Primary Lymphosarcoma of Cerebral Meninges*

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Primary lymphosarcoma of the cerebral meninges occurs only rarely, in contrast to the more frequently encountered primary epidural spinal lymphosarcoma which is a well documented entity.1,2,9,11,16 The absence of a true intracranial epidural space is a major factor accounting for the incidence differential between meningeal or dural lymphosarcoma involving the cranial and spinal portions of the central nervous system. According to Whisnant et al.,10 the 3 main categories of cranial lymphomatous disease are involvement of basal structures via direct extension from lesions of the nasopharynx, diffuse involvement of cranial meninges with or without cranial nerve extensions and intracerebral lymphomas.

In contrast, instances of focal lymphosarcoma arising from the cerebral dura amenable to surgical extirpation are unusual. Kernohan2 recalled having seen a case similar to the one to be presented some 30 years ago, but failed to provide specific elaboration. Zimmerman9 stated that he had seen a number of intracranial epidural malignant lymphomas, but “never showing quite so well the 2 unusual features of bone (diploë) infiltration and the formation of giant germinal centers.” Courville4 felt that the tumor in the case to be presented seemed to be allied to a group of lymphogenous tumors rarely found to have origin in the diploë of the skull. A review of the literature, including standard textbooks of neurology, neurosurgery, pathology and associated subjects revealed a paucity of information as to the pathogenesis of cases such as that which follows—primary lymphosarcoma of the cerebral meninges.

Case Report

A well-developed and nourished 68-year-old negro woman complained of frontal headaches and fatigue for several years. The headaches recurred with ever-increasing frequency and severity, Cornwall4 stating that the facial origin in the diploë of the skull. A review of the literature, including standard textbooks of neurology, neurosurgery, pathology and associated subjects revealed a paucity of information as to the pathogenesis of cases such as that which follows—primary lymphosarcoma of the cerebral meninges.

Case Report

A well-developed and nourished 68-year-old negro woman complained of frontal headaches and fatigue for several years. The headaches recurred with ever-increasing frequency and severity, and were relieved by acetylsalicylic acid and similar drugs. Relatives stated that she had become progressively more confused, irrational and somnolent. They found her on the floor, unable to rise, prior to her admission to the hospital. There was no pertinent past history.

Physical Examination. It was difficult to arouse the patient to any level of cooperative effort. Upward gaze was restricted. The optic fundi were normal. There was a left-sided hemiparesis including left facial weakness and a positive left Babinski sign. The neck was supple with normal carotid pulses. There was no cervical, axillary or inguinal adenopathy. Examination of the heart, lungs, and abdomen was normal.

Laboratory Data. The complete blood count, urinalysis, serological tests for syphilis, fasting blood glucose, urea nitrogen and protein bound iodine studies were all within normal limits. Cerebrospinal fluid pressure, dynamics and appearance were normal with a cell count of 1 lymphocyte per cmm. and the protein was 75 mg. per cent. The electroencephalogram revealed a dominant rhythm of 7-9 c/s waves at 10-60 mvs from all regions of the cortex with definite disorganization and suppression in the right frontoparietal area.

Roentgenogram of the chest demonstrated only slight pulmonic emphysema and cardiomegaly with tortuosity of the thoracic aorta. There was no apparent increase in the breadth of the mediastinum or structures at the tracheobronchial bifurcation.

Roentgenographic studies of the skull showed a triangular area of increased density in the right frontoparietal region with an associated osseous proliferative reaction (Fig. 1). The pineal body was displaced slightly to the left. These changes were confirmed by the cerebral angiogram which also displayed increased vascularity about the density in the right frontoparietal region (Fig. 2).

Operation. A neoplasm which had caused erosion and hyperostosis of the inner table of the skull, and which was obviously incorporated with the subjacent dura, made elevation of the bone flap difficult. The well-circumscribed tumor was enucleated. The adjacent cerebral cortex was apparently intact and uninvolved.

Fig. 1. Triangular area of increased density in the right frontoparietal region due to involvement by the cerebromeningeal lymphosarcoma.
FIG. 2. Frontal view in cerebral arteriogram showing extent of involvement of the right frontoparietal region by the lymphosarcoma.

except for slight softening due to prolonged compression by the lesion.

