemical investigations showed the following levels of steroid excretion: urinary ketosteroids, 7.1 mg/24 hrs; hydrocortisone, 3.0 mg/24 hrs; and oxogenic steroids, 1.1 mg/24 hrs in 1300 ml of urine. These levels are, for this laboratory, low normal ketosteroids, low hydrocorticosteroids,
and low oxogenic steroids. Fasting blood sugar was 66 mg%, serum cholesterol, 169 mg%. Protein-bound iodine was 4.6 μg (the normal range for the laboratory being 3.3 to 7.8 μg). The CSF examination showed no cellular or serological abnormality. The protein level was 40 mg%.

Radiological examination showed on plain films a large sella with ghostly dorsum and undercut anterior clinoids (Fig. 2). A right carotid arteriogram showed normal termination of the carotid vessels, but evidence of several small, spidery vessels passing into the large sella from the parasellar carotid artery, together with some doubtful pathological circulation in the sella itself (Fig. 3). The air encephalogram showed partial occlusion of the interpeduncular and pontine cisterns by an intrasellar mass, with the mass outlined in the chiasmatic cisterns. The anterior end of the third ventricle was slightly elevated and the recesses blunted off (Fig. 4). The clinical picture was thought typical of an intrasellar tumor, presumably chromophobe adenoma.

**Operation.** Right frontal craniotomy (Mr. Lindsay Symon) disclosed a hard, pinkish tumor emerging from the sella, elevating the optic chiasm, and in close contact with the right optic nerve. The salient feature at operation was the toughness of the lesion. The entire suprasellar portion of the tumor was removed, and the greater part of the tumor was cleared from the sella. Considerable bleeding from the intrasellar portion of the lesion was experienced during the operation. The histological characteristics of the tumor are reviewed below.

**Postoperative Course.** Recovery was uncomplicated except for an episode of headache and neck stiffness 5 days postoperatively, proven by lumbar puncture to be due to reactionary hemorrhage. Within a few days of operation, the patient developed polyuria, necessitating treatment with pitressin. Over the course of 3 weeks he appeared to be slightly lethargic, and at discharge his medication included routine replacement
Myoblastoma of the neurohypophysis

with cortisone, 12.5 mg twice a day, and supplementary thyroxine, 0.1 mg per day. At that time, visual acuity was 6/6 bilaterally, and the visual fields were full to white and red objects. At 18 months following operation, the patient remains well with no symptoms of headache, although the reactionary polyuria still requires occasional pitressin snuff at night. Radiotherapy has not been advised in this case.

**Histological Examinations**

The tissue resected from the two cases under discussion was received in the laboratory fixed in 4% neutral formaldehyde. On both occasions, it consisted of irregular pieces of firm gray tissue devoid of characteristic macroscopic features. Tissue was embedded in paraffin wax, and sections were cut at 5 µ and stained with hematoxylin and eosin (H & E), hematoxylin and van Gieson's stain, Mallory’s phosphotungstic acid-hematoxyline (PTAH), and the periodic acid-Schiff (PAS) method of Hotchkiss. Frozen sections were also prepared from Case 1 and stained with Scharlach R and hematoxylin.

**Case 1.** The lesion was composed of rather large polyhedral rarely elongated cells with round or ovoid open-textured nuclei in some of which were small nucleoli (Fig. 5). Some variation in nuclear size was apparent and occasional larger hyperchromatic nuclei and binucleate cells were also present, although mitoses were not seen. All of the cells had finely granular cytoplasm, the granules being eosinophilic and positively stained by the PAS method. Cytoplasmic membranes were usually distinct, although in places they were blurred. Throughout the lesion, the cells were in close contact with one another, the elongated cells tending to form strands and whorls. Capillaries, although not conspicuous, were fairly numerous throughout.

**Case 2.** This lesion was composed of prominent strands of elongated slender cells (Fig. 6 left), although there were also solid alveoli of large polyhedral cells (Fig. 6 right). Nuclei in the former were ovoid or elongated with a dense nuclear membrane and heavy chromatin stippling, the nuclei in the polyhedral cells being smaller, round, and open-textured. Mitoses were not seen. Cell cytoplasm was fairly abundant and finely granular, the granules being eosino-
philic and intensely stained with PTAH but not with PAS. Cytoplasmic membranes were often indistinct, and there was apparent anastomosis of some of the elongated cells. Groups of cells lay in close contact with one another, the groups being delineated by strands of reticulin and fine collagen. Along the edge of two of the fragments of tissue, there was a dense band of collagen and groups of cells were disrupting this at one point (Fig. 7). Capillaries, some of which were sinusoidal, were present throughout the lesion.

