Intracerebral neurilemmoma

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SUMMARY Two examples of intracerebral neurilemmoma occurred in the absence of von Recklinghausen's disease. The first case was unique because the patient was clinically asymptomatic, and the second case was unusual with a combination of oligodendroglioma and neurilemmoma in the same mass. The latter lesion arising in persons without stigmata of neurofibromatosis has not been described. The nature of nerve sheath neoplasms in both instances has been verified by electron-microscopy. Clinical features of this rare neoplasm differ from those of acoustic or other cranial nerve tumour, particularly in relation to age and sex. Intracerebral neurilemmoma has been found most often in the first two decades of life and more often in males. Seizures and paresis, although non-specific are common signs and symptoms. Probable histogenesis of this neoplasm from perivascular elements in brain has been suggested.

The acoustic nerve has long been known as the most frequent site of intracranial neurilemmoma.¹ Nerve sheath neoplasm may, however, rarely arise from within the parenchyma of brain and spinal cord.²⁻⁶ Intramedullary neurilemmomas occur more frequently than within the brain. Nine examples of the latter neoplasm have been reported since 1965,³⁻¹¹ although in only one instance was ultrastructural confirmation as to its origin from the sheath.⁵ Two additional cases of such lesions are described here. The nature of the neoplastic cells has been analysed by both light and electron microscopy. Additionally, the mass in one example (case 2) contained foci of glial neoplasm.

Case reports

Case 1

A 23-year-old man was admitted to UCLA Hospital for an acute episode in the course of chronic schizophrenia. Circumscribed delusional beliefs began 3 years before admission. Psychiatric symptoms were difficult to control and several drugs, including haloperidol, fluphenazine

and benzodiazepines were tried. He later experienced auditory hallucinations, depression and insomnia. Physical examination revealed neither neurologic deficit nor signs and stigmata of von Recklinghausen's disease. Routine laboratory investigations, including blood and urine, were normal. Computed tomography (CT) to evaluate his complaints of headaches while in hospital disclosed a mass in the right parietal lobe (fig 1). Metastatic neoplasm was suspected, but chest radiographs, axial skeletal survey, and liver-spleen scan were normal. There was no family history of mental disease, epilepsy, or skin lesions. At craniotomy a 3 × 4 cm mass was found beneath the pia and was well demarcated from the surrounding brain. The lesion was excised piece-meal. Recovery was uneventful and the patient was doing well when seen 6 months after surgery, although his psychiatric problem remained.

The surgical specimen consisted of multiple fragments of a firm but friable mass. Microscopically, the lesion was characterised by dense cellular interlacing streams and loops of elongated cells (fig 2A). Anaplasia was pronounced and rare mitotic figures were observed. Special stains, including Masson's trichrome and phosphotungstic acid hematoxylin (PTAH) demonstrated finely dispersed extracellular collagenous fibres coursing throughout the neoplasm. The PTAH and Holzer's preparations did not indicate any glial component. Reticulin impregnation revealed an abundance of delicate argyrophilic fibres which encircled individual cells (fig 2B). Ultrastructurally, the neoplastic cells contained abundant cytoplasm with interdigitating processes (fig 3). Most of the cytoplasm formed long, thin profiles in intimate contact with each other. The cell surfaces as well as neoplastic cell processes were covered with well

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defined basement membranes. The anatomical diagnosis was atypical intracerebral neurilemmoma.

Case 2

A 21-year-old man was admitted to UCLA Hospital because of intractable partial complex seizures for five years. Early development had been normal. Symptoms began at age 16 years and were described as intermittent, blank staring spells with immobile standing. Electroencephalogram showed a left temporal spike focus. Skull radiographs and CT scans were normal. The patient received many anticonvulsants but no success was achieved in seizure control. Symptoms continued becoming more protracted with occasional semi-purposeful movements such as gentle swaying. Depth electrodes were emplaced at UCLA and epileptogenic abnormality in the left temporal lobe was disclosed. Physical and neurological examinations were normal. There were no stigmata of von Recklinghausen's disease. Laboratory data were unrevealing. There was no family history of neurologic disease. Since seizures were refractory to drugs, a left temporal lobectomy was performed. The course after operation was uncomplicated and there were no speech difficulties.

