Intramedullary spinal cord glioma with intracranial seeding

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SUMMARY Two cases of intracranial dissemination of primary intramedullary spinal cord gliomas are reported, with a review of the literature. One patient had a post mortem confirmation and in the second, cerebral CT scan and CSF examination demonstrated the occurrence of intracranial dissemination. CSF protein was elevated on both patients and malignant cells were found late in only the one patient. Both patients had raised intracranial pressure. The mechanisms of dissemination and of raised intracranial pressure are discussed. Such dissemination may be more common than previously realised.

Dissemination of spinal cord gliomas into the cranial cavity has been reported infrequently while spread from intracranial glial tumours to the spinal sub-arachnoid space is not uncommon. We report two cases in young women which were seen within one year of each other and speculate on the mechanism of the extensive ventricular seeding that occurred.

Case reports

Case 1

In December 1981, a 38-year-old woman presented with a six weeks history of right leg weakness and left leg paraesthesiae. There was no sphincter disturbance. Examination revealed mild weakness of right hip flexors, brisk knee jerks, flexor plantar responses and impaired appreciation of pinprick below T11 on the left. Neurological examination was otherwise normal. A myelogram to T3 was normal. CSF revealed no malignant cells but many lymphocytes and macrophages and total protein was raised to 0.65 g/l. IgG/Albumin ratio was normal. A diagnosis of possible transverse myelitis was made.

In late January 1982 the patient re-presented with sudden onset of severe headache, vomiting and neck stiffness. Neurological examination was unchanged apart from increased weakness of right leg. Examination of CSF revealed no white blood cells, 222 red blood cells with no xanthochromia, protein of 18.8 g/l and glucose of 2.2 mmol/l. The headache was rapidly relieved by lumbar puncture. Headache and vomiting soon recurred and florid

bilateral papilloedema developed. Lower limb reflexes became bilaterally brisk, plantar responses remained flexor and sensory loss extended to the costal margin bilaterally being most marked on the left. A cerebral CT scan was normal. At this state the diagnosis was uncertain. Infective causes were extensively searched for, but none were found. Scalene node and skeletal muscle biopsies were performed in a search for sarcoid but these were negative. Repeated lumbar punctures were done to relieve headache and drowsiness. CSF examination continued to show high protein levels, with a peak of 66 g/l, lack of malignant cells and no evidence of infection. Over a few days sensory loss in the right T2-T4 dermatomes developed and bilateral abducens nerve palsies were noted. It was then recognised that the previous myelogram did not extend far enough rostrally, and a repeat myelogram was performed. This showed an intramedullary lesion in the thoracic cord with a complete block at T3, and an upper level at T2 (fig 1), while a repeat cerebral CT scan showed mild ventricular dilatation.

She was treated with dexamethasone and in April 1982 a ventriculo-jugular shunt was inserted with temporary improvement. Owing to the patient's poor condition further surgery was deferred and a course of 5000 rads deep X-ray therapy over four weeks was commenced to the cervical and thoracic cord. Lower limb sensory and motor loss progressed and urinary incontinence developed.

In June 1982 the patient was able to undergo an exploration and decompression of the spinal cord from C3 to T6. The cord was seen to be diffusely swollen and soft throughout the length of exploration. No definable tumour margin was seen. Biopsies revealed only non-specific degenerative changes and oedema. After operation the patient developed pneumonia and died in early July 1982.

Pathology Case 1:

At necropsy signs of severe bronchopneumonia were

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Fig 1 Myelogram of Case 1 showing an intramedullary cord lesion extending from T2 to T3.

found with a right upper lobe lung abscess. No tumour or other significant abnormality was found in the general necropsy. The brain weighed 1480 g and showed mild diffuse symmetrical oedema. The leptomeninges over the base of the brain and brainstem were opaque and in the quadrigeminal cistern were markedly thickened. The tuber cinereum was expanded and firm. The cut surfaces of the brain revealed obliteration of the infundibular recess of the third ventricle by firm variegated tumour measuring 15 mm in diameter. The pineal gland was normal in size but very firm in consistency. The lateral ventricles were compressed and there was patchy fine granularity of the

Fig 2 Low power photomicrographs of primary malignant astrocytoma of spinal cord in Case 1. H & E $\times 4$.

