BRAIN TUMORS SIMULATING MENINGITIS

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With the advent of chemotherapy, the treatment of meningitis has, for the most part, become quite stereotyped. Many patients presenting the most elementary symptoms of meningeal involvement are subjected to intensive doses of the various chemotherapeutic agents and in many cases very little further attempt is made to trace the detailed etiology of the meningeal involvement. In those cases of meningitis due to bacterial organisms this type of procedure may be successful, but because many causes of meningeal irritation are encountered in the practice of medicine that are not infectious in origin, a word of caution must be inserted as to such a therapeutic procedure. Failure to investigate a patient thoroughly at the onset for the specific cause of the meningeal involvement may well result in the neglect of a neurological condition that obviously cannot respond to chemotherapy. This should particularly be kept in mind when the patient fails to respond in an adequate fashion to the therapeutic procedures instituted. Such an unusual course of the illness should make the doctor suspect that the cause of the meningitis might be atypical and that further detailed investigation is indicated. The following 3 cases are reported to emphasize the above facts. In all 3 cases the patients suffered from brain tumors which presented themselves as a meningitis.


Summary. Dermoid cyst involving inferior portions of both frontal lobes, with a long history of sinusitis. Onset of acute illness upon blowing of nose, with severe meningeal reaction, fever, leucocytosis and spinal fluid pleocytosis. Fulminating increased intracranial pressure after encephalography. Partial removal and evacuation of an intracerebral cyst. Recovery.

History of Illness. A white male of 22 years was admitted to the Student Health Service in March 1950 with complaints of severe headache which had come on suddenly after he had blown his nose. Initially the headache was felt all over the head, but soon became localized to the frontal areas with no predilection for one side or the other. The patient felt very ill and retired to bed, remaining there without abatement of his complaints until the next morning when he reported to one of his classes in order to take an examination. Following this he returned to bed. Shortly thereafter he became nauseated, vomited and felt that he had a fever. Forty-eight hours after the onset, he was admitted to the hospital.

Past History. Although the patient had suffered from sinusitis for many years, he was first treated for that disability in 1945 while in the service. During Naval training he had a high fever with a headache and rash which was diagnosed as scarlet fever. During convalescence migratory joint pains and a cardiac murmure developed.
with another episode of fever and headache. A diagnosis of rheumatic fever was made. Under salicylates he made a slow recovery but remained in the hospital because of the persistence of headache, joint pains and increased sedimentation rate. The headache was felt to be sinusal in origin and a Luc-Caldwell procedure was performed on the left side.

Nine months later he was given sea duty and during that period the sinuses were drained several times. Upon discharge he returned to school where he played 3 years of intercollegiate football and 1 year of professional football. During his athletic career he was knocked unconscious on 2 or 3 occasions, and he recalled a similar episode at the age of 13.

Examination. The patient appeared ill, complained of pain on movements of the eyes and photophobia, and had a temperature of 100.6°F. Cardiovascular, respiratory and gastro-intestinal systems were within normal limits. Positive neurological findings were: nuchal rigidity, engorgement of the retinal veins without papilloedema, and areflexia.

Laboratory Data. WBC 12,900: 92 per cent polymorphonuclear leucocytes, 7 per cent lymphocytes and 1 per cent monocytes. Sedimentation rate was elevated. Blood chemistries and urines were normal. CSF pressure was 26 mm. of mercury; the fluid showed 1,744 WBC/c.mm.: 97 per cent polymorphonuclear cells, and 3 per cent mononuclear cells. There were 76 RBC. CSF protein was 41 mg. per cent; sugar 56 mg. per cent; and chlorides 127 milli equivalents/1. Smear of the fluid showed no organisms and culture was sterile.

Diagnosis. In view of the sudden onset of the symptomatology, the physical findings and the antecedent history of sinusitis it was thought that the patient had a meningitis probably secondary to a ruptured epidural abscess.

Course. The patient was treated with antibiotics and sulfa compounds. He received intravenous feedings and required demerol for relief of his headache. Under this regime he responded quite well and the temperature slowly returned to normal. CSF pressure on the 3rd hospital day was 20 mm. of mercury; the fluid showed 220 cells, of which 90 per cent were polymorphonuclear leucocytes. Attempts to culture organisms from the CSF were unsuccessful. Despite general improvement his temperature continued to spike nearly every day and he occasionally complained of chills.