The temporal lobe measured 5.5 cm from pole to resection line. A small focus of discolouration located in the inferior temporal gyrus was found. Microscopically, this lesion was largely confined to the gray matter and characterised by the proliferation of two distinct cell types (fig 4A). A large cluster of uniform oligodendroglia cells with regular spheroidal nuclei surrounded by clear cytoplasm gave the typical "honeycomb" appearance (fig 4B). Adjacent to the focus of oligodendroglioma was a zone of spindle cells with nuclei arranged in parallel rows and palisades. The PTAH, Masson's trichrome stains and Wilder's impregnation revealed collagenous fibres with abundant reticulin dispersed among individual fusiform cells (fig 4C). Electron microscopic examination of these spindle cells and their processes showed thin, even basement membranes (fig 5A) on which the cells were attached. Unusually composed bundles of collagen fibres were scattered in the extracellular spaces (fig 5B). The diagnosis was combined intracerebral neurilemmoma and oligodendroglioma.

Discussion

The pattern of palisaded spindle cell nuclei, collagenous cytoplasmic fibrils and dense reticulin networks amidst neoplastic cells pointed to neurilemmoma in both instances. The demonstration of definite basement membranes covering the neoplastic cells and their processes¹² provides additional and more certain verification of the diagnosis than the use of chemical dyes and impregnations alone.

A review of the literature revealed eleven case reports of intracerebral neurilemmoma including the two present cases (table). In 1965 David *et al*³ published the case of a 15-year-old boy with a lesion in the right parietal lobe. The histologic

appearance was characteristic of nerve sheath neoplasm. Gibson *et al*⁵ described the ultrastructural features of neoplastic cells obtained from a temporal lobe mass in a 6-year-old boy. The cells were sheathed with basement membranes similar to the present cases. Seven additional cases have been recorded but the diagnosis has been based essentially on light microscopic criteria, though confirmed by reticulin impregnation and PTAH stains.^{4 6-11} The clinical features of intracerebral neurilemmoma are of interest because of a peculiar age and sex preponderance. The age of most patients of this group

Fig 1 Case 1: Cerebral computed tomogram showing a right parietal mass with slight central lucency and surrounded by oedema.

Fig 2(A) Case 1: Proliferation of spindle cells in the brain tissue. Note pleomorphism of neoplastic cells. H and E $\times 100$. (B) Dense reticulin network seen in the neoplasm. Reticulin impregnation. $\times 250$.

Fig 3 Case 1: Ultrastructural features showing a well defined basement membrane (*) surrounding spindle-shaped neoplastic cell and processes (P). Abundant extracellular collagenous fibrils (C). $\times 35\,000$.

Fig 4(A) Case 2: The lesion confined to the inferior temporal gyrus on right. Middle temporal gyrus (M) is normal. PTAH. $\times 16$. **(B)** Higher power view showing zone of oligodendroglioma. H and E $\times 250$. **(C)** Dense reticulin fibres parallel to longitudinal axes of spindle cells. Reticulin impregnation. $\times 100$.

were in the first two decades, the youngest being 6 years. Ghatak *et al*⁴ described a case of a 63-year-old woman, who, however, had an unusually long clinical history spanning 40 years suggesting that the lesion may have been present since the age of 23. Nine of

eleven instances have been men; the other two women. In contrast, acoustic neurilemmoma occurs predominantly in women ranging from 54%¹³ to 76%¹⁴ of cases. Approximately two-thirds of patients in most series are in the fourth and fifth decades.^{1 13–15}

Fig 5(A) Electron micrograph from the area of spindle cells (see fig 4C) showing a thin basement membrane attached to the neoplastic cells and processes (P). $\times 13\,200$. (B) Extracellular fibrous long-spacing collagen with cross-banding periodicity. $\times 64\,800$.

