Gliosarcoma after a non-Hodgkin splenic lymphoma

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Introduction

Gliosarcoma (GSM) is classified by the World Health Organization (WHO) as a variant of glioblastoma and shares histological characteristics with differentiated glial and mesenchymal (sarcomatous) cells[1]. GSM was initially described in detail by Feigen and Gross in 1955[2] and may occur as primary or secondary tumors[1]. The epidemiology and natural history of GSM are similar to those of glioblastoma and account for 1-8% of all gliomas.[3] The interpretation of survival and treatment response data for GSM is unreliable because of the small number cases for this type of tumor.[3]

Case report

A 67-year-old female patient with lymphadenopathy was diagnosed with a splenic marginal zone lymphoma (non-Hodgkin lymphoma) in 2009, based on bone marrow biopsy. The lymphoma was already widely disseminated but there was no specific recommendation for treatment.[4] During her clinical follow-up, the patient showed visual field and memory loss, behavioral changes, emotional lability and tinnitus; she underwent magnetic resonance imaging (MRI) 15 days later.

MRI revealed an infiltrative lesion in the deep white matter of the left temporo-occipital lobe (Figs 1; 2), an intraparenchymal peripheral nodule in the left occipital lobe (not biopsied) (Fig 3) and subependymal dissemination (Fig 2). Spectroscopy in the temporo-occipital mass showed a decrease in N-acetyl-aspartate and an increase in the choline/creatine ratio, the latter indicative of neuronal or axonal damage, dysfunction and increased cellular turnover/proliferation; there was also an increase in the lipid/lactate peak, indicative of necrosis and anerobiosis (Fig 4). Assessment of perfusion showed a high relative cerebral blood volume in the mass and in the perilesional white matter, indicative of tumor infiltration (Fig 5).

Only the tumoral area in the temporo-occipital lobe was resected. Histopathologic analysis revealed malignant spindle cells with necrosis and neoplastic astrocytes that stained positively for glial fibrillary acidic protein (GFAP) and merged with fusocellular GFAP-negative areas (Fig 6). These histopathologic findings led to the diagnosis of gliosarcoma (WHO Grade IV).

In the postoperative follow-up, the patient underwent radiotherapy and chemotherapy for GSM (6-12 cycles of cisplatin and temozolomide). After the first treatment session, the patient experienced progressive worsening of her neurological symptoms that culminated in hospitalization. She evolved with superior vena cava syndrome and cardiopulmonary arrest that led to her death.

Discussion

Various studies have investigated the genetic characteristics, epidemiology, predisposing factors and prognosis of GSM[1,3,5,6]. GSM generally affects individuals 60-70 years old and is more common in males, a profile similar to glioblastoma[7,8]. The most affected region is the supratentorial brain, although not all regions are equally affected; the temporal lobes are the most affected, followed by the parietal, frontal and occipital lobes[7].

MRI indicates that GSM generally manifests as a well-defined solid lesion, with irregular margins, with or without central necrosis or cystic areas, and perilesional edema[5]. Contrast enhancement is heterogeneous, often showing a ring-like contour. Non-contrast computed tomography generally shows a heterogeneous tumor mass that is iso- to hypo-attenuating. Non-contrast MRI reveals hypointensity on T1-weighted and hyperintensity on T2-weighted sequences compared to the white matter. Sarcomatous and glial components usually have a high signal on T2, but the former shows little enhancement because of foci of necrosis[5].

Advanced magnetic resonance-based analyses (spectroscopy and perfusion) generally show that there is similarity between the peritumoral portion of GSM and high-grade gliomas, a characteristic than can be used to differentiate these tumors from solitary metastases. GSM shows a high relative cerebral blood volume in perfusion, with an increase in the choline/creatine ratio that extends to peritumoral tissue, indicating potential infiltration[9,10]. Many of these features were found in our patient, except that GSM was already widespread to the ependyma.

Conclusion

GSM remains a poorly understood tumor, despite current technological advances in imaging and cytogenetics. The radiological and histopathological findings of the case reported here highlight the aggressiveness of GSM and its poor prognosis.