(a) Extensive tumour replacement of cord and leptomeningeal invasion in the third thoracic segment. (b) Thick subarachnoid tumour infiltrate encasing normal lumbar spinal cord. (c) Infiltrate around nerve roots of the cauda equina.

ependymal surfaces. No other intracerebral tumour deposits were identified macroscopically. The spinal cord showed extensive swelling and softening in the cervical segments with herniation through the recent laminectomy

Fig 3 Case 1 (a) Microscopic appearance of primary malignant astrocytoma in thoracic spinal cord. H & E $\times 90$. (b) Subarachnoid tumour infiltrate overlying anterior surface of medulla. H & E $\times 20$. (c) Ependymal tumour deposits in third ventricle. H & E $\times 60$. (d) Tumour infiltrate surrounding infundibular recess of third ventricle. H & E $\times 20$.

defect. The upper thoracic cord was expanded by tumour which extended into the subarachnoid space, forming a dense collar around the distal cord and cauda equina (fig 2).

Microscopically the thoracic cord tumour was a malignant astrocytoma showing marked cellularity, nuclear pleomorphism and hyperchromatism, vascular endothelial proliferation and areas of necrosis. Numerous bizarre giant cells with swollen eosinophilic cytoplasm and intracytoplasmic inclusion were probably the result of irradiation (fig 3a). Radiation may also have contributed to the oedema, necrosis and vascular reaction. Maximal tumour involvement was found in the third thoracic cord segment where there was replacement of the normal structures of the right side of the cord and extension across the midline anteriorly. Intramedullary tumour infiltrate extended distally to the seventh thoracic segment. There was leptomeningeal invasion with dense subarachnoid infiltrate encasing spinal nerve roots and blood vessels at all levels and invading the nerve roots of the cauda equina. Ascending spread in the intracranial subarachnoid space involved cranial nerve roots and there was direct invasion of the pineal gland from tumour in the quadrigeminal cistern. Multiple microscopic ependymal tumour deposits were present throughout the ventricular system with scattered

superficial foci of subependymal infiltration. There was more extensive subependymal infiltration surrounding the infundibular recess of the third ventricle to form the tumour nodule which had been observed macroscopically (figs 3b, 3c, 3d). The histological features of the intracranial deposits were those of malignant astrocytoma, consistent with spread from the intramedullary spinal cord tumour. The tumour deposits were highly cellular with pleomorphic hyperchromatic nuclei, moderate mitotic activity, associated capillary endothelial proliferation and small foci of necrosis. The appearances were similar to those in the spinal cord tumour but there was an absence of the bizarre giant cells attributed to irradiation in the primary lesion. The cranium had not been irradiated.

Case 2

A 19-year-old girl presented in April 1981 with a three months history of left quadriceps weakness and wasting and dull low thoracic pain. Prolonged sitting produced pain and paraesthesiae in both legs. She walked with the aid of a stick. There was no disturbance of sphincters. Neurological examination revealed that the left mid-thigh diameter was 4 cm less than the right, left knee jerk was absent, and plantar responses were flexor. The left leg was moderately weak, particularly the hip flexors, and sensation was

Fig 4 Myelogram of Case 2 showing an intramedullary lesion of the conus.

impaired on the lower anterior thigh.

A myelogram revealed an intramedullary lesion of the conus extending over 5–6 cm at the T11 level (fig 4). The CSF did not reveal any malignant cells nor excess of white blood cells and protein was 0.38 g/l with glucose of 4.3 mmol/l. A thoracic laminectomy exposed a swollen cord

Fig 5 CT scan of Case 2 showing contrast enhancing periventricular lesions, January, 1983.

and on opening of the pia abnormal, undermarked intramedullary tissue was apparent. A biopsy specimen was taken and the dura closed. The pathology was that of a moderately cellular astrocytoma with no significant anaplastic features. A 4500 rads course of radiotherapy was given over five weeks to the lower thoracic spine, following which there was improvement.

In September 1982 she re-presented with increased pain, numbness and weakness in the left leg. A repeat myelogram showed marked enlargement of the conus from T11 to T12. CSF protein was 0.86 g/l, glucose 2.9 mmol/l and microscopy and cytology were normal. A further 6500 rads were given to the lower cord over seven weeks. Again there was improvement in strength.

