Case reports

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Congenital gliosarcoma; so-called sarcoglioma

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Abstract. A mixed glioma and sarcoma in a 3-month-old infant is presented as a rare case of gliosarcoma with a good response to treatment. This congenital case is quite different from those in adults: the tumor cells were mainly composed of sarcomatous elements; glial components were not anaplastic without obvious endothelial hyperplasia, but presented as reticulin-free islands, mimicking a reactive glioma in a sarcoma. It may be termed "sarcoglioma" to distinguish from a classic gliosarcoma. The origin of the rare mixed tumor may be related to a dysgenesis of both mesenchymal and glial elements.

Key words: Congenital brain tumor – Gliosarcoma – Primary sarcoma – Sarcoglioma

Gliosarcoma is a brain tumor composed of neoplastic glial cells in association with spindle-celled sarcomatous elements. It usually occurs in adults and is associated with a poor prognosis. We managed an infant with a glial and sarcomatous tumor in the left temporoparietal lobe. The patient was successfully treated by surgery and radiation. This unusual case is described in detail, and the clinicopathological features are discussed with reference to the relevant literature.

Case report

The patient was a female infant born without complications at full term on 16 June 1987 after a normal pregnancy and vaginal delivery. Her initial head circumference was 34 cm, consistent with her weight and chest measurements. At the age of 3 months, when her neck was not yet fixed, the head circumference was 43 cm, well above the 95th percentile. She was admitted to the Tone Central Hospital on 13 October 1987, following a generalized convulsion. The episode lasted for a few minutes. On admission, she was alert with a large, bulging anterior fontanel. The deep tendon reflexes were increased, and the plantar reflexes were upgoing on the right side. The neurological examination gave otherwise normal results. Laboratory findings were unremarkable.

The computed tomographic (CT) scans (Fig. 1) showed a large cystic mass involving the left temporoparietal lobe and basal ganglia with contrast-enhancing lesions in the cortical surface and significant peritumoral edema. The midline structures were markedly shifted to the right side.

On 22 October 1987, the patient underwent craniotomy for excision of the brain tumor and a cyst-peritoneal shunt. The tumor was not attached to the dura, but was in fact a well-circumscribed firm, gray mass surrounded by multilobulated large cysts. The slightly yellowish cystic fluid contained 3500 mg/ml of protein and one-third white blood cells. The patient postoperatively developed a left subdural hygroma and right subdural hematoma with slit ventricles and a residual contrast-enhancing tumor shown by the CT scans (Fig. 2) in January, 1988, when she was referred to Gunma University Hospital for further treatment. The next operation was performed on 25 January 1988, this time at our institute. The residual tumor was totally removed and the left subduroperitoneal shunt was placed to revise the last shunting system. Postoperative local radiation of 30 Gy to the tumor site was administered to eradicate the tumor. The recent CT scans (Fig. 3) revealed no residual tumor or subdural fluid collection. At the age of 2 years, she is now able to walk without assistance, to talk, and there are no apparent neurological deficits.

Microscopically, sheets of spindle-shaped cells with elongated nuclei and fibrous cytoplasmic processes were interweaving with collagen fibers (Fig. 4). Most of the tumor showed the histological features of a fibrosarcoma, accompanied by rich intercellular reticulin fiber network. Reticulin-free islands of glial cells were commonly entrapped in the sarcomatous tissue (Fig. 5). Some of the islands showed various degrees of cellular atypia and an increase in astrocytic cell density with proliferated endothelial cells (Fig. 6) and acidophilic hyalin droplets, suggesting neoplastic change. The glial part was clearly identified by the immunohistochemical demonstration of glial fibrilary acidic protein (GFAP) (Fig. 7) and S-100 protein. Islands of GFAP-positive cells were often surrounded by negative sarcomatous tissue. Vimentin was not immunohistochemically positive in the glial cells, but in the mesenchymal components. Neurofilament proteins were not found in any tumor cells. Cell proliferation potential was assessed by measuring the labeling index of the monoclonal antibody of 5-bromodeoxyuridine (BUdR), using an ethanol-fixed paraffin-embedded BUdR-labeled specimen. The BUdR labeling index was lower than 1%.