References

1. Reis RM, Könü-Leblebicioglu D, Lopes JM, Kleihues P, *et al*. Genetic profiles of gliosarcomas. Am J Pathol. 2000; 156:425-432.
2. Feigen IH, Gross SW. Sarcoma arising in glioblastoma of the brain. Am J Pathol. 1955; 31:633-653.
3. Kozak KR, Mahadevan A, Moody JS. Adult gliosarcoma: epidemiology, natural history, and factors associated with outcome. Neuro-Oncology. 2009; 11:183-191.
4. Dreyling M, Thieblemont C, Gallamini A, *et al.* ESMO Consensus Conferences: Guidelines on malignant lymphoma. Part 2: Marginal zone lymphoma, mantle cell lymphoma, peripheral T-cell lymphoma. Ann Oncol. 2013; 24:857-877.
5. Zhang BY, Chen H, Geng DY, *et al*. Computed tomography and magnetic resonance features of gliosarcoma: a study of 54 cases. J Comput Assist Tomogr. 2011; 35:667-673.
6. Han SJ, Yang I, Tihan T, *et al*. Secondary gliosarcoma: a review of clinical features and pathological diagnosis. J Neurosurg. 2010; 112:26-32.
7. Lutterbach J, Guttenberger R, Pagenstecher A. Gliosarcoma: a clinical study. Radiother Oncol. 2001; 61:57-64.
8. Beaumont TL, Kupsky WJ, Barger GR, Sloan AE. Gliosarcoma with multiple extracranial metastases: case report and review of literature. J Neurooncol. 2007; 83:39-46.
9. Lin JN, Chiang IC, Tsai TC, Hsieh FC. 3T-Magnetic resonance imaging and proton magnetic resonance spectroscopy findings in gliosarcoma: a case report. Chin J Radiol. 2007; 32:81-85.
10. Steen RG. Edema and tumor perfusion: characterization by quantitative HMR imaging. Am J Roentgenol. 1992; 158:259-264.

Figures

Figure 1: Axial T2-weighted image showing an irregular lesion with mixed central hypointensity and hyperintensity. The mass is surrounded by perilesional edema.

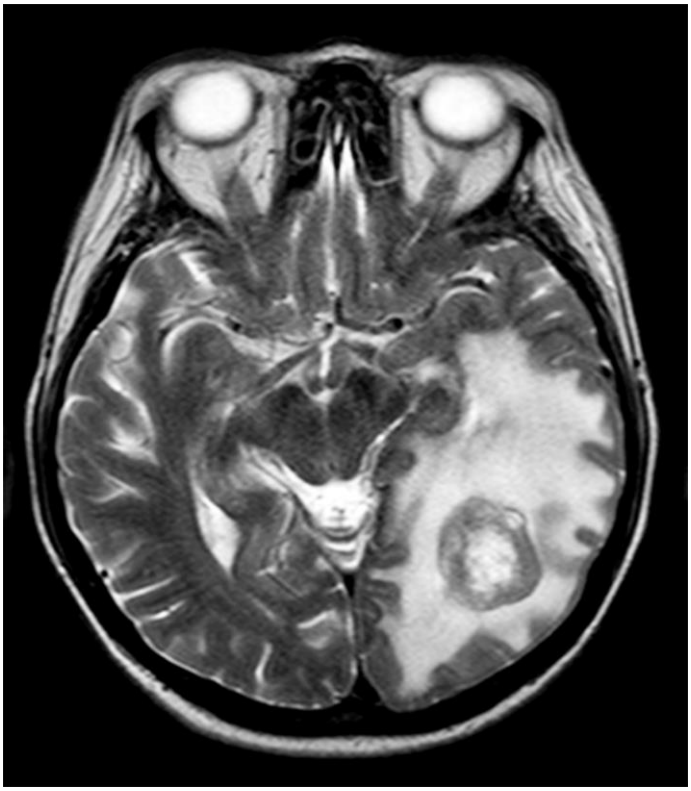


Figure 2: A. Axial T1 fat-sat after contrast showing subependymal enhancement involving the left lateral ventricle. There is also enhancement in the irregular expansive lesion in the left temporo-occipital lesion. B. Axial T1 fat-sat after contrast, following surgery and biopsy, showing residual lesion and postoperative changes (pachymeningeal enhancement).