There was a smaller tumor in the antero-mesial portion of the exposed dura. The craniotomy was extended and the exposed tumor removed, together with the attached dura. This second separate lesion was about \( \frac{1}{3} \) the size of the larger one. It appeared to slightly compress the superior extremity of the pre-central convolu-

FIG. 4. Giant follicular lymphosarcomatous pattern of the tumor as it appears to arise from dural tissue replete with so-called "cracking phenomenon." H & E: \( \times 35. \)

tion. Both of the bone flaps were discarded because of their obvious involvement by the neoplasm and the dural defect was not repaired at the time.

Pathology. Two portions of bone from the frontoparietal region were studied. The convex external aspects were denuded of periosteum and appeared normal. Con-

FIG. 3. Inner concave aspect of right frontoparietal bone flap depicting gross appearance of the cerebromeningeal lymphosarcoma.
Primary Lymphosarcoma of Cerebral Meninges

Primary lymphosarcoma of cerebral meninges, however, were involved diffusely by pink-white, moderately firm, glistening, homogeneous tumor. The latter was integrally associated with the dura and appeared to invade the inner table of the skull (Fig. 3).

Cells characteristic of lymphocytic lymphosarcoma were noted to infiltrate the dural elements of the diploë of adjacent bone. In some areas, there was growth suggesting giant follicles (Fig. 4). In other regions, the largest tumor cells were consistent with lymphoblastic lymphosarcoma or perhaps even so-called reticulum cell (histiocytic) sarcoma as they enveloped portions of the dura (Fig. 5). Classic Sternberg-Reed cells could not be identified. This same pattern of cells was noted in those portions of the tumor which appeared to invade the adjacent osseous tissue (Fig. 6). There were no recognizable cerebral elements in the specimens (Fig. 7).

Postoperative Course. The patient's progress was good and in several weeks she was discharged with a moderate residual left hemiplegia. She was readmitted some 5 months later for cranioplasty. Re-exploration of the recent operative site in the right frontoparietal area revealed extensive softening and gliosis of the tumor bed without gross evidence of residual and/or recurrent neoplasm. A tantalum prosthesis was accomplished after random biopsies of the old tumor bed were obtained. Examination of these substantiated the operative impression that there was no evidence of residual or recurrent tumor. Thoracic roentgenograms and routine laboratory tests were again normal.

It is now 20 months since the first operation. During this time the patient improved and has shown no evidence of recurrence or metastasis.
Discussion

Any consideration of tumors arising primarily in the meninges necessitates reference to anatomical differences that exist between the leptomeninges and dura mater of the brain as contrasted with those of the spinal cord. The dura adheres to the inner table of the skull, functioning as endosteum (periosteum). At the level of the foramen magnum, however, only the outermost layer of the dura continues as the peristeum of the vertebral canal, while the dura proper becomes separated from the bone by a space-containing fibroareolar tissue replete with vascular and lymphatic structures. Also, the pia-arachnoid (leptomeninges) are fused by a fine lattice of delicate trabeculae over the brain except where the subarachnoid cisterns effect their separation. In the spinal cord, however, the pia and arachnoid are definite layers separated by the subarachnoid space everywhere except where it is traversed by nerve roots and certain ligaments. Leptomeningeal extensions into the interior of the brain form the tela choroidea and stroma of the choroid plexuses. The pia mater acts as the outer component of the Virchow-Robin extra-adventitial space penetrating the brain and spinal cord in relation to nutrient blood vessels.

Most meningeal tumors are attached to the dura, whether within the cranium or the spinal canal. It is generally held that they arise in this structure from the included arachnoid villi. Cells of the arachnoid villi are considered to be constituents of the reticuloendothelial system. This system is composed of fixed primitive reticular cells supported by a framework of fibrils. Neoplastic disease of this widely distributed tissue includes such conditions as follicular lymphoma, Hodgkin's disease and reticulum cell sarcomas.

So-called "round cell sarcomas" of the spinal epidural space have been recognized for years. In fact, malignant lymphomatous involvement of this spinal epidural space by malignant lymphoma secondary to disease elsewhere in the body is common. Furthermore, reports of series of cases of primary epidural spinal lymphosarcoma have increased in the last decade, thus indicating that this disease exists as an entity.

