Primary glioblastoma multiforme of the spinal cord in infancy and childhood

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TUMOUR WITHIN THE spinal cord is rare in infancy and childhood [5, 12, 13, 19, 24, 25]. In 1944, Hamby [13] reviewed a total of 214 cases of intraspinal tumors in children under 16 years of age. There were 44 gliomas (20.6%) in that group. However, he did not delve into the nature, biology or pathologic features in any of the 44 cases. It is not possible, therefore, to state the number amongst them that may have been glioblastomas. Stookey's [25] 165 cases yielded 8 intraspinal tumors in children. One was an intramedullary tumor. Again, no specific diagnosis or details were given regarding it. Of the 5 astrocytomas in children reported by Elsberg [7], there was also no instance of a glioblastoma multiforme. Similarly in the following series of spinal cord tumors in children, 16 cases of Richardson [23], 12 cases of Arseni et al [1] and the 40 proven cases of Svien et al [26], there was no documented case of a glioblastoma multiforme.

It is obvious from a review of the literature that in pediatric practice, the occurrence of primary intraspinal glioblastoma multiforme is uncommon. There are only 9 documented cases in children. It is often taken for granted that like their intracranial counterpart, their clinical course, pathologic features and biological behaviour distinguish them from the benign astrocytomas, ependymomas and oligodendrogliomas. They are grouped here separately to examine if this indeed be true for such tumors of the spinal cord. Again, the

radical extirpation of intramedullary tumors advocated for better long-term results, [15] while being true for the benign tumors, does not hold for the glioblastomas. This impression is reinforced by the present review and a case report.

Geisner[11], Lowenberg[17] and Tauber et al[27] reported cases in which glioblastoma multiforme was found in the spinal cord. However, these were not primary intraspinal tumors and are hence excluded from the present study. They were clearly intracranial tumors that secondarily involved the spinal cord. Further, a number of cases were excluded for want of sufficient data. Case 15 of Ford[9] that of a spongioblastoma reported by Grant et al[12], case 1 of Geisler et al[10], case 14 of Iraci[15] and the two cases of Dereymaker et al[6] (2 and 15-year-old girls) are not being included for this reason. The diagnosis in each instance was spongioblastoma. Excepting the 2 cases of Dereymaker et al[6], there was no indication in the rest as to the exact tumor type. Therefore, it was not possible to confirm if they belonged to the benign spongioblastoma polare group or if they were meant to designate the malignant multiforme variety. The first two of the above cases besides lacking adequate pathologic verification had no comments as to the location, specific follow-up or clinical course. Quite similarly, Parkinson et al[20] described a "malignant glioma? neuroepithelioma" in a newborn. Besides mitotic figures, there were no features one would ordinarily ascribe to a glioblastoma multiforme. Moreover, there was no consensus amongst the various pathologists who examined the sections as to the diagnosis. It is, therefore, being excluded from the present series.

Astrocytomas with localised areas of malignant change with none of the features of a glioblastoma multiforme have also been excluded from this study. The relatively long survivals in these cases would attest to their being a different type of a tumor from the glioblastoma multiforme. Ingraham et al[14] had 9 astrocytomas in their series of 63 intraspinal tumors in children. None of them was stated to be a glioblastoma multiforme. In a subsequent report, Matson et al[18] illustrate a 6-year-old girl operated upon at the age of 2 years for a malignant astrocytoma. An identical case was reported by Ver Brugghen[28] in a 13-year-old girl.

Case Report

The patient, a six-year-old girl, was admitted following complaints of intermittent neck pain of one-and-one-half years' duration. Her pain had been insidious in onset and was described as being sharp and knife-like. It was aggravated by looking upward or on extending her neck. It was relieved by holding her head somewhat forward.

