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Congenital Glioblastoma Multiforme

— Report of an Autopsy Case —

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A congenital neoplasm arising in the central nervous system is rarely encountered, and the majority of case reports that have dealt with intracranial tumors have been divided almost equally between teratomas and various gliomas. We experienced a rare case of congenital glioblastoma multiforme encountered in a three day-old male infant who presented with hydrocephalus since birth. Postmortem examination revealed that the tumor seemed to have originated from the right thalamic region extending centrifugally to the cerebral cortex and through the brain-stem down to the cerebellum.

Key Words: *Glioblastoma multiforme, Congenital intracranial neoplasm, Hydrocephalus*

INTRODUCTION

Congenital tumors are divided into three categories, i.e., definite, probable, and possible, according to the time of presentation of symptoms (Wells, 1940), and those present or producing symptoms at birth are called definitely congenital (Solitare and Krig man, 1964). Especially congenital tumors of the central nervous system are rare and amount to only 5% of all congenital tumors. Among congenital intracranial neoplasms, teratoma is the most common histologic type, followed by glial tumors and mesenchymal tumors (Solitare and Krigman, 1964; Sabet, 1982). Moreover, glioblastomas are extremely rare among glial tumors.

We report here a case of definite congenital glioblastoma multiforme presented with hydrocephalus of the obstructive type. This case appears as the tenth documented example of congenital glioblastoma multiforme.

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CASE REPORT

A male infant of 38 weeks gestation was born to a 30-year-old G3 P2 L1 A1 woman whose pregnancy course was uneventful, without a history of drug ingestion, or exposure to radiation or trauma. Family his tory was also non-contributory. The infant was delivered by repeated Cesarean section. The first baby has been doing well so far since birth. The birth weight of the infant in our case was 4,100 grams (over the 90th percentile) and the total body length 52cm (over the 90th percentile). The apgar score was 2 at one minute and 6 at five minutes, and both Moro and sucking reflexes were poor. Because of cyanosis since birth, he was placed in an incubator, and an artificial respirator was instituted.

Laboratory data revealed hemoglobin 9.5gm/dl, hematocrit 27.8, WBC 52,300/mm^3 (poly 59%, band 12%, lymphocyte 20%, monocyte 3%, eosinophil 1%, atypical lymphocyte 1%, metamyelocyte 3%, myelocyte 1%), platelet 259,000/mm^3, nucleated RBC 24/100 WBC, reticulocyte 2.1%, blood glucose 48mg%, SGOT/SGPT 44/135IU, creatinine 2.0mg%, BUN 36.3mg%, uric acid 15.3mg% inorganic phosphate 13.9mg%, total protein/albumin 3.5/2.6 g/dl, K 9.8 meq/L. Blood gas study showed pH 7.029, PO2 52.9 mmHg, PC02 27.2 mmHg, and HC03 6.9 mM/L.

Computed axial tomograms of the brain showed that

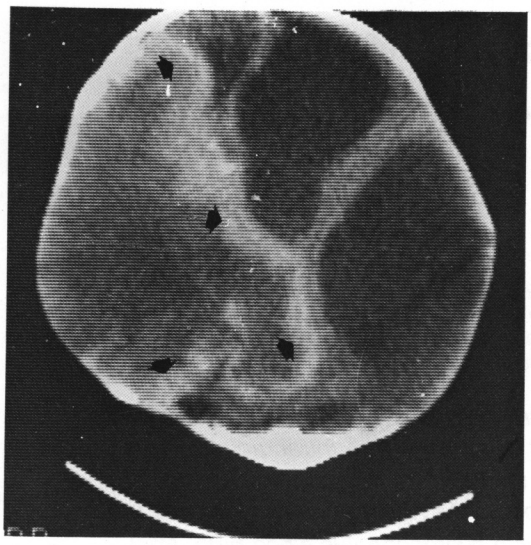

Fig. 1. Contrast-enhanced computed tomogram shows huge hypoechoic mass replacing right cerebral hemisphere. A post-contrast study shows that the peripheral margin of the mass is enhanced (arrows).