By electron microscopy, the sarcomatous areas were composed of spindle-shaped cells with oval nuclei and slender elongated processes (Fig. 8). Their cytoplasm had markedly abundant, rough

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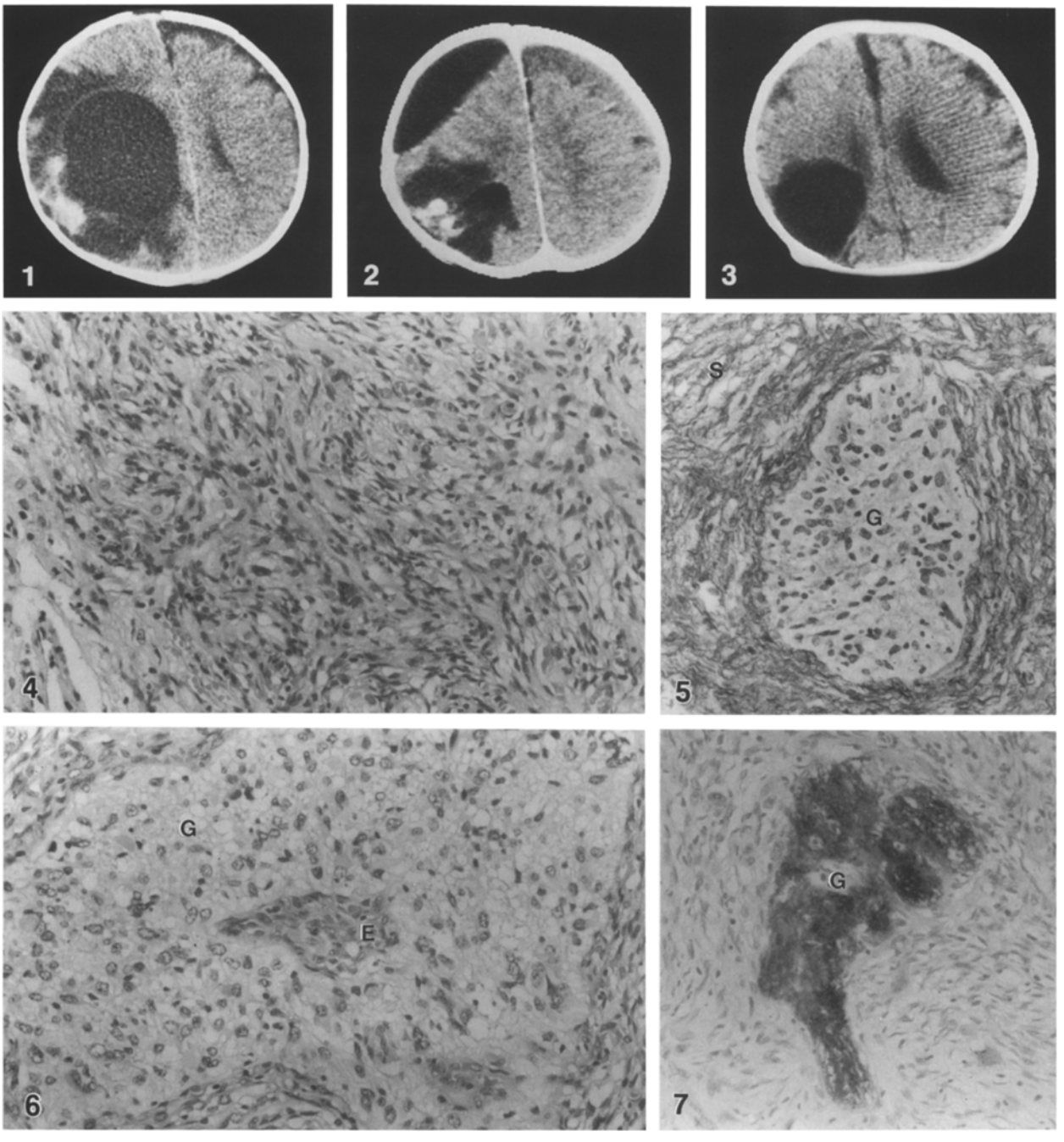


Fig. 1. Preoperative CT scan on 14 October 1987, showing a large cystic mass with contrast-enhancing lesions in the cortical surface

Fig. 2. CT scan on admission of Gunma University Hospital showing a left subdural hygroma and right subdural hematoma with a residual contrast-enhancing tumor

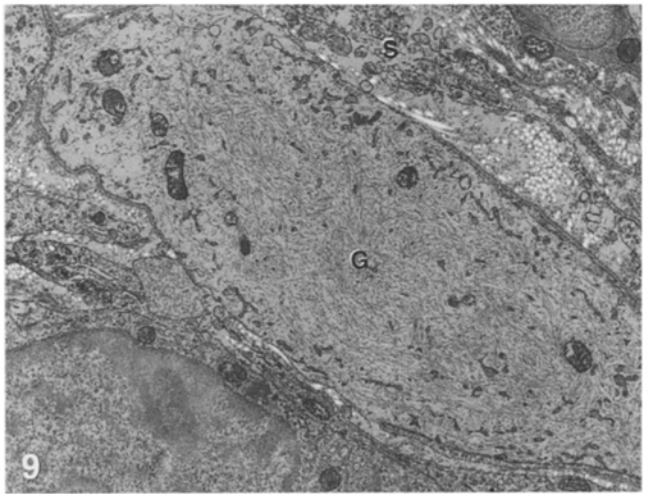
Fig. 3. Post-treated CT scan showing no residual tumor or subdural fluid collection

