**Glioblastoma multiforme with extracranial metastases in the absence of previous craniotomy**

**Case report**

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Although the occurrence of extracranial spread from intracranial tumors is common knowledge, this event still deserves reporting whenever observed. While craniotomy and shunt operations have been blamed for extracranial seeding from primary intracranial tumors, it is less well known that more than 10% of all cases reported have shown remote metastases in the absence of any previous surgical manipulation.

From a review of 89 intracranial tumors with extracranial metastases published by Glasauer and Yuan and from 78 additional cases found in the literature since the completion of their survey, it appears that cases of metastasis of neuroectodermal tumors without craniotomy make up a distinct minority. Within this small group are a few cases of glioblastoma. This is particularly noteworthy considering the relative frequency and high malignancy of this oncotype. I am reporting another such case.

**Case Report**

A 53-year-old woman was first admitted to the Medical Service of the Hôpital Cantonal Universitaire in Lausanne, Switzerland, on August 25, 1965. Family history and past personal history were unremarkable except for frequent migraine attacks since early adult life. Five days prior to admission, she had noticed sudden, intense, occipital headache, progressively associated with nausea and vomiting.

First Examination. There was bradicardia, and a blood pressure of 220/100 mm Hg, a Babinski sign on the left, and bilateral papilledema more marked on the left. A spinal tap yielded clear normal fluid under a pressure of 310 mm H₂O. An electroencephalogram showed a very abnormal tracing over the left frontal region. A left carotid angiogram furnished evidence of a large tumor mass in the same area. The over-all impression obtained from the angiographic study was that of a malignant tumor, probably of a gliomatous nature.

The patient was not operated on, and she was transferred to the Radiology Service for further care. Over a period of about 8 weeks, she received a total amount of 8000 rads (Betatron) over the left frontal and temporal regions. Additional medication during this time consisted of Vitamin C, corticosteroids, and acetazolamide.

Second Examination. The patient was re-admitted on December 12 because of renewed headache, vomiting, and failing vision. She now showed some loss of memory, mild sensory aphasia, diminished deep tendon reflexes and muscular strength on the
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right, and persistent bilateral papilledema. Bradicardia was again noticed, with a peripheral pulse of 60/min, but the blood pressure was not elevated. Chest x-ray films showed no tumor. Plain x-ray films of the skull revealed some demineralization of the sella turcica. A brain scan with I-131 showed marked uptake over the left frontal region and was interpreted as indicative of a malignant glioma (Dr. Roland Oberson). In another scintigraphic study obtained with Tc-99m a few weeks later, the previous findings were confirmed and completed. The focus of the left frontal uptake appeared to cross the midline and extend about 2 cm into the right frontal region.

Third Examination. When admitted for the third time on April 14, 1966, the patient was restless, disoriented, and complained of headache and pain in her left arm. All the previous signs and symptoms were worse. The knee jerks were now absent bilaterally, and the Babinski was positive bilaterally. X-rays of the cervical spine were normal. There was a mild hyperglycemia and elevated serum alkaline phosphatase. The patient's condition deteriorated steadily, and she died on September 14, 1966. The clinical diagnosis was brain tumor, most likely glioblastoma multiforme of the left frontal lobe. A diagnosis of a neoplasm elsewhere in the body was never made nor suspected.

Postmortem Examination. Autopsy was performed by Dr. Michel Monti of the Insti-

tut d'Anatomie Pathologique of Lausanne. There was confluent bronchopneumonia in both lungs, cholethiasis of the gall bladder, chronic passive congestion of the liver and spleen. The main findings were the following: dura was tightly adherent to the left frontal lobe; the brain weighed 1570 gm and was asymmetric, with the rostral portion of the left hemisphere bulkier than that of the right. In the body of the 11th thoracic vertebra, there was a round, grayish-white area about 1.5 cm in diameter. In cutting through the liver, five widely-separated, round, well-circumscribed, grayish-white nodules ranging from 0.4 to 1.5 cm in diameter were found. Since none of these extraneural tumors had the appearance of a primary neoplasm, an extensive and careful search was pursued by taking numerous sections from the different organs. No other tumors were ever found macroscopically or microscopically.

Macroscopic Examination. The brain was fixed in formalin and cut in the usual manner. The tumor occupied the rostral portion of the centrum semiovale; it extended forward into the frontal pole and backward into the parietal and temporal lobes, measuring approximately $6 \times 6 \times 13$ cm. The cut surface was granular, ragged, variegated with necrotic patches of grayish and yellowish color, and dotted focally with small hemorrhagic extravasation (Fig. 1). At the periphery, the tumor became more grayish-white in color and firm in consistency, blending imperceptibly with the surrounding tissue, blurring the usual cortical markings, joining and retaining the meningeal coverings up to the overlying dura. Medially, the tumor encroached on the lateral aspect of the putamen, overrunning the cau- strum but leaving the basal gray essentially untouched. Ros- trally, the knee and body of the corpus callosum, as well as the septum pellucidum and fornix, appeared stouter than usual and had a finely granular cut surface with slightly prominent vascular markings. Also, the adjoining portion of the right corona radiata displayed focally some of these changes, suggesting neoplastic involvement. Perifocal edema was noticed, as well as the usual signs of increased intracranial pressure, such as narrowing of the left lateral ventricle, left subfascial herniation, and temporal herniation more prominent on the left than on the right side. The midbrain appeared somewhat flattened and compressed on the left side, with a slit-like slightly bowed aqueduct. However, none of the usual secondary lesions in the brain stem and occipital lobes was seen.

Microscopic Study. Many sections were taken from the intracerebral tumor. Necrosis and hemorrhage were very widespread throughout the tumor mass. The viable parts of the neoplasm offered a picture that varied from field to field, and whose salient features were high cellular density and polymorphism. Some fields were occupied by masses of more or less round, small and large nuclei, embedded in a scanty, finely fibrillar matrix (Fig. 2 left). In other fields, the cells were predominantly spindle-shaped, often packed into short interwoven bundles (Fig.