Four months prior to her admission, she was noticed to hold her head tilted to the left. At this time, she was seen by a doctor who placed her on cervical traction. This relieved her pain but her head tilt persisted. However, the week following, she complained of difficulty in raising her left arm above her shoulder. It was also noticed that she was not as deft with her left hand as she had been previously. Her grip became progressively weaker in that hand. Soon she experienced considerable difficulty in handling a spoon or holding a glass to her mouth.

A week prior to her admission, she had difficulty in walking. She required support to bear weight on the left leg.

There was no history of trauma to the head or neck. There had been no febrile episodes of significance. She volunteered no bladder or bowel problems. There was no history of recent weight loss. Her past history was unremarkable.

On examination, the child was normal mentally for her age. She was afebrile. In obvious pain, she resented any movement or manipulation of her head or neck. Her blood pressure was 120/70 mm. of mercury. There was no lymphadenopathy.

Her pupils were equal and reactive to light and accomodation. There was no papilloedema. A Horner's syndrome was not present.

Examination of the left hand showed considerable wasting. The thenar, hypothenar and interossei muscles were atrophic. No fasciculations were seen. Her left grip was extremely weak. In addition, there was marked weakness of her left biceps, triceps and brachioradialis muscles. By measurement, there was no disparity between the sizes of the left and right arms. Her left arm was somewhat hypotonic.

Her left leg was weaker than her right. This weakness was not confined to any one muscle group. There was some increase in tone but the leg could not be described as being spastic. There was no wasting apparent in the leg. She had difficulty standing on her left leg and needed some support and assistance in walking.

She had a sensory level to light touch, pain and temperature at T6. The superficial abdominal reflexes were intact. There was marked hypereflexia and a Babinski response could be elicited on the left side.

Radiologic studies

X-rays of her chest and skull were normal and unremarkable. X-rays of the cervical spines

revealed a 5 mm. forward subluxation of C3 on C4. There was no widening of the interpedicular distance. The intervertebral foramina were also normal.

A pantopaque (diiodophenylundecylate) myelogram was done. The cerebrospinal fluid opening pressure was 70 mm. of water. No Queckenstedt test was attempted. Fluoroscopy revealed a complete subarachnoid block at T4. In view of this, the pantopaque was not removed from the spinal subarachnoid space. The cerebrospinal fluid within the manometer was estimated for protein content. It was 98 mg.%. The myelographic defect and the clinical findings referable to the arm indicated a rather extensive intramedullary tumor

Operation

Under general anaesthesia, a wide laminectomy was performed in the sitting position. The laminectomy extended from C5 to T5. This exposed a tight dura mater. The latter did not pulsate. On opening the dura mater, the spinal cord was seen to fill the canal. As the exposure progressed, it was obvious that the cord was hypertrophied and edematous. It was the seat of a fusiform swelling. It was maximally dilated at about the C6 C7 interspace. An intramedullary mass was now obvious. A posterolateral myelotomy was now done on the left side. As this neared completion, a purplish-blue mass began to extrude. It was obvious that the spinal cord was reduced to a mere shell, having been compressed and stretched by the expanding neoplasm. There were no cysts to be identified. Spatulas and various blunt dissectors were used in an attempt to preserve what appeared to be the semblance of a cleavage plane between the tumor and the spinal cord.

As this was done, it was quite apparent that the tumor was frankly infiltrative. This was especially so at the upper and lower poles of the tumor and also on its anterior surface. All gross evidence of tumor was removed. Care was taken not to interrupt large vessels in the spinal cord or those accompanying the nerve roots.

Hemostasis assured, the dura mater was closed. The wound was then apposed in layers.

Histopathology

Hematoxy and eosin preparations of both small and large fragments of the tumor showed considerable numbers of neoplastic glial cells. These cells had ovoid to elongated nuclei and were pleomorphic. They were quite hyperchromatic.