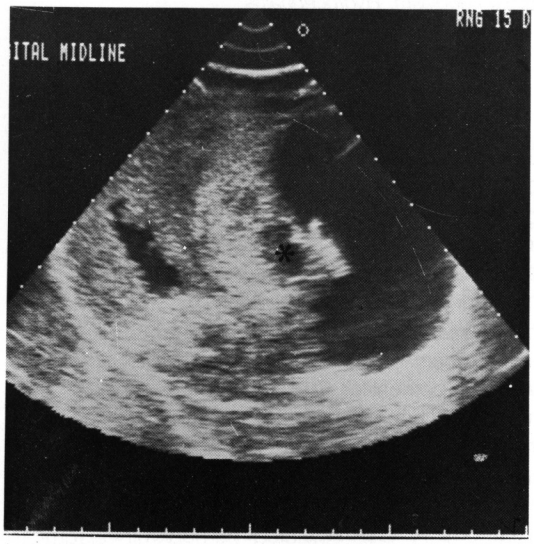

Fig. 2. Neurosonogram reveals irregularly mixed echogenic and echolucent areas in the right hemisphere and a dilated third ventricle (asterisk).

the entire right hemisphere was replaced by a solid mass with alternating high and low attenuation density, which obliterated the right lateral ventricle and shifted the midline to the left side. Postcontrast study showed a markedly enhanced irregular peripheral margin of the mass (Fig. 1). The lateral ventricle on the left side was markedly dilated, and the normal density of the brain could be appreciated only peripherally. The third ventricle was well delineated and rather dilated posteriorly. A neurosonogram also revealed irregular mixed echogenic and echolucent areas in the right hemispehre, which were considered anechoic necrotic changes in mass (Fig. 2).

Despite intensive care, the baby continued to deteriorate and died 72 hours after birth.

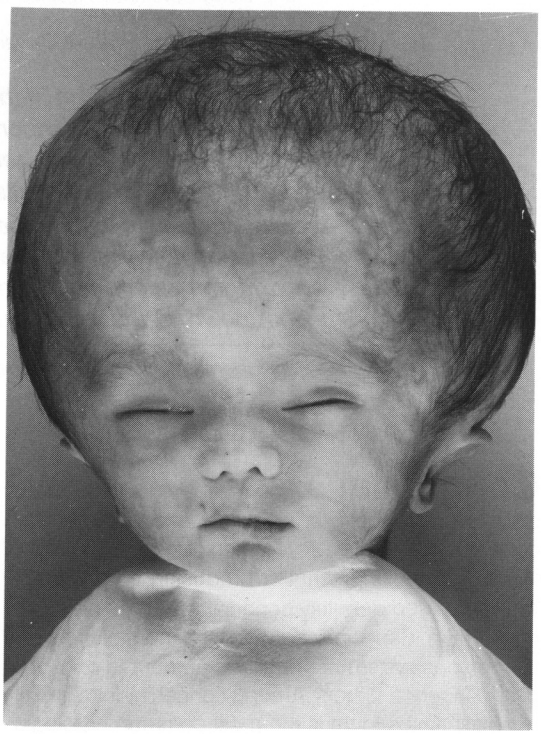

Fig. 3. Postmortem picture of the patient with hydrocephalus

Postmortem Findings

The head was symmetrically and markedly enlarged (circumference 51cm; expected circumference 34cm Fig. 3). When removing the brain, the left hemisphere was bluish and cystic, and the right temporal lobe was bulging. After removing the brain, the anterior cranial fossa appeared enlarged with thinning of bone due to longstanding hydrocephalus compared to the posterior fossa. The brain weighed 700 grams (about 1.7 times heavier than that of normal full-term baby). The dura was loosely attached to the underlying leptomeninges only by bridging veins. However, in the base, around the floor of the third ventricle, there were gray white protrusions that partly adherred to the dura.

The cerebral hemispheres were markedly enlarged rather symmetrically, but the right hemisphere was far more solid compared to the left, which was more cystic and easily collapsed. The cortical surface of right hemisphere had irregular hemorrhagic areas intermingled with fine granular yellowish speckles over the frontal and parietotemporal area (Fig. 4). The cortical surface of the left hemisphere was smooth with flattening of gyri and bluish due to hemorrhagic content, with clot formation in the left lateral ventricle. There was no gross disfigurement of the brain except for the posterior thalamic region where the masses extended toward the posterior fossa content.