On the 27th hospital day pneumoencephalography was done; 25 cc. of air were introduced into the spinal canal and an equal amount of CSF was withdrawn. During this procedure the patient had one convolution. Roentgenograms showed a small pocket of air in the left frontal lobe anterior to the lateral ventricle, but no communication with the lateral ventricles was visible. Following this procedure the patient became worse. Nausea, vomiting and severe headache were persistent and in the course of 24 to 36 hours papilloedema appeared bilaterally, associated with paresis and hyperactive reflexes on the right side. In view of this unsatisfactory turn of events immediate surgical intervention was carried out. The pre-operative diagnosis was probable left frontal lobe abscess.

1st Operation. Under general anaesthesia a trephine opening was made over the left frontal eminence and a brain needle inserted to a depth of 4 cm., where a cyst was encountered, from which sebaceous material with hair was evacuated.

Course. It was expected that the patient would be relieved by this evacuation until a definitive operation could be performed at an elected time. However, during the next 24 to 36 hours he showed evidence of increasing intracranial pressure
with the development of bilateral abducens paralysis, an increase in papilloedema and retinal hemorrhages.

2nd Operation. Under intratracheal anaesthesia a left transfrontal craniotomy was performed. Decompression of the cyst by another evacuation through a brain cannula was necessary prior to reflection of the bone because of extreme intracranial pressure with herniation of cerebral tissue through the trephine opening previously made. The anterior portion of the left frontal lobe and an anterior projection of the cyst were amputated. The remainder of the cyst extended posteriorly in the frontal lobe across the midline behind the falx and expanded into the right frontal lobe (Fig. 1). The bulk of the cyst was in and near the midline, situated above the optic nerves, chiasm and pituitary gland and beneath the hypothalamus and 3rd ventricle. An attempt was made to dissect out the wall of the cyst and this was partially successful but it soon became evident that a complete removal would be impossible. A small raised plaque containing hair was encountered in the cyst wall (Fig. 2).

Microscopic Diagnosis. Dermoid cyst (Figs. 3 and 4).

Postoperative Course. The patient’s course was complicated with convulsions which were controlled with anticonvulsant drugs. He made steady satisfactory progress despite mild diabetes insipidus which subsequently subsided. It was noted that he was blind in the right eye. He had a mild paresis of the right leg but was able to walk with the aid of a cane. He was discharged on the 25th day after operation and has returned to school.

Discussion. This case of a large dermoid cyst of the frontal lobes presented itself as a meningitis. It is well known that the contents of dermoid and epidermoid cysts of the brain are very irritating to the ependymal lining. In this case it was thought that the acute exacerbation of symptoms after
encephalography unrelieved by evacuation of the cyst was due to ependymitis with obstruction of the aqueduct. Such an obstruction of the aqueduct resulting from the irritating effect of the contents of a dermoid cyst was found at postmortem examination in a case reported by Miller. 16 Had the cerebrospinal fluid been examined by a physician instead of a laboratory technician the significance of the fat and epithelial cells would have been appreciated and an early diagnosis made, since such elements were present in quantity but not recorded.


Summary. Semicomatose patient with marked spinal fluid pleocytosis and signs suggestive of meningitis. Abnormal course prompted further investigation, which revealed brain tumor of frontal lobes. Diagnosis: glioblastoma multiforme.

History of Illness. A female of 69 years was admitted to the University Hospital in a semicomatose condition in November, 1949. She had first complained of severe unlocalized headaches 5 months previously. Two months before admission she had had "flu" which was unresponsive to the usual household remedies. Upon signs of confusion and disorientation she was entered in a local hospital with a diagnosis of atypical pneumonia. Penicillin therapy was instituted with considerable improvement and against advice the patient left the hospital, only to be readmitted 1 week later in a semicomatose condition. At this time there was marked nuchal rigidity, with bilaterally fixed and dilated pupils, a right hemiparesis with hyperactive reflexes and ankle clonus. The patient was febrile. The blood urea nitrogen was 40 mg. per cent. There was a leucocytosis of 13,400 cells, of which 85 per cent were polymorphonuclear leucocytes. CSF showed 122 WBC; 73 per cent were polymorphonuclear leucocytes. Three days later the CSF showed 560 WBC; 96 per cent were
polymorphonuclear leucocytes. At this point she was transferred to the University Hospital.

Examination. The patient was unable to cooperate, muttered unintelligently but responded reflexly to noxious stimulation. Temperature was 99.6°F, and pulse 50. Positive neurological findings were: marked nuchal rigidity, left hemiparesis with a positive Babinski reflex, ankle clonus and a grasping reflex on the right. There were no cranial nerve abnormalities.

Past History. With the exception of a nephrectomy at the age of 17 for renal tuberculosis the past history was not contributory.

