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GLIOSARCOMA ASSOCIATED WITH NEUROFIBROMATOSIS TYPE I: A CASE REPORT

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Neurofibromatosis type I (NF I) is the most common hereditary syndrome predisposing to neoplasia. We report the third case in the literature, documenting the combination of gliosarcoma with NF I. The patient's son was known at our center because of a history of pleomorphic xanthoastrocytoma (PXA) with NF I.

A 48-year-old man who had a number of café-au-lait spots with neurofibroma since birth presented with severe headache. Neuroradiological studies revealed a cystic tumor of the right temporal lobe of high grade nature. Surgical excision was performed and the tumor was found to be located on the surface of the temporoparietal area with cystic formation and vascular and infiltrative features. Postoperative MRI showed no detectable contrast enhancing tissue. Immunohistochemical examination evidenced the characteristics of typical gliosarcoma. The patient received radiation therapy but five months following surgery recurrence of the tumor was diagnosed. Reoperation was performed and histopathological studies confirmed the diagnosis of gliosarcoma. We believe that the neurofibromatosis was inherited by the son with PXA from the father with gliosarcoma.

The rarity of the combined occurrence of gliosarcoma and NF I, in addition to this uncommon family history, makes this case remarkable. Our findings suggest that NF I is a multifaceted disease associated with benign as well as malignant astrocytic tumors.

Key words: gliosarcoma, neurofibromatosis I, temporal lobe.

Introduction

Gliosarcoma is a glioblastoma with a sarcomatous component. It constitutes 2% of all glioblastomas[1-3]. Its occurrence in neurofibromatosis type I is so rare that only two cases have been reported in the literature to date[4,5]. In this paper we report on a patient with gliosarcoma associated with von Recklinghausen's disease whose son was known at our clinic because of a history of pleomorphic xanthoastrocytoma associated with von Recklinghausen's disease[6].

Case report

The patient was a 48-year-old male. He had a family history of neurofibromatosis type I, including his son and daughter. He presented with a chief complaint of severe headaches of one month's duration. Physical examination revealed neurofibromas all over the body, more than 20 café-au-lait spots larger than 10 mm and Lisch nodules. Neurological examination did not reveal any pathological signs. Magnetic resonance imaging (MRI) demonstrated a right temporal mass of 50 x 44 x 44 mm with peripheral contrast enhancement and central necrosis causing a midline shift of 11 mm (Figure 1).

The patient underwent surgery. A right temporal craniotomy was performed. The dura mater had a tense appearance. The temporal lobe cortex was incised using a bipolar coagulator and a red-gray, easily suckable tumor showing poor demarcation but infiltrating the surrounding brain parenchyma was exposed. Gross total resection was performed (Figure 2). Tumor tissue was fixed in 10% buffered formalin and embedded in paraffin. The sections were stained with hematoxylin-eosin; in addition, selected sections were stained with reticulin. Glial acidic protein (GFAP, BioGenex) was performed on selected sections with ap-

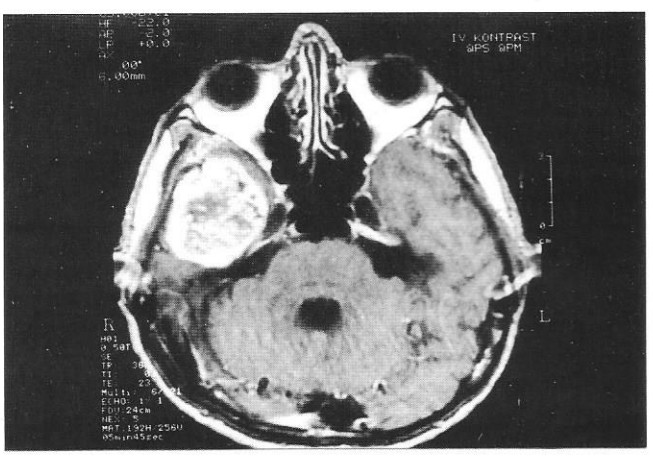

Figure 1 - Magnetic resonance image showing a right temporal mass of 50 x 44 x 44 mm with peripheral contrast enhancement and central necrosis causing a midline shift of 11 mm.