In January 1983 she presented with a ten day history of diffuse headache and drowsiness. There was early papilloedema but no other change. CT scan of brain revealed multiple periventricular lesions which showed a marked contrast enhancement (fig 5). Examination of CSF revealed malignant cells consistent with astrocytoma, protein was 10 g/l and glucose was 3.4 mmol/l. The patient was treated with dexamethasone and metoclopramide but returned one month later with headache, vomiting and drowsiness. On examination papilloedema was marked, left leg weakness had progressed and there was mild right leg weakness. Grand mal seizures were treated with phenytoin sodium. The patient elected to have chemotherapy and an Omayia reservoir was inserted. The protocol of intrathecal methotrexate 15 mg, cytosine arabinoside 70

Fig 6 CT scan of Case 2 showing right cerebellopontine angle and right cerebellar hemisphere lesion and less marked periventricular lesions.

mg and hydrocortisone 100 mg plus leucovorin rescue was commenced on days 1, 3 and 5 for three weeks, then days 1 and 5 for one week and then weekly for three weeks. Also intravenous BCNU 80 mg/m² on days 1 to 3 and vincristine 2 mg on days 1 to 8 were given plus procarbazine 100 mg/m² on days 1 to 10 at six weekly intervals. CSF examination after one week revealed no malignant cells and a protein of 0.3 g/l. The patient became alert and free of headache.

In mid March 1983 right cerebellar signs and right trigeminal and abducens nerve palsies were noted. CT scan showed that the ependymal and periventricular areas of contrast enhancement were less marked but that there was a region of contrast enhancement adjacent to the right cerebello-pontine angle and extending to the right cerebellar hemisphere (fig 6). Chemotherapy and dexamethasone were continued. One month later there was progression of papilloedema, decreased visual acuity bilaterally, right trigeminal, abducens and facial palsies and increasing bilateral leg weakness, sensory loss in right leg and frequent headaches. CT scan did not demonstrate the cerebello-pontine lesion but there were large periventricular deposits in the frontal horns and the appearance of butterfly spread along the corpus callosum bilaterally. There were also regions of contrast enhancement in the left fronto-parietal region and left basal ganglia (fig 7). The patient died in May 1983 in her home town and necropsy was not performed.

Discussion

Gliomas account for 8% of primary spinal cord tumours.¹ Their spread from spinal cord to the cranial cavity has seldom been documented while spread of intracranial gliomas to the spinal canal has been repeatedly noted.²⁻⁵ A review of the literature reveals that 14 necropsy-proven cases of spinal cord tumours with intracranial dissemination have been reported: see table. The patients were generally young with an age range from 5 to 48 years and duration of illness was less than one year in most cases.

The time course for the progression of symptoms in our patients makes it unlikely that the primary lesion was intracranial, or that the lesions were multifocal in origin. In Case 1 the initial symptoms in the lower limbs preceded the symptoms of increased intracranial pressure by three months. Cerebral CT scans from the onset of intracranial symptoms failed to reveal any evidence of a primary intracranial lesion. Necropsy demonstrated a picture consistent with invasion by tumour deposits from the ventricular system but no evidence of a primary intracranial neoplasm. Case 2 had symptoms related to a

Fig 7 CT scan of Case 2 showing large periventricular deposits and bilateral spread along the corpus callosum.

biopsy-proven intramedullary conus tumour for 24 months prior to the development of any cerebral symptoms. A cerebral CT scan was performed with the advent of cerebral symptoms and showed multiple periventricular deposits but no evidence of a primary intracerebral lesion. Serial CT scans then showed evidence of intracerebral invasion. Although necropsy was not performed in Case 2, it is most improbable that a primary cerebral lesion was present that could seed to the conus and yet remain otherwise clinically silent for 24 months, particularly given the pattern of ventricular to cerebral spread of the deposits seen on serial cerebral CT scans.

Meningeal invasion paves the way for spread in the CSF pathways. Other factors may then determine the extent and rate of dissemination and the site of metastatic deposits. All four of Eade and Ulrich's metastasising spinal cord gliomas were histologically malignant.¹⁴ Kopelson and Linggood have also stressed the prognostic importance of the histological grade of intramedullary spinal cord gliomas.¹⁸ This appears to apply to our two cases. Case 1, with malignant astrocytoma, survived only nine months from the onset of her illness, whereas

Case 2, with the lower grade tumour survived for 28 months. In Case 2, however, in the absence of necropsy examination we cannot exclude sampling error in the biopsy or subsequent anaplastic change in the tumour.

Another possible histological determinant of tumour behaviour is oligodendroglial differentiation.¹⁹ Oligodendrogliomas are noted for their propensity for spread. Eade and Ulrich described oligodendroglial differentiation in three of their four cases of disseminated spinal cord gliomas. No evidence of such differentiation was found in our two cases but, again, the small biopsy in Case 2 may not have been representative of the tumour and its numerous deposits. We note that in two of the three cases with oligodendroglial differentiation in Eade and Ulrich's report the initial biopsies contained only astrocytoma.

