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Sarcomas in the Central Nervous System of Children

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Introduction

The neurosurgeon encounters sarcomatous lesions either as primary diseases of the central nervous system or its coverings or as lesions originating elsewhere, secondarily involving the nervous system often after having been diagnosed and treated at their primary site. The former, usually manifested as rapidly progressive space-occupying lesions, fall obviously in his domain but he is also frequently sought for palliative treatment of neurologic manifestations of extraneural neoplasms. Moreover, extraneu-ral tumors not infrequently manifest themselves initially with neurologic signs and symptoms. Patients with these infrequent and highly aggressive lesions usually undergo a conventional neurosurgical approach and it is the pathological examination that reveals the unsuspected nature of the tumor and determines further therapeutic decisions. Thus, a collective review of both primary and secondary sarcomatous lesions involving the nervous system, although nosologically unorthodox, claims the practical advantage of grouping together diverse lesions that share common problems for the neurosurgeon. Intracranial and intraspinal sarcomas constitute an ill-defined group in terms both of taxonomy and nomenclature. Classifications have varied according to the personal view-point of different authors [1-5] and the boundaries of the group are as yet not completely established. Lesions such as the so-called monstnuocellular sarcoma [1] are considered as either a form of glioblastoma or as a sarcoma of the blood vessel origin. Reticulum cell sarcomas/microgliomas are in the process of being incorporated into the lymphomas [6] but this view is not unanimous. The purpose of this paper is to report on the analysis of a group of 26 patients with intracranial or intraspinal sarcomas attended over a 10-year period at the Instituto Nacional de Pediatría-DIF in Mexico City. We included in this series all patients with sarcomatous lesions identified either at surgery or at autopsy as involving the central nervous system. Lesions considered lymphomatous in nature were excluded.

Case Material

Frequency and Distribution

One of our patients had both intraspinal and intracranial involvement giving a total of 27 lesions; 15 of these were intracranial and 12 were intraspinal. Sarcomas thus represent 5.5% of our series of 270 intracranial tumors. This figure is higher than Matson’s [7] 8 sarcomas

in 750 intracranial tumors (1.06%) and of Koos and Miller [8] who list 29 sarcomas in 700 tumors, representing 4.14% of their series.

Our 12 intraspinal sarcomas amount to 19.04% of our series of 63 intraspinal tumors.

Corresponding figures in the literature include a proportion of 19% in 214 intraspinal tumors in childhood reported in the literature up to 1944 and reviewed by Hamby [9]; Matson's [7] figure of 13% in 115 intraspinal tumors; 15.6% in Rand and Rand's [10] series of 64 patients, and 11 sarcomas in 81 intraspinal tumors (13.5%) recently reported by De Sousa et al. [11].

All the above figures give a rough indication of relative frequencies but must be interpreted with caution in view of the lack of uniform criteria for including specific types in the different series.

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Age and Sex Distribution

The male-to-female ratio was 10:5 in 15 intracranial sarcomas and 7:5 for the 12 intraspinal lesions. Children with intracranial sarcomas ranged in age from 8 months to 17 years, and those with spinal neoplasms from 3 to 17 years.

Pathologic Aspects

The histologic diagnosis appears in tables 1 and 2. Four of the five intracranial meningeal sarcomas and one of the three spinal meningeal sarcomas were of the polymorphic cell type. One instance in each location exhibited features suggestive of origin in a meningioma and could be considered malignant meningiomas, albeit with unequivocal sarcomatous changes. The remaining case, involving the cervical spinal cord, had features of meningeal sarcomatosis (fig. 1).

The four unclassified sarcomas were tumors of undetermined histogenesis, some of them originally considered reticulum cell sarcomas but in which, on reclassification in the light of current taxonomic opinion, a lymphomatous origin could not be substantiated (fig. 2). Others were of probable meningeal origin but did not conform to the conventional features of meningeal sarcomas (fig. 3). All four were intradural and involved the brain. One was multicentric with diffuse meningeal and intraventricular involvement (fig. 4).

Consultations with other neuropathologists about some of these cases did not lead to conclusive diagnoses; the lesions were considered very primitive neoplasms of uncertain histogenesis. With the exception of one intraspinal and one intracranial rhabdomyosarcoma, which were of the alveolar variety, the other lesions encountered were embryonal rhabdomyosarcomas. Both cases of rhabdomyosarcoma involving the skull arose from lesions in the face. One of them originated in the maxillary antrum and manifested itself initially with neurologic symptoms. The other case originated in the soft tissues of the face; remission was achieved with surgery and radiotherapy and after an asymptomatic period of 5 months, presented with signs of increased intracranial pressure and focalization. On surgery, an extradural growth was found involving the temporal region and approaching the midline basally. Three of the four spinal rhabdomyosarcomas were hourglass lesions that originated in the retroperitoneum. The fourth case arose in the soft tissues of the face and metastasized to the dorsal spine. One of the three cases of Ewing sarcoma originated in the bones of the skull, with extensive involvement of the cranial cavity. One case was metastatic from a lesion in the humerus and involved the brainstem, as discussed below. The third case, previously mentioned as the patient with both intracranial and intraspinal lesions, had an

initial lesion involving the spinal canal with minimal bone involvement and might represent a case of extraosseous Ewing sarcoma.
The sole case of a malignant neurogenic sarcoma had areas of plexiform neurofibroma, which probably represented the original lesion.