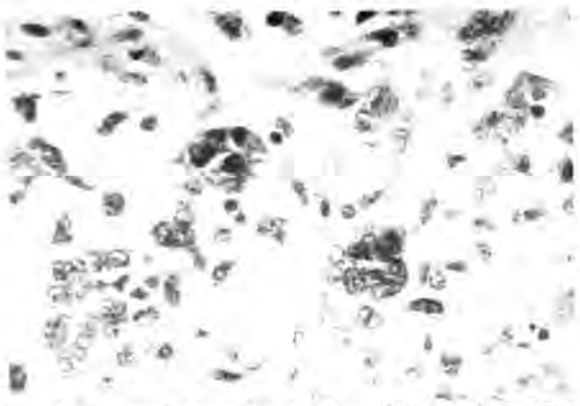

Fig. 1: Photomicrograph of the spinal cord tumour. Hematoxylin and eosin stain. Multinucleated giant cells and pleomorphism of the glial cells support the diagnosis of glioblastoma multiforme x 350.

In addition, there were large areas of necrosis. In the more cellular areas, multinucleated giant cells and abnormal mitotic figures were abundant (see photomicrograph). In yet other areas, there were large atypical astroblasts which showed tendencies to form a cartwheel-like arrangement about vessels. Endothelial proliferation with vascular hyperplasia was evident in many of the sections examined. There was no sarcomatous component to the tumor. In some areas, "gitter cells" were seen impregnated with hemosiderin pigment attesting to small past bleeds within the tumor.

Examination of all the speciments failed to reveal evidence of recognizable spinal cord tissue or nerve roots.

Diagnosis: Glioblastoma multiforme.

Postoperative course

On the day following surgery, a tracheostomy was performed to help with her airway. On the 14th postoperative day, she developed hyperthermia (T° 105F). This was, in part, due to her inability to sweat below her neck. In addition, she had abdominal distension, no doubt secondary to the loss of intestinal tone.

Her progress was slow but steady. In two weeks, she was able to sit out of bed. At this time, cobalt treatments were begun to her entire spine. She received a total of 3,000 rads over a 6-week period. Her neurological status, however, was unchanged from that previous to surgery. Seven months later, she complained of neck pain again. Examination at this time revealed a quadriplegia. Her progressive downhill course continued. Intercurrent urinary tract infection complicated exten-

No.	Year	Author	Sex	Age	Location	Survival Postop	Diagnasis
1	1901	Fischer[8]	F	8 yrs.	C.T.	—	**Glioblastoma multiforme**
2	1930	Bergonzi[3]	M	12 yrs.	C.T.L.	—	"
3	1934	Berkwitz[2]	F	14 yrs.	C.T.L.	3½ mos.	"
4	1934	Browder[4]	F	10 yrs.	C.	3 mos.	"
5	1935	Weil et al[29]	?	5 yrs.	C.T.	—	"
6	1944	Klackenberg[16]	M	11 mos.	C.	10 mos.	"
7	1960	Rand et al[22]	F	11 yrs.	T.	3 mos.	"
8	1960	Rand et al[22]	F	7 yrs.	C.	25 days	"
9	1966	Iraci[15]	F	13 yrs.	T.	12 mos.	"
10	1969	Arumugasamy	F	6 yrs.	C.T.	9 mos.	"

C = Cervical
T = Thoracic
L = Lumbar

Table of documented cases of primary spinal cord glioblastoma multiforme in the literature.

sion of her tumor into the medulla oblongata. She died 9 months after her surgery.

Autopsy

A post-mortem was performed on 1.19.68. Besides bilateral chronic pyelonephritis and cystitis, there was tumor recurrence at the site of the surgery. In addition, there was considerable contiguous extension of the tumor into the medulla oblongata and cisterna magna. The microscopic appearance of this tumor was identical to that of the operative specimens.