Fig. 4. Mesenchymal components showing histologic features of a fibrosarcoma. H&E stain, ×62.5

Fig. 5. A reticulin-free island of glial cells (*G*) is entrapped in the sarcomatous tissue (*S*). Silver impregnation for reticulin, ×62.5

Fig. 6. A glial island (*G*) including cellular atypia and mild endothelial proliferation (*E*). H&E stain, ×62.5

Fig. 7. A glial island (*G*) demonstrated by immunoperoxidase, whereas the sarcomatous tumor (*S*) is immunonegative. Immunoperoxidase stain for GFAP, ×62.5



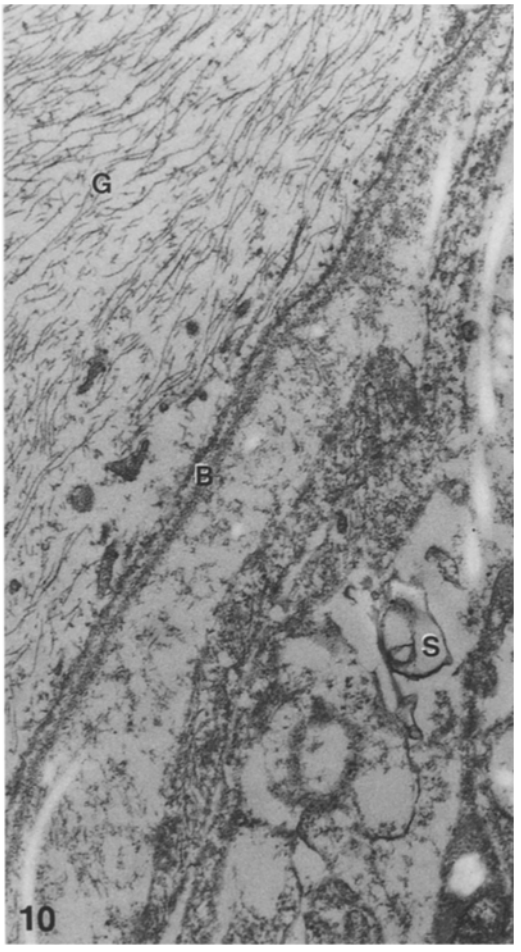


Fig. 8. A sarcomatous area with spindle-shaped cells including abundant rough endoplasmic reticulum in the cytoplasm. The interstitial spaces contain many collagen fibrils, showing fibroblastic characters. Electron micrograph, × 11 000

Fig. 9. A glial cell (*G*) in the sarcomatous tissue (*S*) contains intracytoplasmic intermediate filament, 8–9 nm in diameter. Electron micrograph, × 11 000

Fig. 10. A basement membrane (*B*) borders the sarcomatous (*S*) and glial (*G*) components. Electron micrograph, × 33 000

endoplasmic reticulum. The interstitial spaces contained a large amount of collagen fibrils, showing fibroblastic characters. On the other hand, the glial cells contained many bundles of intracytoplasmic intermediate filaments, 8–9 nm in diameter, with short cytoplasmic processes (Fig. 9). The sarcomatous and glial cells were well bordered by basement membranes (Fig. 10).

Discussion

Gliosarcoma is a well-recognized neoplasm of mixed glial and mesenchymal origin and is included in the WHO classification of central nervous system tumors [13]. It usually contains apparent components of anaplastic glioma or glioblastoma. Exuberant vascular endothelial proliferation in the stroma of an anaplastic glioma is considered the common route to formation of a sarcomatous component [4]. That type of gliosarcoma was estimated to occur with a frequency of approximately 8% of all glioblastomas [10]. The majority of patients with these tumors were between 40 and 70 years old. The most common site is the temporal lobe. The second- and third-most common sites are the parietal and frontal lobes. The sarcomatous element tends to have a different biological behavior – metastasizing outside the neuroaxis [1]; however, the survival rate for gliosarcoma is essentially the same as that of glioblastoma, depending on the grade of gliomas.