Table 1. Intracranial sarcomas: pathology

Meningeal sarcoma	5
Sarcoma, unclassified	4
Ewing sarcoma	3
Rhabdomyosarcoma	2
Alveolar sarcoma of the orbit	1

Table 2. Intraspinal sarcomas: pathology

Rhabdomyosarcoma	Ewing sarcoma	Meningeal sarcoma	Neurogenic sarcoma	Osteogenic sarcoma
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Table 3. Intracranial sarcomas: symptoms

Vomiting	Headache	9	8
Impaired visual acuity		5	4
Motor disturbances			
Tumor		3	
Restlessness		3	
Seizures, gait disturbances,		2	

Table 4. Intracranial sarcomas: signs

Papilledema	MacEwen sign	Pyramidal signs	Strabismus	Hemiparesis	Tumor	Pupillary signs
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Clinical Aspects

The primary topography of the intracranial lesions was intradural in nine cases and extradural in six. Four of the five meningeal sarcomas present in the skull were intradural in location. All four sarcomas of uncertain histogenesis were intradural, whereas both rabdomyosarcomas and two Ewing sarcomas were extradural. The sole intradural tumor represented metastasis from a primary lesion in the humerus. This was the only case in our series without histologic verification; the primary lesion was adequately documented and, shortly after amputation, clinical and radiologic evidence of a brainstem mass, documented by CT scan, appeared. The patient died after receiving mas-

Fig. 1. Small spindle cells diffusely involve cervical spinal cord in meningeal sarcomatosis.
 Fig. 2. Sarcoma of undetermined histogenesis with features suggestive but not conclusive of lymphomatous origin.

sive radiotherapy to the brainstem. At autopsy, extensive necrosis of the brainstem was found, and neoplastic cells were not unequivocally documented. The single case of alveolar soft part sarcoma of the orbit was extradural, most of it intraorbital, but a neurosurgical approach to the tumor was required so that the roof of the orbit was excised. With the sole exception of the brainstem metastatic Ewing sarcoma, previously mentioned, all other intracranial sarcomas were supratentorial in location. One of the unclassified sarcomas was multicentric, with diffuse peri-vascular and meningeal involvement (fig. 4). It was originally considered a reticulum cell sarcoma but, as men-

Fig. 3. Sarcoma of undetermined histogenesis with compact, large clear cells that could represent a meningeal origin.

Fig. 4. Coronal section of brain in a patient with sarcoma of undetermined histogenesis but expected multicentric appearance for reticulum cell sarcoma lacking histologic features of a lymphomatous nature. tioned above, the cytologic features do not suggest a lymphomatous proliferation. Nine of the twelve spinal tumors were dorsolumbar; two involved the cervical spinal canal and one was lumbosacral. In contrast to meningeal sarcomas in the skull, two of the three

spinal meningeal sarcomas were extradural in location and the remaining case represented an example of meningeal sarcomatosis diffusely involving the dura in the upper cervical spinal cord. All other spinal tumors were extradural. Symptoms and signs for the intracranial neoplasms appear in tables 3 and 4. Tumor in this location mani-
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Fig. 5. Lateral view of an 8-year-old girl with enormous menin-geal sarcoma.
Fig. 6. Spinal x-ray in a patient with osteogenic sarcoma (arrow points to most important part of osseus lesion).
Table 5. Intraspinal sarcomas: symptoms
Motor disturbances in legs 12
Sphincter impairment 9
Pain 8
Paresthesia 2
Tumor 1
Table 6. Intraspinal sarcomas: signs
Sphincter incontinence 9
Sensory impairment 9 (3)

Spastic paralysis	6
Pyramidal signs	6
Flaccid paralysis	5
Tumor	2
Quadriplegia	1

fested mainly as increased intracranial pressure and signs of focalization or lateralization were present in only four cases. In 3 patients an outstanding manifestation was a visible mass in the skull (fig. 5).
 Spinal tumors (tables 5, 6) usually presented with motor disturbances in the legs, abnormalities in sphincter function and pain in the back or lower limbs. In only 1 patient was a visible mass the presenting complaint. Sensory disturbances were present in 9 patients, but a definite level of sensorial loss was established only in 3 of them. Six children exhibited spastic paralysis or paresis, 5 had flaccid paralysis, and in 1 case there was a flaccid quadriplegia.

