TUMOR CELLS IN THE CEREBROSPINAL FLUID*

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The armamentarium of the neurosurgeon in the diagnosis of intracranial neoplasm has increased considerably in the past 4 decades. However, the considerable number of “negative” surgical explorations and intracranial neoplasms actually missed indicate that new techniques are still needed.

During the last 7 years we have become interested in the examination of the sediment of the spinal fluid as an aid in the diagnosis of intracranial tumors. It seemed clear that cytologic examination of the cerebrospinal fluid for tumor cells might play a significant role in the recognition of these neoplasms. While most of the reported studies described cells from metastatic brain lesions, only a few investigations demonstrated tumor cells derived from primary intracranial tumors in the spinal fluid.

We propose to present a short review of the pertinent literature followed by a detailed description of 3 cases in which the cytologic findings in the spinal fluid aided in the diagnosis of intracranial tumor. Subsequently, the over-all result of a study on 2,270 cases in which the patient was suspected of having a neoplasm of the central nervous system is mentioned briefly.

At Michael Reese Hospital all specimens of spinal fluid from the neurosurgical and neurological services are sent routinely for cytologic examination. The fluid, usually 3 to 6 cc., is centrifuged rapidly for 5 min. The sediment, which frequently is only microscopic in amount, then is smeared at once on two albumin-coated slides and immersed immediately in a solution of 95 per cent alcohol. The slides are stained according to Papanicolaou’s method. In addition, all ventricular fluid obtained from ventriculography is sent for cytologic diagnosis. This specimen is prepared in the same manner as the cerebrospinal fluid from spinal puncture. The cells present in the ventricular fluid are interpreted in the same manner as those in the fluid obtained by spinal puncture. It is clear that there will be many more and better preserved tumor cells in the ventricular fluid if the tumor has extended into the ventricles.

Platt, citing a number of older studies, remarked that cytologic examination of spinal fluid does not supplant other neurologic procedures in the diagnosis and localization of tumors of the central nervous system, but should be used in combination with other existing methods. He reported 8 cases in which cytologic examination of the spinal fluid disclosed atypical cells. The sediment in the spinal fluid of 1 patient with glioblastoma multiforme showed atypical pleomorphic nuclei and of another, sheets of malignant tumor cells. The spinal fluid of a patient with medulloblastoma revealed cells with hyperchromatic nuclei and numerous mitoses. Atypical cells with hyperchromatic nuclei were found in an instance of sarcomatosis of the meninges. Hyperchromatic cells with pyknotic nuclei (Class IV–V of Papanicolaou's classification) were derived from a Rathke's pouch cyst. Cells suggestive of malignant tumors were present in cases of glioblastoma multiforme, astrocytoma and oligodendroglioma.

McCormack et al., in 1953, demonstrated carcinoma cells in the spinal fluid in 9 of 40

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patients with metastatic carcinoma. Larson et al.\textsuperscript{2} reported tumor cells in 5 instances: 3 metastatic carcinomas and 2 gliomas. Spriggs\textsuperscript{11} found carcinoma cells in the spinal fluid in a high proportion of his cases. He also reported positive findings in patients with a glioblastoma multiforme, a medulloblastoma, a reticulum-cell sarcoma, and a myeloma, respectively.

Murphy\textsuperscript{7} stressed clumping of tumor cells in the spinal-fluid sediment in instances of carcinomatosis of the meninges. McCormack et al.,\textsuperscript{2} in 1957, found neoplastic cells in the spinal-fluid sediment in 27 out of 320 patients. The majority of these patients had metastatic carcinoma. McMenemey and Cumings,\textsuperscript{5} in 1959, described 13 cases in which there were tumor cells in the spinal fluid. There were 8 metastatic carcinomas and 5 primary tumors—an astrocytoma, a meningioma, an oligodendroglioma, a chromophobe adenoma, and a chordoma. Marks and Marrack\textsuperscript{4} reported 7 instances of metastatic carcinoma with positive findings in the spinal fluid.

From these reports it is evident that carcinoma cells from metastatic brain lesions are detected much more commonly than cells from other tumors.

**CASE REPORTS**

**Case 1.** A 59-year-old white male was admitted to Michael Reese Hospital because of intermittent nonprojectile vomiting of 3 months' duration, lethargy, and generalized weakness. Eighteen months previously he had fallen down a stairway and dislocated his shoulder; there was no loss of consciousness. A radiologic diagnosis of peptic ulcer of the lesser curvature of the stomach was made 3 months prior to admission.

Examination revealed bilateral papilledema with unequal pupils, the left being large and reacting slowly to light, while the right one was pinpoint. The cranial nerves were normal except for a right central facial weakness. Abdominal reflexes were present but cremasteric and deep tendon reflexes were absent. Bilateral Gordon and Oppenheim reflexes were present. There was general weakness of muscles in all extremities. Vibratory and pain sensations were intact.

Lumbar puncture revealed an opening pressure of 600 mm. of water, the fluid being clear and colorless. Cytologic examination of the cerebrospinal fluid disclosed 1–2 lymphocytes per high power field. In addition, scattered over the slides were occasional, large, single cells, approximately 20 micra in diameter. The nuclei were enlarged, hyperchromatic and somewhat irregular in shape. Often there was only a rim of cytoplasm (Fig. 1).

The laboratory data were normal except for a hemoglobin of 10.8 gm. Films of the skull showed no cranial or intracranial abnormality. The roentgen-ray findings of the gastrointestinal tract revealed a gastric ulcer in a lesser curvature, penetrating into the pancreas.

On the 3rd hospital day ventriculography was performed via parietal burr holes. The ventriculogram showed no localizing evidence of tumor. A right subtemporal decompression was then performed.

Cytologic examination of the ventricular fluid obtained at operation revealed isolated malignant tumor cells of the same type as were seen in the cerebrospinal fluid. However, the cells were somewhat better preserved and more numerous (Fig. 2). These cells were interpreted as metastatic carcinoma cells. The patient’s condition deteriorated progressively. Based on the cytologic findings, a diagnosis of gastric malignancy with...