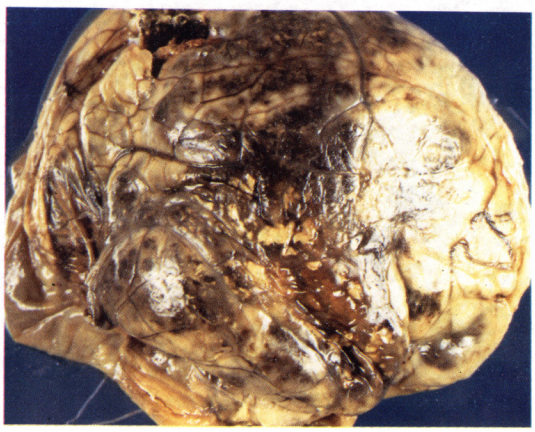

Fig. 4. Right lateral view of the brain shows bulged out temporal lobe and cortical surface with irregular hemorrhagic areas intermingled with whitish calcific flecks.

A coronal cut in its fresh state showed a gush of blood and necrotic material from the right hemisphere. The main tumor mass was located in the central portion of the brain obscuring the right lateral ventricle and growing toward the cortical surface of the right cerebral hemisphere (Fig. 5). The tumor blended into the brain parenchyma in most areas. The tumor measured 12.5cm in maximum extent. It was largely necrotic and hemorrhagic with a granular cut surface. In some areas it was almost totally blood clot. The basal ganglia and thalamus were not discernible due to tumor invasion. The choroid plexus was not identified. However, the posterior portion of third ventricle was markedly dilated. The foramen of Monro and aqueduct of Sylvius could not be identified. The tumor in the right hemisphere extended down into the posterior cranial fossa structure, displacing the right cerebellar hemisphere and obliterating the fourth ventricle. It appeared that the tumor in the cerebrum crossed the

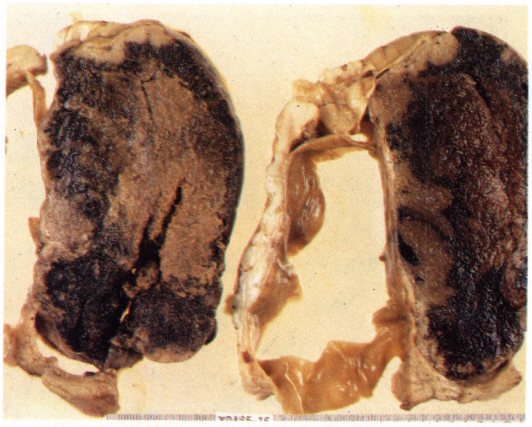

Fig. 5. Coronal section of the brain discloses huge hemorrhagic and necrotic tumor mass replacing the entire right hemisphere and obliterating the lateral ventricle. The left lateral ventricle markedly dilated.

tentorium cerebelli through the parapineal space from the thalamus and extended directly to the right cerebellum. The pons and medulla oblongata were not involved by the tumor.

Meanwhile, the left cerebral hemisphere showed only an extreme hydrocephalus. The foramen of Monro was obliterated by the tumor, and the lateral ventricular surface was smooth and glistening. The cerebral mantle was thinned and compressed. Other than patchy subarachnoid hemorrhage, no gross tumor mass was noted in the left hemisphere. The choroid plexus was identified as normal in size and shape.

There were no grossly discernible abnormalities or malformations in the other organs. Careful search for the thoracic cage and its contents, the abdominal viscera, genitalia, and spinal cord revealed no tumor metastasis.

Microscopically, the tumor was composed of uniformly elongated or fusiform cells with deeply eosinophilic cytoplasm with occasional cytoplasmic processes, arranged in a streaming or fasciculating pattern (Fig. 6). Pleomorphism of the nuclei was not remarkable, and mitotic figures, often atypical, could be seen infrequently. Typical geographic necroses with pseudopalisadings of glioblastoma multiforme as well as hemorhages were commonly found (Fig. 7). In some areas, gemistocytic differentiation of the cells with abundant deeply eosinophilic cytoplasm was also noted. Although PTAH or Van Gieson stain failed to show the evidence of astrocytic differentiation of tumor cells, immunoperoxidase staining for glial fibrillary acidic protein (GFAP) demonstrated focal areas of positive reac-