Ancillary Studies

Plain skull x-rays were abnormal in 11 of the patients with intracranial masses. This finding ranged from nonspecific evidence of increased intracranial pressure to clearly defined bone lesions, suggesting localization of the tumor. Spinal x-rays were abnormal in 10 of the 12 cases of spinal lesions. Involvement of the vertebral facets was the usual finding. An example of a more severe lesion appears in figure 6 and belongs to a patient with an osteogenic sarcoma affecting vertebral bodies.

Echoencephalograms of the intracranial lesions revealed pathologic deviations of the midline structures in 8 of 11 patients in which the procedure was performed, while the electroencephalogram was abnormal in 13 of the 14 patients in whom it was done. In only 2, was there evidence of focalization. Nuclear scans with technetium-99 revealed abnormalities in 11 of 15 patients and exhibited abnormal concentrations of the radionuclide, particularly in intradural lesions.

Fig. 7. CT scan in a patient with alveolar sarcoma of orbit (arrow points to mass).
 Fig. 8. Enhanced CT scan of 2-year-old boy with a meningeal sarcoma. Fig. 9. Enhanced CT scan of a 7-year-old girl with an Ewing sarcoma. Note tumors inside and outside skull.

Neuroradiologic Aspects

CT scans in our last 6 patients have been of value in localizing the tumor in all instances. Representative findings in CT scans are shown in figures 7-9. Cerebral angi-ography was abnormal in all 13 patients in whom it was performed; in most cases it offered precise localization of the tumor, revealing important vascularization of these lesions, especially in meningeal sarcomas (fig. 10-13).

Myelograms were performed in 11 of the 12 patients with spinal lesions; in all of them abnormalities, with partial or total block of contrast medium in the spinal canal, were documented.

Treatment

Surgical removal of the tumor was attempted in all patients except one with an intracranial tumor and one with intraspinal tumor. Six patients in each group also received radiotherapy and 4 patients in each group received chemotherapy in addition to the other two procedures. who died 13 months after surgery. The shortest survival was that of a 2-year-old child, who died 1 month after surgery. All 3 patients with Ewing sarcoma involving the skull died, as did the patients with rhabdomyosarcoma. The patient with alveolar soft tissue sarcoma is alive, with no evidence of recurrence 11 months after radical surgery, which consisted in exenteration of the orbital contents.

Regarding the spinal tumors, the only surviving patient with rhabdomyosarcoma is well and free of tumor activity 3 years and 4 months after surgery.

All 3 patients with meningeal sarcomas died between 2 and 10 months after surgery.

Survival in patients with Ewing tumors was slightly longer; deaths occurred between 7 months and 2 years after surgery. The girl with neurogenic sarcoma died 5 years after surgery, with recurrence appearing after 4 years and 5 months of tumor-free interval. The patient with osteogenic sarcoma of the vertebral body is alive and has no signs of recurrence 6 months after surgery. She is, at present, undergoing chemotherapy.

Results of Treatment and Survival

Survival for patients with cranial and spinal tumors appears in tables 7 and 8. Three of the 5 patients with cranial meningeal sarcomas died 2-8 months after surgery. Two of them are alive, one with recent local recurrence 1 year after surgery. The other patient is alive with no clinical evidence of tumor activity 10 months after surgery. All 4 patients with sarcomas of undetermined histogenesis died. The one who survived longest was a 17-year-old girl

Concluding Remarks

The proportion of sarcomas among our intracranial and intraspinal tumors is somewhat higher than in other published series. Some variation may be expected because not all authors include the same tumors under the heading of sarcomas. With increasingly sophisticated surgical techniques and therapeutic resources, more extraneural

Fig. 10. Cerebral angiogram, AP view, in a patient with alveolar sarcoma of orbit (arrow points to vascularized mass).

Fig. 11. Lateral view of angiogram in figure 10, venous phase. Arrow points to draining veins of orbit.

Fig. 12. Lateral view, internal carotid angiogram, late phase in 7-year-old girl with Ewing sarcoma. Arrow points to abnormal vessels.

Fig. 13. Lateral view, external carotid angiogram. Same patient as in figure 12. Arrow points to feeding artery to external mass.

sarcomas, previously fatal over the short term, may be expected to invade the central nervous system and fall in the domain of the neurosurgeon.