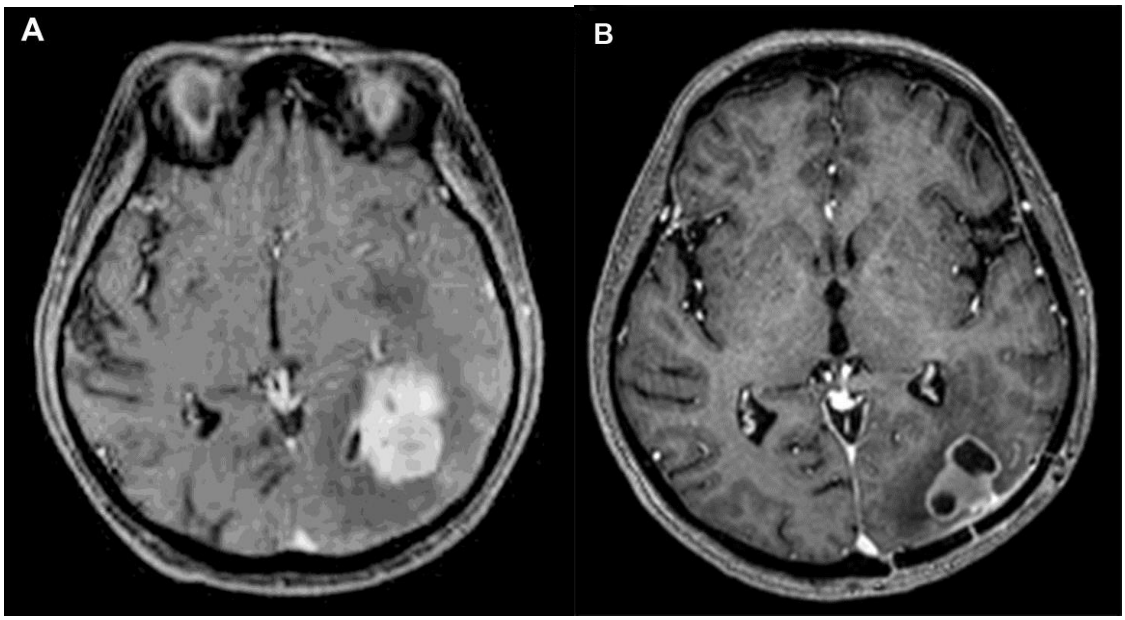


Figure 3: Sagittal T1 fat-sat after contrast revealed a mass in the deep white matter of the left temporo-occipital lobe (histologically shown to be GSM) and also a peripheric nodule in the occipital region.

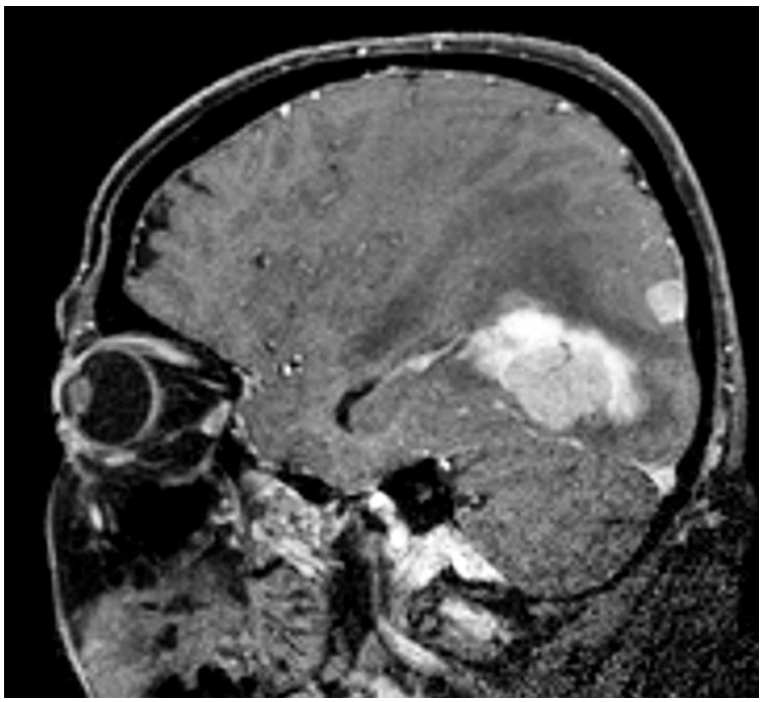


Figure 4: A. Short TE (31 ms) proton-spectroscopy sequence showing a decrease in N-acetyl-aspartate (NAA) and an increase in the choline/creatine (Cho/Cr) and lipid/lactate ratios. B. Axial image showing where the voxel was placed.