Laboratory Data. Hb. 15.2 gm. WBC 8,250 with a normal differential. Blood urea nitrogen 13 mg. per cent, CO₂ combining power 24, chlorides 104 milliequivalents/l. and serum protein 6.1 gm. Roentgenograms of the chest were normal except for an insignificant congenital rib anomaly.

CSF pressure was 200 mm. of water. WBC was 154, of which 123 were polymorphonuclear leucocytes. CSF protein, 154 mg. per cent. The culture was sterile.

Diagnosis. On the basis of the foregoing a diagnosis of tuberculous meningitis was made and treatment instituted accordingly.

Course. The patient continued in a semicomatose state throughout her hospitalization. Aureomycin, streptomycin and penicillin produced no significant change. In view of the lack of change under chemotherapy and the localization of findings to the right frontal area, further investigation was felt necessary. Angiography showed no alteration in the vascular pattern. Pneumoencephalography showed
definite evidence of a large mass in the right lateral ventricle. No air entered the left lateral ventricle. In an attempt to obtain more satisfactory visualization of the ventricular system, ventriculography was done which showed a large mass involving the corpus callosum, septum pellucidum and projecting from the roof of both lateral ventricles, which were dilated.

**Operation.** Upon exposure of the right lateral ventricle the tumor was observed involving the ventricular wall and projecting into the ventricular cavity. A partial removal was effected.

**Course.** The patient remained comatose and expired 1 week postoperatively.

**Autopsy Report.** There was a large, diffuse, poorly circumscribed, necrotic and hemorrhagic tumor extending into the frontal and parietal lobes bilaterally with destruction of the corpus callosum, septum pellucidum and obliteration of the 3rd ventricle.

**Microscopic Diagnosis.** Glioblastoma multiforme (Fig. 5).

**Discussion.** The onset of signs of meningeal irritation and the high proportion of polymorphonuclear leucocytes in the spinal fluid suggested a primary meningitis. The failure to respond to antibiotics and the abnormal course prompted further investigation which led to the proper diagnosis. The cause of the meningeal reaction was felt to be due to both tumor necrosis and the products of hemoglobin breakdown. Myelin destruction may also have contributed to this response. Fig. 6 shows the meningeal reaction in the vicinity of the tumor.

**Case 3. E.R., V.A. 80512.**

**Summary.** Cerebral varix involving the 3rd ventricle, producing clinical and laboratory signs of meningitis. Fatal outcome.

**History of Illness.** A white male of 23 years was admitted to the hospital with complaints of occipital headache and stiff neck accompanied by nausea and vomiting. The onset was dated 1 week previously. Since the age of 13, the patient had suffered periodically from headaches confined to the left side of his head; symptomatic relief had been obtained from large doses of sodium amytal. The pain on admission was not related or similar to his previous headaches. He also complained of pain in the posterior neck muscles, and staggering had been noted by relatives during the last 2 days.

**Past History.** With the exception of the headaches previously described the past history was noncontributory.

**Examination.** The patient was acutely ill, restless, drowsy, slightly febrile and complained bitterly of headache. The only abnormal neurological findings were nuchal rigidity and an equivocal Babinski reflex on the right side.

**Laboratory Data.** WBC 17,000: 81 per cent polymorphonuclear leucocytes, and 19 per cent lymphocytes. The CSF was under a pressure of 400 mm. of water and showed a pleocytosis of 694 WBC: 89 per cent polymorphonuclear leucocytes and 11 per cent lymphocytes. A smear of the CSF showed gram positive cocci resembling pneumococci. CSF sugar was 73 mg. per cent, protein 38 mg. per cent, and chlorides 102 milli equivalents/1. Urinalysis, blood serology and roentgenograms of chest and skull were normal.

**Diagnosis.** On the basis of the clinical findings substantiated by the presence of organisms in the spinal fluid a diagnosis of pneumococcic meningitis was made.
Course. The patient was treated with large doses of penicillin intramuscularly and intrathecally. Daily spinal punctures were performed, each of which showed a blood-tinged fluid under pressures ranging from 400 mm.-600 mm. of water. No organisms were grown and the gram positive cocci first observed were never seen on subsequent smears. No additional neurological findings appeared with the exception of papilloedema of 1 D. which subsided after a period of 3 days. Shortly thereafter, however, bilateral choked discs of 3–4 D. developed with retinal hemorrhages. Ventriculography showed bilateral symmetrical hydrocephalus. Two days following this procedure the patient suddenly became cyanotic with shallow gasping irregular

Fig. 7. Case 3. Horizontal section of brain showing large central varix, displaced 3rd ventricle and dilated lateral ventricles.

respirations and passed into a semicomatose condition which terminated fatally. A presumptive diagnosis of tumor of the 3rd ventricle was made.