The two groups of primary tumors – meningeal sarcomas and unclassified sarcomas – presented as rapidly progressive, highly aggressive lesions, as reflected by the

usually brief survival of patients. Further studies of unclassified sarcomas, currently in progress, particularly electron microscopy and immunohistochemical procedures, may well reveal the nature of these sarcomas. Nevertheless, this information is not usually forthcoming while the neurosurgeon is involved in the case. It is impor-

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Table 7. Intracranial sarcomas: survival
Table 8. Intraspinal sarcomas: survival

Sarcoma
Pa- Survival tients
Sarcoma
Patients
Survival

Meningeal sarcoma	5	4/12. 1/12. 8/12. 1 vr.	Rhabdomvosarcoma	4	1-8/12. 1 vr. 1 vr. 3-
Sarcoma unclassified	4	6/12 4/12 1/12 11/12	Ewing sarcoma	3	5/12 10/12 2/12
Ewing sarcoma	3	1-11/12 4/12 4/12	Meningeal sarcoma	3	1-11/12 7/12 9/12
Rhabdomvosarcoma	2	1 vr. 1-2/12	Neurogenic sarcoma	1	5vr
Alveolar sarcoma of	1	11/12	Osteogenic sarcoma	1	6/12

tant for the neurosurgeon to be aware that some degree of controversy exists as to the pathologic classification of these lesions.
It is noteworthy that whereas meningeal sarcomas in the skull were usually intradural, spinal lesions of the same type tended to be extradural in the few cases examined. Physical examination of the skull revealed a visible mass in 2 cases with Ewing sarcoma involving the skull and in the only case of intracranial meningeal sarcoma of extradural location (fig. 1).
Plain films may, at times, help to identify the presence and location of the lesion. CT scans offer great resolution and should complement but not replace the usual neuro-radiologic studies, such as angiography for intracranial lesions and myelography for those in the spine; the information provided by these studies is indispensable for decisions as to surgical approach. Cerebral angiography is required so as to visualize the external as well as the internal circulation, especially in patients with a suspicious bone or meningeal lesion, as in meningeal sarcoma, Ewing tumor, and so forth. We do not have experience with spinal angiography.
In general, resistance treatment was the rule in most of these tumors; radiotherapy and chemotherapy are of limited benefit. In view of the rapid progression and biologic behavior of these tumors, a more timely diagnosis in these patients will probably not extend the survival or cure rate significantly. Nevertheless, with a timely diagnosis the palliative effects of surgery, especially in spinal lesions, may convey considerable benefit to the patients.

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Author's Comment

Names of things change at different rates than do their other features. The pathology of primary meningeal sarcomas is a case in point. These patients would still have their signs and symptoms, imaging techniques have since advanced but would produce essentially the same information and the surgical strategy for their management is probably unchanged. But the way the pathologist names them is completely different. At the time of the original publication (the material was collected from 1971 to 1980) primary meningeal sarcomas were classified, according to Rubinstein [1] and the *AFIP Atlas of Tumor Pathology*, into spindle cell, round cell and polymorphic types. Many of these tumors with prominent chondroid areas are now considered mesenchymal chondrosarcomas but others have not been reassigned to a particular category in spite of the fact that the term 'meningeal sarcoma' has practically vanished from the literature with no reference made to its previous existence and its official presence in the *AFIP Atlas*. Be they a specific entity or a group of neoplasms arising in a particular site, this group of tumors is ripe for a reassessment, both with modern techniques of molecular pathology and the review of large groups of cases from several institutions. Immunohisto-chemistry may detect some tumors which are actually glial in origin but with a prominent desmoplastic reaction and may further characterize those which are truly meningeal. A substantial change has also taken place with the group formerly named reticulum cell sarcoma. At the time of the original publication, these growths were al-

ready suspected of being lymphomas and the reticulum cell and its derived neoplasms were conceptually blurring. We were thus reluctant to use that term and referred to them as sarcomas of undetermined origin. At present, the morphologic definition of lymphomas goes far beyond routine histologic analysis. This group of neoplasms can now undergo detailed assessment by immunohistochemistry and by molecular analysis in its different modalities, i.e. in situ hybridization, blotting, flow cytometry. A great deal of recent work on CNS lymphomas has been done in immunosuppressed patients. Similarly detailed studies of other patients with lymphomas of the brain are expected. With these ideas in mind, from 1981 to

1993, we have collected 17 more intracranial sarcomas and 7 intraspinal sarcomas. The incidence of these lesions decreased: 32 cases among 857 intracranial tumors, now representing only 3.85% in comparison to the 5% in the Original' series. For the spinal sarcomas there are 19 cases among 170 intraspinal tumors which accounts for 11.2% in comparison with the 19.04% in the Original' series. All the above facts remind me that: Jesus Christ taught that God was everything; Marx thought that the economy was everything; Freud said that sex was everything; and finally Einstein demonstrated that everything is relative.

Reference 1 Rubinstein LJ: AFIP Atlas of Tumor Pathology. Washington, 1972.