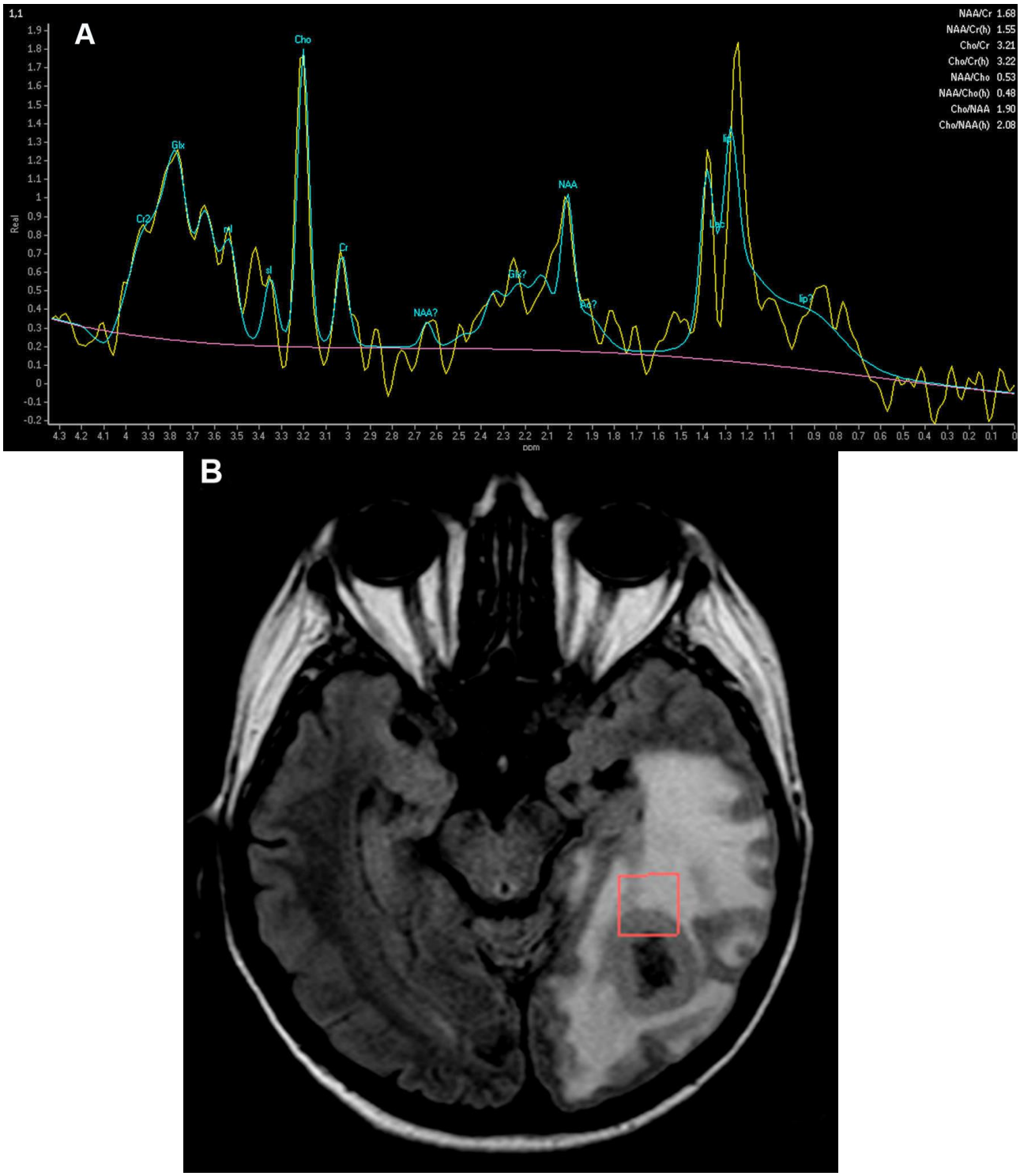


Figure 5: Perfusion analysis showing a significantly increased relative cerebral blood volume corresponding to the irregular wall of the lesion in the left temporo-occipital lobe.