Postmortem Report. Horizontal sections of brain showed dilatation of the lateral ventricles. Immediately posterior to the optic chiasm and displacing the 3rd ventricle was a large subependymal hemorrhagic mass 3 cm. in diameter. Fig. 7 shows the gross appearance of the lesion.

Microscopic Diagnosis. Cerebral varix.

Discussion of Case. The meningeal reaction and spinal fluid pleocytosis are assumed to have been due to the breakdown products of hemoglobin. Hydrocephalus was the cause of death. A very similar case was reported by Merwarth and Freiman,12 of a child who died at the age of 4 months of communicating type of hydrocephalus due to intraventricular hemorrhage from a small angioma in the thalamus.
It is known that meningeal irritation with associated meningitis can be caused by numerous agents. Acute demyelinating diseases may elicit intense lymphocytic, polymorphonuclear and plasma cell reactions. The disintegration products of nerve tissue have been accepted as a cause for such reactions. Bender injected lipoid fractions derived from myelin into the subarachnoid space and obtained a polymorphonuclear response in the cerebrospinal fluid. Cholesterin was found to be more potent in activating such a response than cerebrosides. It is now well appreciated that the CSF may contain large numbers of polymorphonuclear cells following operations upon cholesteatomas or cholesterin-containing cysts of the brain. The rapid disintegration of myelin due to embolism or thrombosis of a vessel is followed by a polymorphonuclear response in the meninges. Such a reaction was experimentally reproduced by Cone and Barrera, who blocked the cerebral vessels with aseptic emboli.

Bagley reported both clinical and experimental evidence of chronic meningitis in the dog following repeated injections of blood into the subarachnoid space. Aseptic meningitis following subarachnoid hemorrhage has been reported by Lamb, Strauss, Globus and Ginsburg, Bagley, Cookson, Sands, Dandy, Richardson and Hyland, Collier, and Bramwell. Mallory reported a case of intracranial varices in which symptoms of meningeal irritation followed each episode of rupture. Spurling described aseptic meningitis following cranio cerebrar injuries. Bedford showed that isotonic sodium chloride injected into the cisterna magna caused a pleocytosis. Jackson, in a comparative study of the reaction of blood and its breakdown products in the subarachnoid space, has shown that bilirubin is probably the specific agent in blood that is responsible for the meningeal reaction.

Although meningitis occurring as a result of bacterial invasion, viral invasion and demyelinating processes is frequently sought for in the routine investigation, the fact that a similar process may be caused by brain tumors is generally not appreciated. Cerebral tumors as a rule produce no change in the cell count of the cerebrospinal fluid. When, however, intracranial tumor is associated with large numbers of cells in the CSF, necrosis of the tumor or myelin destruction in the perineoplastic area is presumed to be the cause. When gliomas situated near the ventricles undergo softening the CSF may contain a great excess of polymorphonuclear cells. Pennybacker, speaking of the spinal fluid, has stated that "increase in the protein content is a very common finding in cases of intracranial neoplasms of all sorts and the cell count may be raised with or without an increase in the protein content. Some cases of degenerating and necrotic gliomata situated near the ventricular system or the subarachnoid space may show a marked pleocytosis contributed to by polymorphs as well as by lymphocytes." Bailey states that ordinarily there is no increase in the cell count of the CSF in brain tumor.

An analysis of a report by Henderson and de Gutiérrez-Mahoney on the
CSF in brain tumor shows the greater frequency of spinal fluid pleocytosis in glioblastoma multiforme. Of 43 cases of glioblastoma multiforme, 13 exhibited pleocytosis ranging from 14 to 70 cells, of which large numbers were polymorphonuclear. In all such cases the ventricular walls were infiltrated with tumor. Metastatic tumors were not infrequently accompanied by CSF pleocytosis, whereas other types of cerebral tumor were associated with an increase of only 1 or 2 cells over the normal value.

The clinical courses of the common varieties of meningitis are well known. Any type of meningitis with an abnormal course should be viewed with suspicion and further investigative procedures undertaken in order to determine the etiology. Pneumoencephalography, ventriculography and arteriography are measures available to enable the clinician to arrive at the correct diagnosis. It is equally important to be aware of the fact that meningitis can develop during the course of a brain tumor.

SUMMARY

Three cases of brain tumor of varied pathology presenting as meningitis have been reported.

Intracranial neoplasms are to be accorded an important place in the etiology of meningitis.

Any meningitis of an abnormal course should be viewed with suspicion and further studies done to determine the etiology.

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