The remote sites of tumour deposition in the subarachnoid space and the ventricular system are probably related to CSF flow.²⁰ The marked tumour seeding within the ventricular system in both cases may be due to tumour seeding first to the basal cisterns and cisterna magna with formation of a communicating hydrocephalus. Such flow of CSF into

Table *Previously reported cases of intracranial dissemination of spinal cord gliomas that were proven by necropsy*

Author	Age/sex	Total duration	Site of spinal tumour	Site of dissemination	Histology	Operation
Mallory 1908	Child	?	Lumbar cord	Subarachnoid space invasion of cervical cord, pons and cerebellum	Glioma	?
Greenfield 1934	48 M	6 years	Cauda equina	Subarachnoid space, ventricles	Medullopithelioma	+
Eden 1938	19 M	7 months	Lumbo-sacral cord	Subarachnoid space	Mixed glioma	+
O'Connell 1946	16 M	16 months	Dorsal cord to conus	Subarachnoid space and ventricles	Glioblastoma multiforme	+
Russell 1949	37 M	5 months	Cervical cord	Subarachnoid space and ventricles	Oligodendroglioma	-
Russell & Rubinstein 1959	11 F	6 months	Cervical cord	Subarachnoid space and ventricles	Glioblastoma multiforme	-
Perese, <i>et al</i> 1959	39 M	28 months	Conus	Subarachnoid space and ventricle and invasion of cerebellum	Astrocytoma Grade I-II	+
Russell & Rubinstein 1971	16 F	?	Conus	?	Malignant astrocytoma	?
Eade & Ulrich 1971	21 F	8 months	Dorsal cord	Subarachnoid space and ventricles	Mixed glioma	+
Eade & Ulrich 1971	21 F	11 months	Dorsal cord	Subarachnoid space and ventricles	Mixed glioma	+
Eade & Ulrich 1971	19 M	6 months	Conus	Subarachnoid space and ventricles	Mixed glioma	+
Tashiro, <i>et al</i> 1971	12 F	11 months	Dorsal cord to conus	Subarachnoid space and ventricles and invasion of hypothalamus, thalamus, brainstem and cerebellum	Glioblastoma multiforme	+
Andrews <i>et al</i> 1978	45 M	13 months	Dorsal cord	Subarachnoid space and ventricles and invasion of septum pellucidum	Glioblastoma multiforme	+
Simonati <i>et al</i> 1981	19 F	5 years	Dorsal cord	Subarachnoid space and ventricles	Malignant glioma	+
Current Case 1	38 F	9 months	Dorsal cord	Subarachnoid space and ventricles, invasion of thalamus, hypothalamus midbrain and pineal	Malignant astrocytoma	+
Current Case 2 (No necropsy)	19 F	28 months	Conus	Subarachnoid space and ventricles, invasion of cerebellum, corpus callosum, basal ganglia, frontal lobes	Astrocytoma Grade II	+

the ventricular system does not normally occur without communicating hydrocephalus as has been demonstrated by scintiscisternograms.²¹ Recently Nishio *et al* have described an additional correlation with focal ependymal defects which occur in normal brains but appear to be exaggerated in hydrocephalus.²² Tumour cells became attached to the ependymal cell-free ventricular surface, while normal ependymal surface appears to be inconducive to tumour cell attachment.¹³

The role of surgery in precipitating subarachnoid dissemination is disputed in previously reported cases. In patient 2 it is possible that surgical manipulation of the tumour and the relatively prolonged survival allowed dissemination to occur, but in

patient 1 surgery was performed only nine days prior to death and therefore had no significant role in dissemination.

Both patients had evidence of raised intracranial pressure. Possible mechanisms include obstruction of CSF absorption at the arachnoid villi by increased protein, haemorrhage from tumour or seeded tumour cells. Production of a communicating hydrocephalus or production of excessive fluid as well as protein by the tumour may also be involved. In a patient, such as patient 1, with or without spinal cord symptoms, and with markedly elevated CSF protein, it is necessary to consider the possibility of a spinal cord tumour and then search for it. Raised intracranial pressure is not always indicative of dis-

semination intracranially of spinal tumours but a cerebral CT scan should be performed in such cases.

The place for cranio-spinal irradiation in patients with spinal cord tumours who have malignant cells in CSF or abnormalities on cerebral scanning is uncertain. The efficacy of adjuvant chemotherapy is even less certain and should be used in centres where a trial can be conducted. It should be given via an Omay reservoir to achieve worthwhile intraventricular drug levels.

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