Cytology of Cerebrospinal Fluid in the Diagnosis of Malignancy

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Neoplastic cells have been identified in the cerebrospinal fluid (CSF) since Dufour's report in 1904. Various techniques have been developed to isolate and identify these cells, the most common being the use of dried smears of centrifuged CSF. Within the past 6 years the method of millipore filtration has been applied. The purpose of this paper is to record six cases in which malignant tumor cells were identified in the CSF and in which malignant tumors were subsequently found at biopsy or autopsy. These cases illustrate the importance of routine cytological examination of the CSF; a simple method is described for preparing Romanowsky-stained films using air-dried smears of centrifuged fluid samples.

Material and Method

Clinical Material. Of the 177 patients with verified neoplasm of the nervous system seen at Maida Vale Hospital during the 14-month period from December, 1965, through January, 1967, 93 had examinations of the cerebrospinal fluid (Table 1). The CSF specimens were collected during lumbar puncture, lumbar drainage, pneumoencephalography, ventricular puncture, ventricular drainage, or ventriculography. Stained films were made as part of the routine examination of the CSF.

Preparation of CSF Stained Film. At least 1 ml of CSF is used for a cytological examination which must be done within 2 hours of collection to avoid destruction of the cells. After the color of the fluid has been noted and the bacteriological cultures made, a few drops are lightly colored with 1% toluidine blue for a total count of nucleated cells in the Fuchs-Rosenthal counting chamber. The remaining fluid is centrifuged in a conical tube at low speed (500 to 1000 rpm) for 5 minutes. The supernatant fluid is then decanted by gently inverting the tube into the original container; it can be used for other analyses as well, such as protein, glucose, chloride, or serological tests. After the supernatant fluid has been completely drained and while the tube is still inverted, the cellular deposit is sucked gently into a thin Pasteur pipette with an absolutely level tip and applied on a clean dry slide. It is then sucked up again into the Pasteur pipette and deposited on the slide beside the first application, and so on for two to five applications until no fluid remains in the pipette. In this way the slide dries quickly, as in a blood smear, with no shrinking or distortion of the cells. In damp weather it may be necessary to shake the slide in the air for rapid drying. With a diamond glass marker, the dry drops are marked on the opposite side of the slide. The slide is fixed without delay in methyl alcohol and stained with May-Grunwald and Giemsa as for a blood film. It is then covered with a cover slip and mounted in neutral Canada balsam.

Results

Of the 177 patients in the series (Table 1) 138 had primary and 39 metastatic tumors. The cerebrospinal fluid was examined within 2 hours of collection in 30 cases; in 63 the cytology was less satisfactory since the fluid was either examined later than 2 hours or its time of collection was not recorded, while in 84 cases no CSF was collected.

During the same period, 1565 samples of CSF were received by the laboratory from the neurological and neurosurgical wards; most of them were examined in this way within 2 hours of collection.

Primary Tumors. From 138 patients with a primary tumor of the nervous system, 23 satisfactory specimens of CSF were collected. Tumor cells were positively identified in only one case (Case 6 in our series); this fluid was removed from the fourth ventricle during an operation on a medulloblastoma.

The finding of astrocytes in the ventricular...
fluid of a patient with an astrocytoma of the corpus callosum (Case 7) has subsequently been discounted since we have now identified astrocytes with comparable morphological characteristics in the ventricular fluid in a variety of conditions. These conditions have included brain metastasis, medulloblastoma, recurrent meningioma, hydrocephalus, myelomeningocele, Arnold-Chiari malformation, and bacterial meningitis; two of these findings are described in our Discussion section under "Normal Cells."

Ependymal or choroidal cells were identified either singly or in masses in a high percentage of fluids irrespective of the primary disease and were especially numerous in cases of intracranial postoperative inflammation (Case 8).

Metastatic Tumors. Out of 39 patients with metastasis in the central nervous system, seven suitable CSF specimens were obtained and examined. Carcinoma cells were identified in five of these (Cases 1–5).

Case Reports

Case 1 (59214). A 46-year-old woman was admitted with a 2½-month history of repeated episodes of headache, confusion, delirium, and right hemiparesis. She was found to have neck rigidity, papilledema with fundal hemorrhages, ataxia, depressed tendon jerks, and a mobile mass in the left breast; there were no palpable lymph nodes. Extensive investigations were normal except for the lumbar spinal fluid which showed carcinoma cells (Fig. 1). The fluid was blood-stained, and the supernatant fluid obtained from centrifuging was pale yellow. There were 165 nucleated