The reason for the difference in age and sex from solitary neurilemmoma of the eighth cranial nerve is not known, although it may be that the intracerebral neoplasms have a congenital origin. Temporal and parietal lobes have been the common sites of parenchymatous neurilemmoma in brain as noted in this review. These lesions may affect brain stem⁸ and cerebellum,⁶ although such effects are rare. Seizures are the first symptoms found in most cases, followed by a high incidence of paresis. The neurologic signs, of course, are related to the anatomic location of the lesion. Absence of epilepsy and other neurologic dysfunction in case 1 is exceptional. The lesion may thus be asymptomatic or produce symptoms for many years suggesting that growth in some instances is extremely slow and damage to adjacent brain structure is minimal. Schizophrenia in our case is probably coincidental. Persistence of mental illness after surgical removal of the neoplasm would support this view.

Considerable controversy exists regarding the histogenesis of these neoplasms. Theories concerning the mode of occurrence have been offered by several authors.^{4,5,10} First is the possibility of

developmental origin because the lesions are found in the young. It should be noted that these patients, including our two cases, had normal birth and childhood development and there were no evidence of associated malformation. Secondly, the growth might be part of von Recklinghausen's disease as suggested by Scharenberg,¹⁶ who stated that such a patient with bilateral acoustic neoplasms might also harbour intracerebral neurilemmoma, but the author gave no further details. Interestingly, family history or physical stigmata of multiple neurofibromatosis has not been found in the recorded examples. Furthermore, the absence of multiple lesions in these cases is evidence against such a possibility. Thirdly, such neoplasms may originate from proliferation of Schwann cells in perivascular nerve plexuses, particularly in cases involving the spinal cord. Hyperplasia of perivascular nerve plexuses has been observed in certain chronic diseases of the cord and in older persons.¹⁷ Foci of Schwann cell proliferation are mainly found in spinal cord.¹⁴ Aberrant peripheral nerve fibres have been observed in the medulla oblongata as a chance-finding on serial sections.¹⁸ Several examples of intramedullary neurilemmomas^{2,17,19} and a remarkable instance of nerve sheath neoplasm occurring in the pons⁸ would strengthen this concept. One considerable weakness of this argument, however, is that abnormal foci of Schwann cell hyperplasia have not been identified in the cerebral hemisphere or the cerebellum. Although some authors^{20,21} observed the presence of Schwann cells and peripheral myelin within human central nervous tissue in multiple sclerosis and at the edge of old infarcts as well as in certain experimental conditions in rats, none of these diseases has been found in patients with intracerebral Schwannoma.

Russell and Rubinstein¹⁴ have observed a resemblance of pial cells to Schwann cells and have suggested that pial cells might undergo conversion to Schwann cells. It is generally accepted that leptomeninges are derivatives of the neural crest.²² Cells of the crest may differentiate into many cell-types, including bone, striated muscle, meningocytes, Schwann cells, and fibroblasts.²³ Occasionally, striated muscle can be found in meninges as well as in brain tissue, along with penetrating vessels.^{24,25} It is conceivable that this ectomesenchyme could give rise to neoplastic transformation. For example, Kasantikul and Brown²⁶ published two instances of meningioangiomatosis restricted to the cerebral cortex in the absence of von Recklinghausen's disease. Cases of intracerebral and intracerebellar "fibroma", as well as primary rhabdomyosarcoma of brain, have been reported.²⁷⁻³¹ Furthermore, islands of ossification, cartilage, and clusters of blood vessels have been found in combination with parenchyma-