Discussion
The appearances of these two lesions, although different in detail, were essentially similar and corresponded with the histological appearances of two of the three pituitary granular cell myoblastomas described by Luse and Kernohan; these authors commented on the faint staining with PAS of the small granules in the elongated cells in 11 of their cases. Sobel and Churg also made the observation that cytoplasmic granules were scanty in "young" cells.

The status of the granular cell myoblastoma has given rise to considerable controversy in the past, and there is still no unanimity as to its nature and histogenesis. Abrikossoff, who first described granular cell myoblastoma in the tongue, thought it arose from degenerating voluntary muscle. This view gained general acceptance but became untenable when lesions in sites where voluntary muscle is not normally found were described. To account for such lesions, Leroux and Delarue suggested a histiocytic origin, although subsequently almost all workers have favored an origin from tissues present in peripheral nerves, such as the internal connective tissue of peripheral nerves, possibly Schwann cells, endo- or perineural fibroblasts, or neural tissue with uncertainty as to the precise cell of origin. A more recent study by Aparicio and Lumsden has repudiated both the myogenic and Schwann-cell origin for these lesions, and

![Image](image-url)

Fig. 6. Case 2. Left: Photomicrograph showing that predominantly elongated cells with indistinct cytoplasmic membranes, granular cytoplasm, and variable nuclei form the bulk of the tumor. H & E, ×240. Right: Another part of the lesion showing poorly defined solid alveoli of polygonal faintly granular cells. H & E, ×240.
Myoblastoma of the neurohypophysis

suggested an origin from an undifferentiated mesenchymal cell with leiomyogenic affinities.

This disputed histogenesis, although clearly of fundamental academic importance, is of less interest in the context of these two cases than is a consideration of the nature of the lesion and its natural history. Is granular cell myoblastoma a true tumor capable of progressive growth or not? An answer to this question is obviously of considerable importance as a guide to prognosis and therapy, especially in a situation where primary surgical clearance may be difficult or impossible.

Abrikossof suggested an opinion that these lesions arose from degenerating voluntary muscle; this view was accepted for many years until the problems which it raised in terms of the expansive nature of the lesion and the absence of any other histological features of degeneration led to a consideration of other modes of pathogenesis. However, there are also difficulties in accepting the myoblastoma as a tumor, for although the lesion is almost invariably benign, most of these lesions are not well circumscribed, lack a capsule, and indeed infiltrate the adjacent structures including nerves. Infiltration, in particular, would not generally be acceptable as a feature of a benign tumor, and yet if these lesions are benign tumors of Schwann cells or neural connective tissue, then an encapsulated tumor adjacent to or encircling a nerve would be expected. Because of these inconsistencies, the view has been taken that the granular cells in this lesion are modified tissue cells which are storing or elaborating substances that appear on histochemical and on electron microscopic examination to be altered myelin.

Acceptance of this view that the granular cell myoblastoma is a local thesaurosis, and not a true neoplasm, would accord well with the histological appearances (including the microscopic lesions in the pituitary where often only a few cells are involved), slow progress of the lesion, and failure to metastasize as observed clinically, and would indicate that conservative resection is the correct form of therapy.

Whereas we feel that the balance of the evidence is strongly in favor of the non-neoplastic nature of granular cell myoblastoma, our observations on these two cases do not allow us to refute the claim made by Apa riccio and Lumsden that granular cell myoblastoma is a true tumor due to the fact that the myoblastoma cells are encircled by basement membranes formed by themselves.

Together with the cases presented here, only six cases of myoblastoma of the neurohypophysis have been identified during life. In 1950, von Luthy and Klingler reported the case of a 34-year-old man with a few months' visual deterioration in his right eye and severe visual impairment in the left eye of many years' duration because of retinal detachment. Clinical examination revealed bitemporal hemianopia. Genital hypoplasia was also noted. Of the endocrine tests performed, only the glucose tolerance test was abnormal, showing a late rise of blood glucose with persistent elevation of the glucose at 2 hours. The CSF examination was normal. Radiographic studies revealed a ballooned sella in plain films, and a suprasellar mass in the air encephalogram. The clinical diagnosis was pituitary adenoma. The tu-

Fig. 7. Case 2. Photomicrograph of the edge of the “myoblastoma” showing granular cells within the fibrous wall of the lesion. Hematoxylin and van Gieson, × 000.
A tumor was explored subfrontally, and a firm lesion, noted for its vascularity, partially removed with chiasmal decompression. The vision was reported as improved postoperatively. The patient was thereafter given 8000 rads to the parasellar area. Histologically, the lesion was classified as a "tumorette," another recognized name for myoblastoma.14

In 1953, Harland10 reported a second case, that of a 32-year-old woman whose symptoms were blindness, optic atrophy, and bilateral third nerve paresis. In the course of the evolution of the clinical picture, she developed hydrocephalus because of obstruction to the third ventricle, drifted into coma, and died. The clinical diagnosis was a third ventricular tumor, and the correct diagnosis, an intrasellar myoblastoma, was established only at autopsy.