Discussion

Poser[21], in his review of syringomyelia with associated neoplasms, drew attention to 4 glioblastomas in children[2, 3, 8, 29]. They were all variously related to intramedullary cystic cavities. Although Fischer[8] does not state the sex of his patient there are definite indications that he was speaking of a girl. Bergonzi's[3] patient had extensive involvement of the cervical, thoracic and lumbar segments of the spinal cord. Berkwitz[2] described a glioblastoma multiforme of proportions identical to that of Bergonzi[3]. His case was included in Hamby's report[13] but not that of Bergonzi.

There are 2 cases in the literature where a spina bifida with a meningocele was associated with a spinal cord glioblastoma multiforme. One is that of a 5-year-old child (the sex of the child is not stated in the report)[29] and the other, an infant reported by Klackenberg[16]. Browder's[4] case I of a cervical glioblastoma multiforme in a 10-year-old girl was surgically verified. The patient died 3 months later but was not autopsied. Iraci's[15] case 19 and the 2 cases of Rand et al[22] are unequivocal examples of spinal cord glioblastoma multiforme. A further case is being added here.

Spinal cord glioblastoma multiforme is rarer in infancy than in childhood. Klackenberg's[16] case (alluded to earlier) of an 11-month-old boy is the youngest patient being reviewed here. Subsequent

reports, of spinal tumors in infancy by Mosberg[19] and Schwartz[24] did not add further new cases, of the type presently under review, to the literature.

It would appear from the cases tabulated, that girls far outnumber the boys (3.5:1). However, the number of cases is too small to warrant any definite conclusion regarding this. All the patients were dead in under a year following surgical verification.

Gliomas of the spinal cord should be removed as completely as possible[15]. Following radical removal, the immediate postoperative course may be trying and stormy, but the long-term results are better than with subtotal resections[15]. While this is true for the benign tumors of the spinal cord, it cannot be extended to include the glioblastomas. Iraci[15] makes no distinction between the glioblastomas and other gliomas in this regard. It is agreed that in each instance as complete a removal as is possible should be done irrespective of the tumor type. However, the prognosis with the glioblastomas has been uniformly poor. In spite of a radical extirpation and X-ray therapy, the patient reported here died nine months after surgery. It is entirely possible that should the tumor have been located in the lumbar or low thoracic area, she may have lived longer.

In general, the duration of survival has been less in those with glioblastomas than those with benign gliomas. Our table would indicate that in all where details were available (7 patients) death occurred in under one year. In the 9 cases of Grade I and II astrocytomas reported by Rand et al[22], seven were alive at the end of one year. The remaining two had been recently operated upon and were alive at the time of their report. Further, one of their patients (case 3) lived 14 years after surgery. But both their patients with a glioblastoma multiforme were dead in under 3 months following surgery. Iraci's[15] surgically verified cases also showed a similar trend for the benign tumors. His girl with the glioblastoma multiforme died 12 months following surgery.

Many earlier reports of intraspinal tumors failed to classify the gliomas into their various type. It is not enough to talk of intramedullary tumors in the broad category of gliomas. Correct histopathologic verification should be obtained in each instance. This is because prognosis and therapy will vary with the tumor type. The glioblastoma multiforme should be considered separately from other gliomas by virtue of its nature, biological behaviour and pathology. This study indicates that as in its intracranial counterpart, the prognosis is uniformly poor. Spinal cord gliomas are rare in children. It is evident from this report that glioblastoma multiforme is more so. That the patient in this report had symptoms only referable to the spinal cord would support the diagnosis of a primary intraspinal neoplasm. On autopsy, other than local contiguous recurrence, there was no evidence of tumor intracranially or elsewhere.

Summary.

1. Reported cases of children with spinal cord glioblastoma multiforme are reviewed and tabulated. A further case has been added making a total of 10 such cases.
2. Girls seem to be more commonly affected. Although the few cases in the literature do not allow firm conclusions regarding these tumors, it is hoped that more meaningful deductions will be forthcoming as more cases are reported.
3. It is evident that with present methods of treatment, the prognosis is uniformly poor. All patients reviewed were dead in under a year.

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