Table Clinical features of brain neurilemmoma

Author(s)	Age of patient (yr)	Sex	Duration of symptoms (yr)	Location	Symptoms and signs
David <i>et al</i> , 1965	15	M	0.3	R parietal lobe	Headache, increased intracranial pressure, L hemiparesis, L hyperreflexia
Gibson <i>et al</i> , 1966	6	M	1	L temporal lobe	R focal seizures and weakness of R arm and leg.
New, 1972	8	M	2	R parietal lobe	Grand mal seizures.
Ghatak <i>et al</i> , 1975	63	F	40	R parietal lobe	L focal seizures, L hemiparesis, L hyperreflexia, L lower facial weakness, L homonymous hemianopsia.
Pialat <i>et al</i> , 1975	24	M	9	R frontal lobe	Grand mal seizures.
van Rensburg <i>et al</i> 1975	21	M	7	R temporal lobe	Uncontrolled behaviour and psychomotor seizures.
Komminoth <i>et al</i> , 1977	15	M	2	Superior vermis of cerebellum	Bilateral exophthalmos, L facial weakness and L cerebellar signs.
Prakash <i>et al</i> , 1980	14	F	3	Pons	Squint and facial asymmetry, ataxia, L lower motor neuron and L CN VI, VII paresis.
Vassilouthis <i>et al</i> 1980	17	M	2	L subfrontal lobe	Increased intracranial pressure, headache, dizziness and amaurosis.
Kasantikul <i>et al</i> (present study)	23	M	—	R parietal lobe	Schizophrenia, absence of neurologic signs and symptoms.
	21	M	5	L temporal lobe	Partial complex seizures.

M = Male, F = Female, R = Right, L = Left.

tous neurilemmoma arising from brain.^{4 32} The presence of nerve sheath neoplasm deep in the cerebral hemisphere then could have arisen from perivascular elements. The fact that ectomesenchyme is also presented in the pericapillary regions in brain tissue further supports such a contention.²⁵

The lesion in case 2 is unusual because of the combination of two completely different types of neoplasm in the same mass. Clusters of neuroglia were mainly situated adjacent to the region of nerve sheath neoplasm. Only two other cases of combined Schwannoma and neuroepithelial tumour in the cerebrum have been reported.^{32 33} Shuangshoti and Netsky³² described a 14-year-old boy with multiple cutaneous café-au-lait spots having a large mass localised in the left temporal lobe. At craniotomy, the lesion consisted of differentiated meningioma, neurilemmoma, and poorly differentiated astrocytoma. Hahn and Netsky³³ reported a 23-year-old man with cutaneous café-au-lait spots and a frontal subcortical mass. The cerebral neoplasm was a mixture of neurilemmoma and astrocytoma. Although these two reported examples were associated with von Recklinghausen's disease, the criteria for a diagnosis of such disorder are insufficient in our patient. The lesion in case 2 thus appears to be unique.

The presence of glial tissue in combination with Schwannoma also poses a question concerning Antoni type B tissue in nerve sheath neoplasms. Many investigators^{1 13} consider Antoni type B tissue to be the result of degeneration in neurilemmoma; though this loose reticular tissue can sometimes be

found associated with a structure similar to the "honeycomb" appearance of oligodendroglioma and could even resemble astroglia. Histologically distinguishing between Antoni type B tissue and neuroglia may at times be difficult.^{34 35} Schiffer³⁶ has induced brain neoplasms in the rat by use of ethyl nitrosourea. In some instances, zones of oligodendroglioma were found in continuity with the neurilemmomatous tissue resembling the lesion described in case 2.

Anatomically, both cranial and peripheral nerves have glial and a peripheral neurilemmal component depending on the site of tissue examination. The glial tissue may extend in a peripheral direction.^{37 38} Glial neoplasms arising from cranial and peripheral nerve have been reported^{34 39 40} and occasionally may mingle with neoplastic Schwann cells.^{34 41-43} We suggest that in some instances Antoni type B tissue could, in reality, be neuroglia.

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