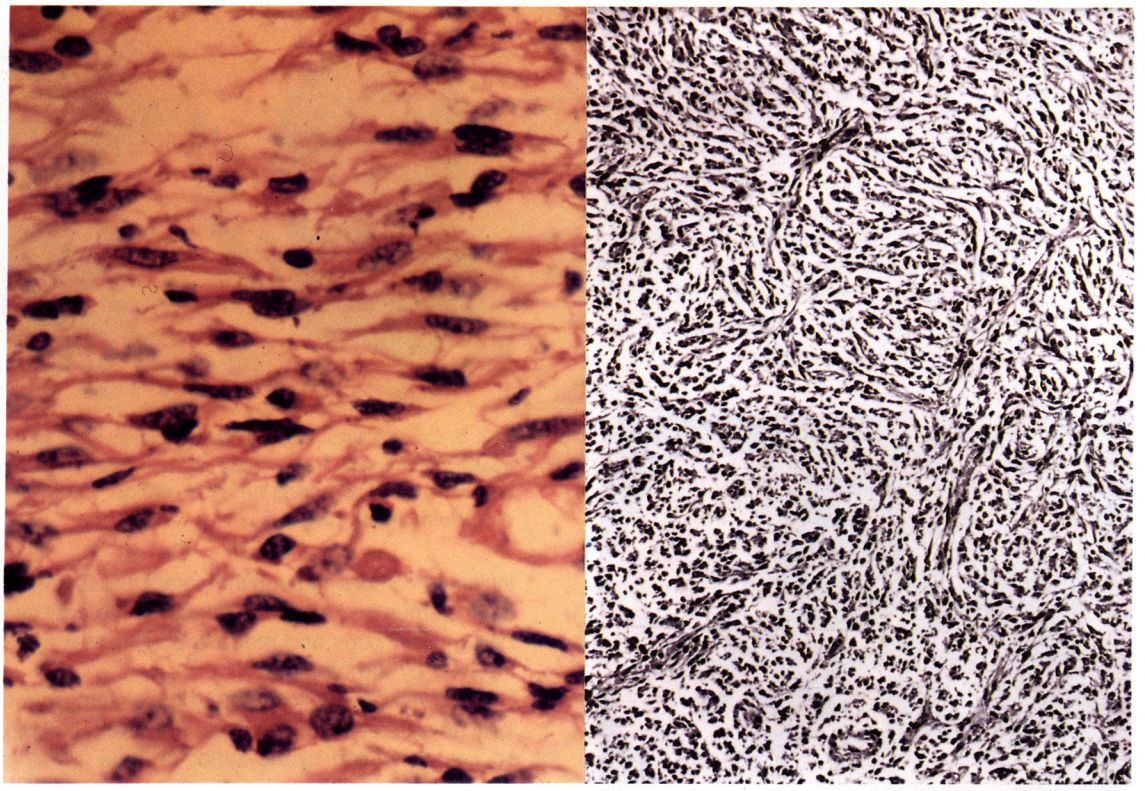

Fig. 6. Shown are uniformly elongated or fuiform cells, some of which are exhibiting cytoplasmic processes (A;H-E, x400), arranged in a steamming or fasciculating pattern (B;H-E, x100).

tion in the cytoplasm of the cells, revealing glial differentiation of the tumor (Fig. 8). Capillaries in the tumor showed a glomeruloid proliferation of the endothelial cells with thrombus formation in the lumen. Some of them were organized. Gomori's reticulin stain revealed a lacy pattern of perivascular proliferation of fibrous tissue. However, this was not enough to be called as sarcomatous transformation. Increased thick-walled capillaries imparted a telangiectatic feature in the focal area. Deeply basophilic granular calcification was superimposed on the tumor necrosis. There were ferruginous materials deposited within or outside of the glial cells in surrounding cortex, considered to be a result of longstanding brain ischemia due to tumor mass.

The choroid plexus in the right hemisphere was invaded by tumor cells. In addition, the burst of tumor cells seemed to spill into the ventricular cavity in some areas.

The left hemisphere showed the findings of chronic ependymitis such as proliferation of the capillaries and perivascular fibrous proliferation in subependymal area. Leptomeninges showed proliferation of fibroconnective tissue.

There were no microscopic foci of metastatic tumor in any organ. However, the features of disseminated intravascular coagulation were found in the lungs, kidneys, and spleen. In addition, extensive uric acid crystals were found in renal tubules.

DISCUSSION

Intracranial neoplasm, with onset before birth, is a rare disease. In 1940, Wells divided the congenital tumors into arbitrary categories of definite, probable, and possible. Thereafter, Solitare and Krigman (1964) defined them those present or producing symptoms at birth, those within the first week of life, and those within the first month of life, respectively. Applying these definitions, these is no doubt in calling this case a "definitely congenital" one, because the infant was born with hydrocephalus of the obstructive type due to massive tumor growth.