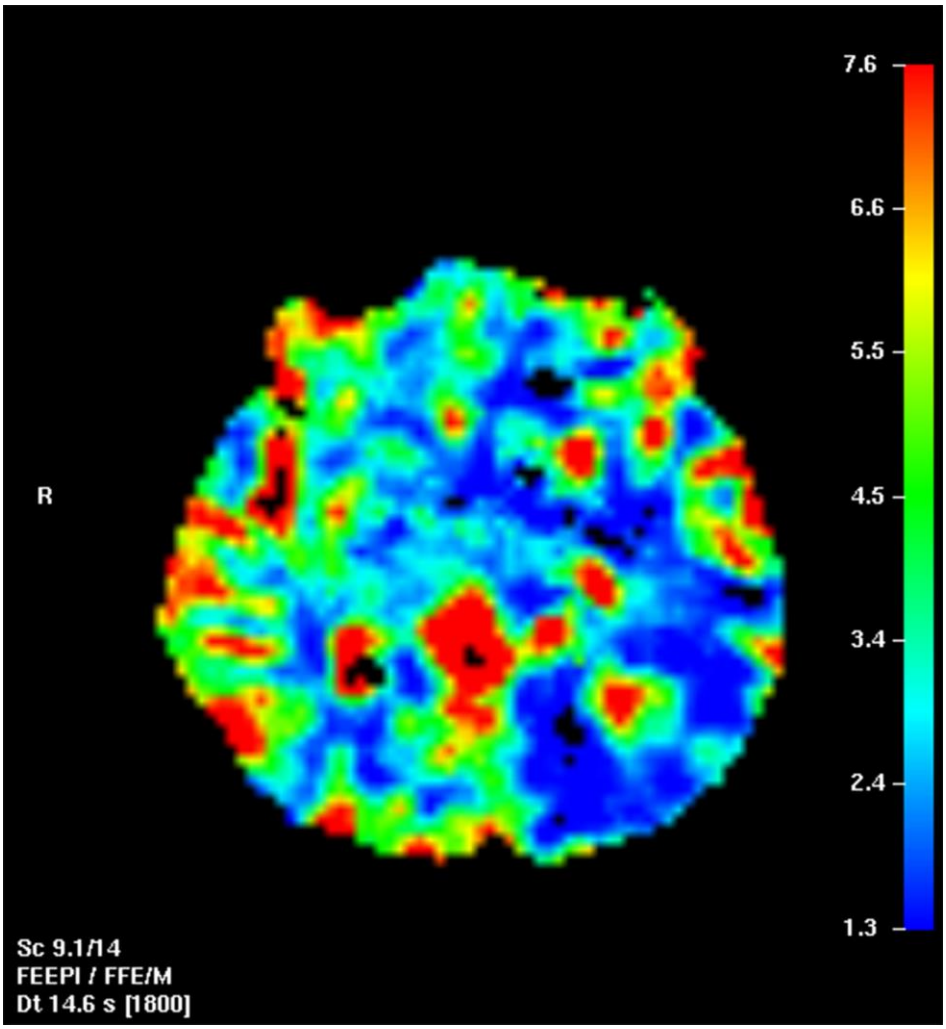


Figure 6: Histopathologic analysis of tumoral tissue. Left panels (A,C,E) – gliomatous area, right panels (B,D,F) – sarcomatous area.

A. High-grade glioma showing loosely arranged atypical astrocytes and capillary proliferation. The capillary in the center shows multiple lumens. HE. x300.