Paradoxically, another form of mixed glioma and sarcoma is histologically characterized by a mainly central location of intracerebral sarcoma in relation to a periph-

Table 1. Differences between gliosarcomas and sarcogliomas

	Gliosarcomas	Sarcogliomas
Incidence	8% of glioblastomas	Much rarer
Age	Usually in adults	Often in infants
Primary	Glioma	Sarcoma
Grade of glioma	3 or 4	Often 2
Endothelial proliferation	Prominent	Mild
BUdR index (%)	>2	<1
CT finding	Solid > cystic	Cystic > solid
Prognosis	Poor	Sometimes good
Dysgenetic factor	Not related	May be related

Table 2. Reported cases of infantile gliosarcomas (sarcogliomas)

Authors (year)	Age (months)/ sex	Histology	Operation	Radiation	Chemo-therapy	Outcome
Holt (1917) [6]	1/M	Gliosarcoma	(−)	(−)	(−)	Autopsied
Lalitha and Rubinstein (1979) [7]	8/M	Meningeal sarcoma with low-grade astrocytoma	Subtotal removal, one-stage	(−)	(−)	Died
Lalitha and Rubinstein (1979) [7]	2/F	Fibrosarcoma with glioblastoma	Total removal, one-stage	(−)	(−)	Autopsied
Goldstein et al. (1981) [5]	4/F	Malignant gliosarcoma	(+)	(?)	(?)	(?)
Chadduck et al. (1987) [2]	1/M	Fibrosarcoma with undifferentiated glioma	Partial removal	(−)	(+)	Alive
Radkowski et al. (1988) [11]	0/M	Malignant gliosarcoma	Total removal, two-stage	(?)	(?)	Alive (21 mo)
This report	3/F	Fibrosarcoma with low-grade glioma	Total removal, two-stage	(+) 30 Gy	(−)	Alive (34 mo)

eral distribution of the gliomatous elements. The reactive astrocytes are considered to be transformed into neoplastic cells in the glial islands within the primary sarcoma. It has been suggested that this type should be termed "sarcoglioma" to distinguish it from the classic type of mixed glioblastoma with sarcomatous components (Table 1) [7]. This form is much rarer than the gliosarcomas with secondary sarcomatous change, because the marked difference between the incidence of primary intracranial sarcoma and that of glioblastoma [12]. Primary sarcomas of the nervous system are not common in adults, but are sometimes found in infants, occurring in 3.9% of infantile brain tumors during the first 2 years of life [8]. Only 6 cases of infantile gliosarcoma have been reported previously (Table 2) [2, 5–7, 11].

In the present case, the tumor cells were mostly composed of sarcomatous elements. The glial components appeared to be low-grade, present as islands segregated within the sarcomatous tissue. The vascular endothelial hyperplasia was not prominent. Although the distinction between sarcomatous change and primary sarcoma is not always clear-cut because of the age of the patient this case would appear to be a primary sarcoma with secondary gliomatous change, such as a sarcoglioma. However, the presence of glial tissue as islands incorporated with sarcomas resembled an ectopic glial cell nest in an infantile skull base or an ectopic subcutaneous glial tissue in a lumbar meningomyelocele. We suggest that this mixed tumor developed from a dysgenesis of both glial and mesenchymal origins, as had been reported in a neonatal gliosarcoma with chromosome abnormalities [2].

Neuroradiologically, the CT observation in this case was consistent with previous CT reports of congenital malignant gliosarcomas, which appear as large, cystic masses [5] or as densely enhancing temporoparietal mass with associated edema, reaching the pial surface of the brain [11]. These are different from those of adult gliosarcomas [9]. However, the CT findings of gliosarcomas cannot be completely differentiated from other types of malignant gliomas.

Clinically, both radiotherapy and chemotherapy have been utilized in the treatment of gliosarcomas, but no definite effect on survival has been noted in adults [10]. Even in primary sarcomas in childhood, the clinical history has been short and deterioration usually rapid [3, 8]. However, infantile gliosarcomas may have a favorable response to the treatments as in the present case [2, 11]. In spite of extensive surgery, the late neuropsychological results were good, unless a one-stage radical operation was performed on a vulnerable infant. In this case we did a two-stage operation, as described previously [11]. Since no effective chemotherapy against gliosarcomas has yet been established, we used radiotherapy, but avoided more than 30 Gy to the hemispheres, which might have undesirable effects on the immature, growing brain in infants [8]. In conclusion, congenital gliosarcomas, so-called sarcogliomas, tend to have several specific characteristics, as mentioned above, and must be regarded as a special form of relatively low-grade malignant gliosarcoma.

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