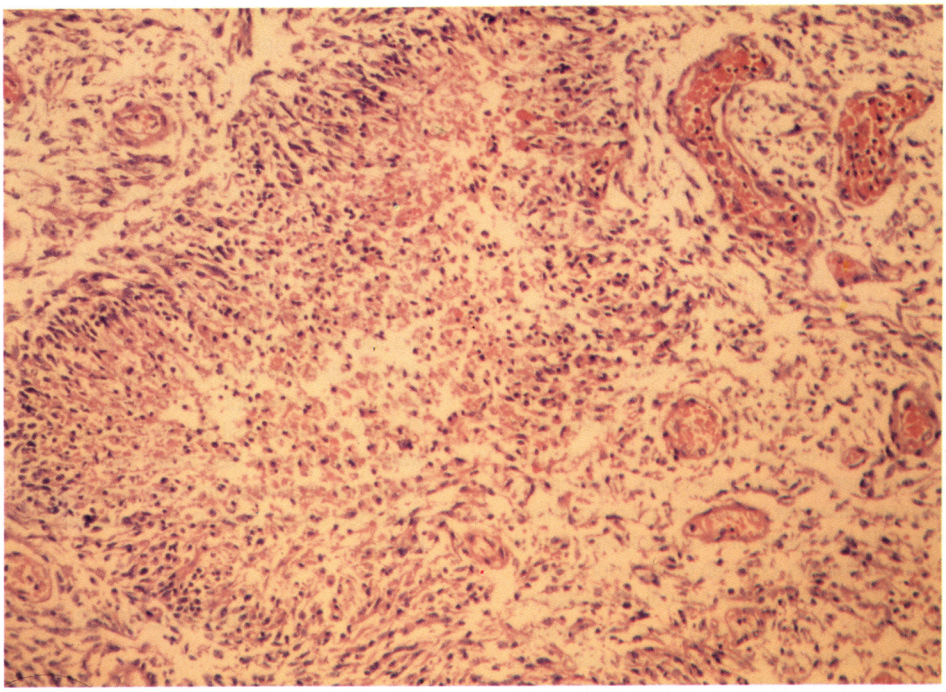

Fig. 7. Geographic necrosis with pseudopalisading is seen (H-E, ×200).

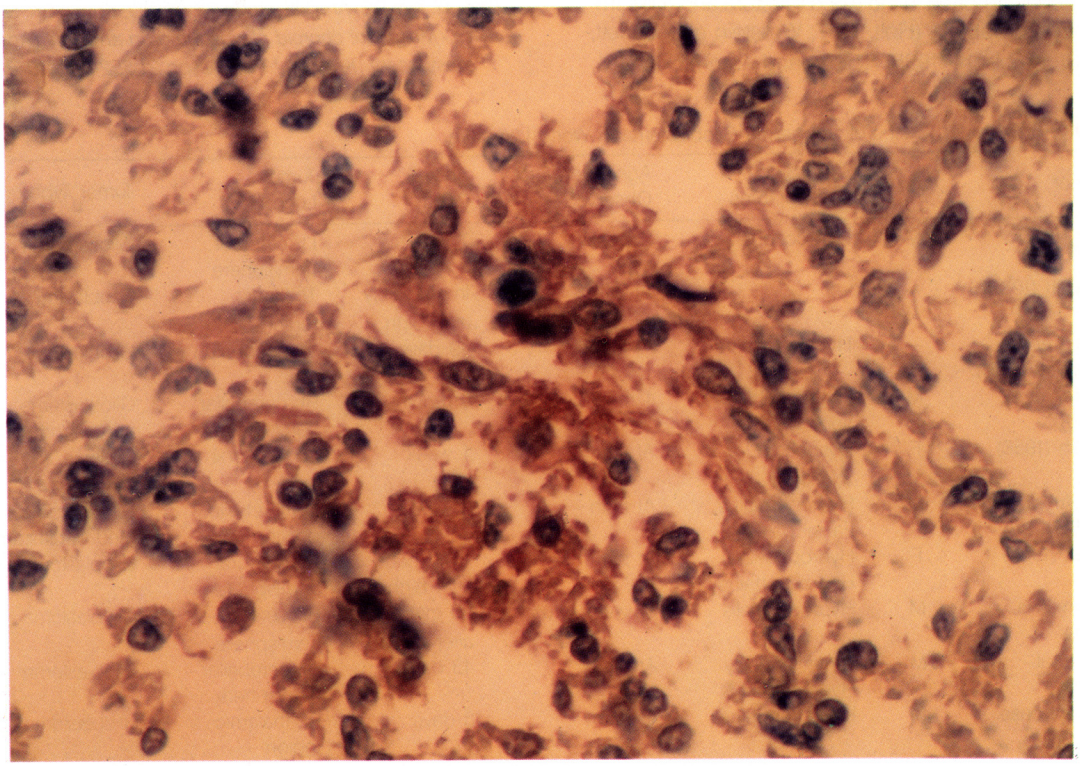

Fig. 8. Immunoperoxidase stain for glial fibrillary acidic protein domonstrates focal areas of positive reaction (GFAP, x400).