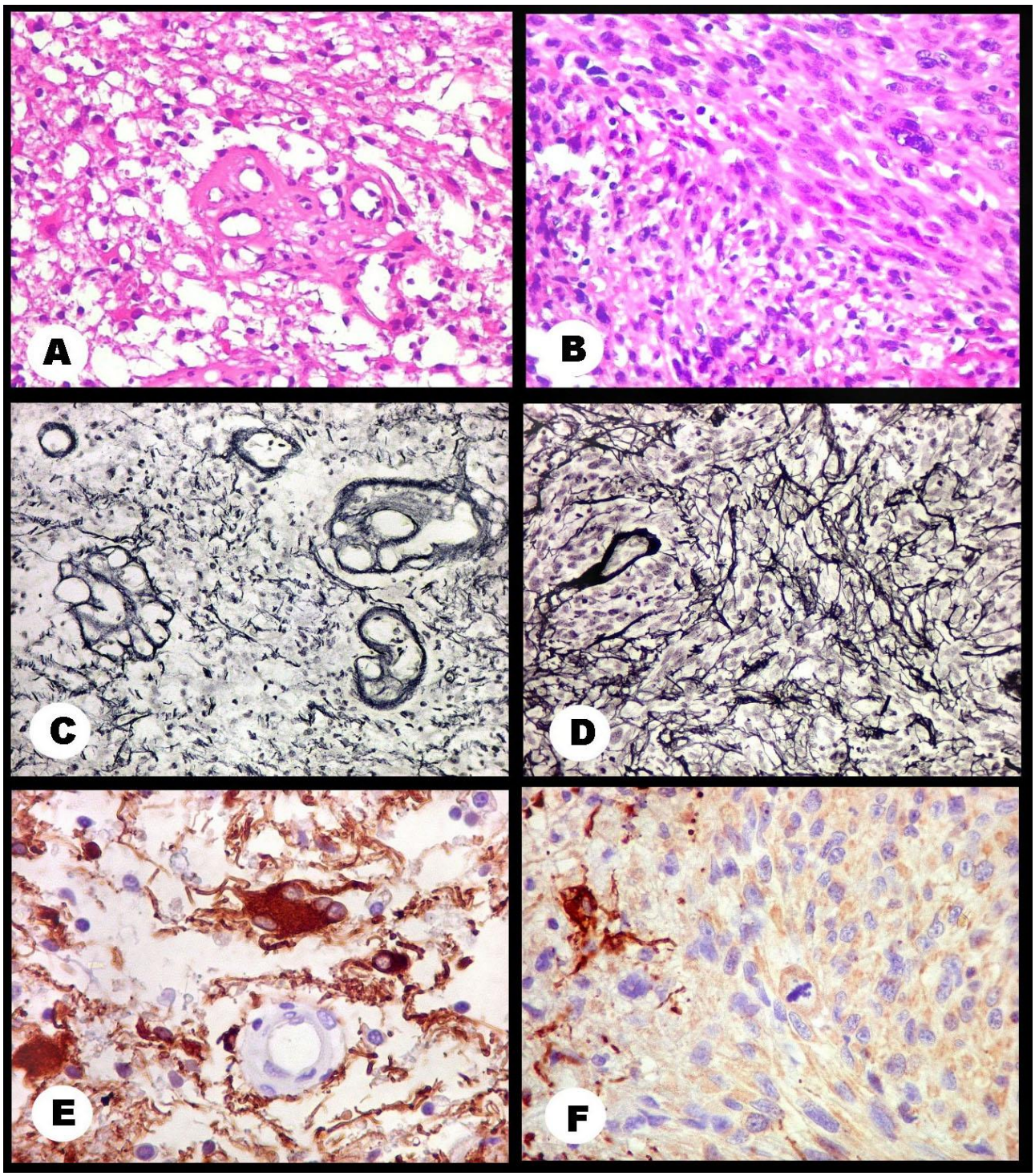
B. Sarcomatous area characterized by spindle-shaped cells with hyperchromatic nuclei densely arranged in perpendicularly crossing bundles. HE. x300.

C. Gliomatous area showing reticulin fibers primarily around small glomeruloid vessels, with reduced presence among tumor cells. Gomori's silver impregnation. x200.

D. Sarcomatous area showing an abundance of reticulin fibers amongst neoplastic cells. Gomori's silver impregnation. x200.

E. Gliomatous area. Atypical, multinucleated, strongly glial fibrillary acidic protein (GFAP)-positive neoplastic astrocytes and their cytoplasmic processes contrast with the GFAP-negative thickened capillary. Immunohistochemistry for GFAP. x200.

F. Sarcomatous area virtually devoid of GFAP-positive cells (some staining is seen on the left of the image). Note atypical mitosis in the center of the image. Immunohistochemistry for GFAP. x200.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