A third case was reported by Glazer, et al., in 1956,9 that of a 31-year-old woman who had had some difficulty with vision for 3 years and had been blind for 1 month before examination. Bilateral optic atrophy was evident, and air encephalogram showed displacement of the third ventricle by a suprasellar mass. The clinical diagnosis was craniopharyngioma. At operation, a hard suprasellar tumor was partially removed and the correct histological diagnosis made. Radiotherapy in a dose of 3200 rads to the tumor was given, but the patient died 5 months postoperatively.

In 1965, Doron, et al.,6 reported a fourth case, that of a 47-year-old woman with a 6-year history of frontal and occipital headache, and a 4-year history of progressive visual disturbance, starting with a defect of the left upper quadrantic visual field. By the time of examination just before surgery, she had developed bitemporal hemianopia. Examination disclosed pallor of the optic discs, a temporal hemianopia in the right eye, and preservation of only an upper nasal quadrant in the left. Plain skull films showed enlargement of the sella, and carotid angiography showed marked elevation of the ipsilateral anterior cerebral artery and well-marked pathological circulation in the pituitary fossa. At subfrontal exploration, an intensely vascular tumor was partially removed, with decompression of the optic nerves and chiasm. Subsequently, deep x-ray therapy with a tumor dose of 4000 rads was given.

The patient showed considerable visual field improvement by 3 months postoperatively, and this improvement has been maintained to the time of writing (personal communication, Prof. A. J. Beller, 1970).

It is clear from the clinical presentation of the six recorded cases that the granular cell myoblastoma may present itself either as a suprasellar or as an intrasellar mass and that there are no reliable clinical features to distinguish it in either of these situations from the other tumors that are considerably more common in both sites. Thus, the suprasellar myoblastoma is commonly mistaken for a craniopharyngioma, and the intrasellar myoblastoma for a pituitary adenoma. The clinical features, those of compression of the optic nerves and of other nerves in the cavernous sinus, patchy moderate pituitary dysfunction, and, possibly with a large lesion and marked suprasellar expansion, hydrocephalus, are also common to many lesions in the area and in no way specific.

The unusual vascularity of Case 4 reported by Doron, et al.,6 caused preoperative comment, and pathological circulation was certainly noted in one of our own cases. However, in our case, we felt that the vascularity was not unusual for a chromophobe adenoma of the pituitary; indeed, we believe that pathological circulation in the sella is occasionally seen in chromophobe adenomata, although its character, namely, fine linear vessels, is usually slightly different from the rather coarse circulation evident in Fig. 3. There has been no calcification reported in this tumor either clinically or at postmortem, so that calcification would appear to exclude granular cell myoblastoma. Two of the six cases presently reviewed showed elevation of the CSF protein, in one instance to 150 mg% and in the other to 244 mg%.

Neurosurgeons are not famous for reporting technical operative difficulties, but in all the cases where operative details have been recorded, subtotal removal of this tumor has occasioned some difficulty because of its hard consistency and considerable vascularity. From the course of the cases detailed here, it would appear, however, that progression of the lesion is slow, and partial removal with decompression of the optic apparatus is all that is required. There is no una-
Myoblastoma of the neurohypophysis

nimity in the literature as to the advisability of postoperative x-ray treatment, but if our present views of the pathology of the lesion are correct, and its origin is indeed from neurectodermal elements of the posterior hypophysis, it would not seem to be highly radiosensitive. The first of our own cases appears to be pursuing a clinically quiescent course, despite the absence of radiotherapy. It does not seem to us, therefore, that radiotherapy should be undertaken with such a diagnosis. Further, at postmortem in Glazer, et al., there was no evidence of any histological change induced by radiotherapy.

It appears likely that the granular cell myoblastoma will continue to be misdiagnosed clinically because of its extreme rarity and lack of specific features, but it seems reasonable to bear the possibility in mind in the differential diagnosis of sellar or suprasellar tumors in middle-aged adults, particularly in the absence of calcification and where there is angiographic demonstration of a pathological circulation.

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References


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