However, it is rare for the cranial meninges or even the skull to be involved with malignant lymphomas of any type. In 1952, Kernohan and Sayre stated that, while lymphoid tumors are extremely rare in the cranial cavity, they are more frequent in the spinal canal, especially in the spinal epidural space. Intracranial involvement by malignant lymphoma is unusual and most reports allude to origin or growth in the skull rather than in the meninges or dura. The occurrence of bone marrow involvement in lymphosarcoma is readily explainable since even in normal marrow preparations isolated islands of lymphocytes, replete with germinal centers, are found. The diploe of the skull, although rarely if ever examined, should prove to be no exception. In 1949, Courville stated that it would seem possible to have primary lymphosarcoma of the skull and reiterated this when he examined the material from the case herein described. He stated further that this tumor seems to be allied to a group of lymphogenous lesions that are rarely found to originate in the diploe of the skull. Piendak and Alder in 1959 apparently substantiated Courville's observations when they reported the 5th case of primary reticulum cell sarcoma of the skull.

Even more rare are the reported instances of malignant lymphoma arising in the cerebral meninges. Most cases are concerned with the unusual secondary involvement of the skull by systemic lymphosarcoma. Different observers report that in 8 to 11 per cent of lymphosarcoma cases studied, skeletal lesions are present, of which only a minor percentage involve the skull. Thus, despite the fact that Kernohan and Zimmerman state that they have seen cases of lymphosarcoma in cerebral meninges, these tumors have not been reported as such in the literature. Wöckel in 1960 describes the rare instance of primary reticulum cell sarcoma, apparently arising in and in-
volving the dura of a 3½-year-old boy. The tumor extended over the convexities of both cerebral hemispheres and was divided into inner and outer lamellae.

The clinical evidence in our case was insufficient to justify preoperative diagnosis of primary intracranial meningeal lymphosarcoma. Lumbar puncture showed normal dynamics; the crystal clear cerebrospinal fluid contained only 1 lymphocyte per cmm. The fluid was not examined for tumor cells. Since the early part of this century there have been numerous reports of the presence of tumor cells in cerebrospinal fluid. Several articles have appeared in the literature between 1931 and the present. Nayler\(^1\) in 1964 detected neoplastic cells in the cerebrospinal fluid from 25.5 per cent of 313 patients with intracranial and intraspinal tumors. The highest percentage of detection was metastatic carcinoma, 42 per cent; next gliomas, 29.4 per cent; and lowest the non-gliomatous primary neoplasms, 11.8 per cent. Important reasons for not being able to detect neoplastic cells in cerebrospinal fluid are that certain tumors do not tend to exfoliate their cells, and that the growth may not have direct contact with the spaces through which the cerebrospinal fluid circulates. Clusters of small cells resembling lymphocytes are normally found in preparations of ventricular cerebrospinal fluid. These are presumed to be from the choroid plexus\(^2\) but could be difficult to differentiate from cells sloughed by a small cell epidural or meningeal lymphosarcoma.

In this case, as soon as a space-occupying lesion in the right frontoparietal area was recognized, a craniectomy was performed and all recognizable tumor removed. When the patient had begun to recover, radiation therapy was instituted. A total of 5,000 r in air was delivered to the head externally over a 5-week period. This is the mode of treatment recommended in primary epidural spinal lymphosarcomas.\(^2\) In the past decade chemotherapy has been used more frequently for the treatment of malignant lymphomas, including lymphoid leukemias, Edzlini and Stutzman\(^4\) in 1963 reported that Chlorambucil (Leukeran), an oral alkylating agent, was administered to 126 patients with lymphoma or chronic lymphocytic leukemia. It benefitted \(\frac{2}{3}\) of the patients with Hodgkin's disease and \(\frac{1}{3}\) of those with leukemia or small cell lymphosarcoma. However, only 1 of the 12 patients with reticulum cell sarcoma responded to Chlorambucil therapy.\(^5\)

**Summary**

An unusual instance of primary lymphosarcoma of the cranial meninges, mixed small and large cell type, with extension into the inner table (diploë) of the right frontoparietal skull, is described. This rare tumor occurred in a 68-year-old negro woman with severe frontal headache and progressive personality change of several years' duration. We believe the primary origin of intracranial lymphosarcoma is the meninges rather than the diploë. Few, if any, comparable cases have been specifically reported.

### References


18. Zimmerman, H. M. Personal communication.