In 1982, Sabet reviewed 110 cases of congenital intracranial neoplasms, including 45 cases reviewed previously by Solitare and Krigman (1964). According to Sabet, 35% were teratoma and 31% were glioma, including four cases of glioblastoma multiforme, followed by medulloblastoma, neuroepithelioma, craniopharyngioma, and mesenchymal tumors. In Korean literature a case of malignant choroid plexus tumor (Choi et al., 1978) and a case of immature teratoma (Park et al., 1990) were found.

Considering the gross and microscopic findings, our case is compatible with glioblastoma multiforme. Microscopically, this tumor is composed of unipolar, bipolar, or apolar spongioblasts and some primitive, undifferentiated cells. Palisading necrosis, proliferation of the capillaries with endothelial reaction, and massive coagulative necrosis are seen very distinctively in a few regions. However, a marked pleomorphism of the tumor cells with giant or multinucleated forms or frequent mitotic figures, often atypical is not impressive compared to the findings of typical glioblastoma multiforme in adults. That seems to be a morphologic characteristic of congenital glioblastoma multiformes, though they behave similarly in children and adults.

Nine cases of congenital glioblastoma multiforme have been reported in the world literature and are summarized in Table 1 (Holt, 1917; Wollstein and Barlett, 1923; Amolsch, 1935; Thiele and Dimmick, 1951; Sacrez et al., 1954; Marsch,1956; Takaku et al., 1978; Riboni et al., 1985; Itoh et al., 1987). Males were affected more frequently than females in a ratio of 3:1, and hydrocephalus was the predominant clinical manifestation. The locations were the cerebrum in five cases, followed by two in the thalamus, two in the cerebellum, and one in the cerebellopontine angle.

The site of origin in this case is uncertain. However, it is unlikely to have originated in the brain stem or cerebellum with upward growth, because the tumor showed massive growth to the posterior fossa pushing the cerebellum. Grossly, the tumor was sharply demarcated from the surrounding normal brain tissue without involvement of the arachnoidal membrane. Therefore, the possibility of cortical origin with downward extension is less likely, too. It is most likely that the tumor originated from the right thalamic region and extended centrifugally to the cerebral cortex and cerebellum.

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Table 1. Reported Cases of Congenital Giloblastoma in World Literature

Author	Sex	Initial Signs or Symptoms	Age when First Observed	Age at Death	Tumor Location	Tumor Type
Holt (1917)*	M	Hydrocephalus	2 weeks	7 weeks	Lt. cerebral hemisphere	Gliosarcoma
Amolsh (1935)	—	—	At birth	Immediately after birth	Thalamic region	Glioblastoma
Thiele and Dimmick (1951)	—	Hydrocephalus	At birth	49 days	Diencephalon	Glioblastoma
Sacrez et al. (1956)	M	Hydrocephalus Vomiting	1 month	9 months	Rt. cerebellar hemisphere	Glioblastoma neurospongiosa
Marsh (1956)	F	Dyspnea Vomiting	At birth	1 week	Lt. temporal lobe	Glioblastoma
Takaku et al. (1978)	M	Hydrocephalus Facial palsy	At birth	3 weeks	Lt. cerebello-pontine angle	Glioblastoma Medulloblastoma
Sabet (1982)	F	Hydrops fetalis Hydrocephalus	At birth	1 1/2 hour after birth	Rt. cerebral hemisphere	Glioblastoma
Riboni et al. (1985)	M	Hydrops fetalis	33-week fetus	20 minutes after birth	Rt. cerebral hemisphere	Glioblastoma
Itoh et al. (1987)	M	Rt. facial palsy Hydrocephalus	At birth	43 days	Rt. cerebellar hemisphere	Glioblastoma
Present case	M	Hydrocephalus	At birth	3 days	Rt. thalamic region	Glioblastoma

*Also reported by Wollstein and Barlett (1923) — Not specified Lt.: Left Rt.: Right

Holt LE: *Gliosarcoma in an infant of seven weeks resembling hydrocephalus. Am J Dis Child 14:219-221, 1917.*

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