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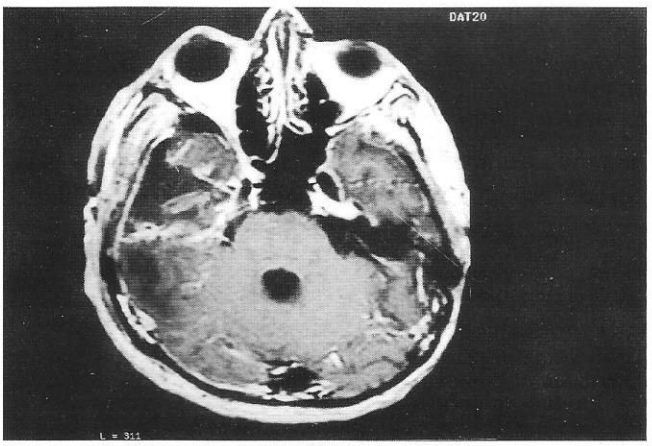

Figure 2 - Postoperative magnetic resonance image showing gross total resection of the tumor.

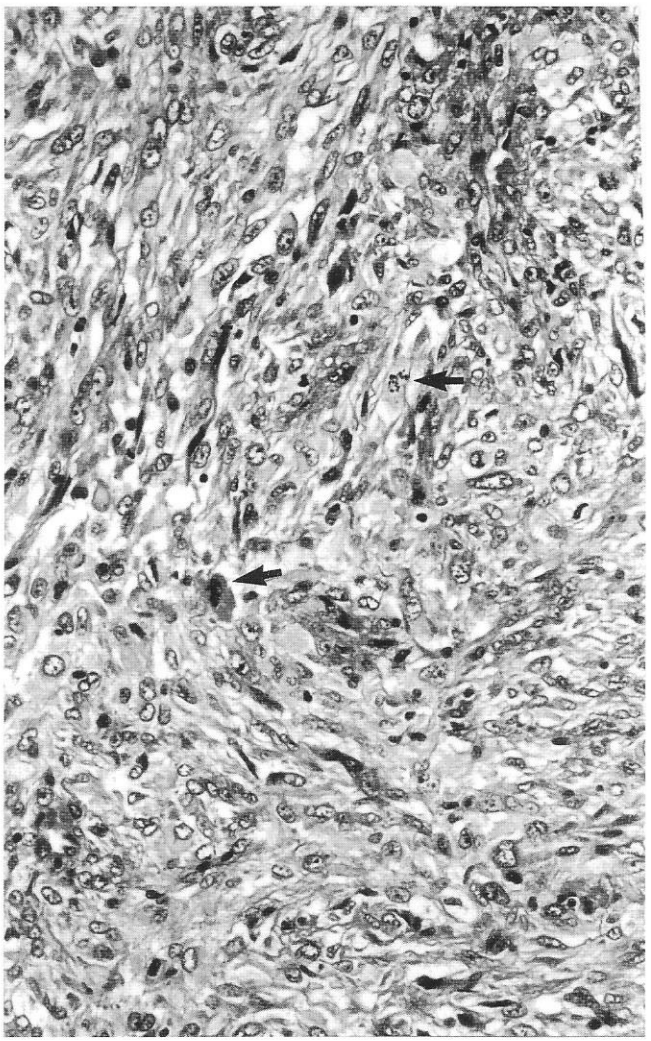

Figure 3 - The mesenchymal component of the tumor resembles a pleomorphic sarcoma and shows pleomorphic cells with mitosis (arrows).

propriate positive and negative controls as an immunohistochemical marker for astrocytes. Histopathologic examination revealed a neoplasm containing both malignant glial and mesenchymal tissue. The histological features included fascicles of sarcomatous transformation interspersed with areas of glioblastoma. In some areas the sarcomatous component of the tumor was composed of spindle cells with a herringbone architecture. This component showed pleomorphic spindle cells with mitosis (Figure 3). The mitotic rate was high in both the glioblastoma and sarcomatous components of the tumor. There was necrosis that surrounded by a distinctive collar of cells, called pseudopalisading, in some parts of the tumor. The cortical tissue was also infiltrated by the tumor and revealed perivascular, perineuronal and subpial accumulations of tumor cells. The spindle cells of the sarcomatous islands of the tumor had a marbled configuration into the glioblastoma and showed strong pericellular reticulogenesis (Figure 4). By contrast, the glioblastoma component of the tumor was characteristically free of reticulin and stained intensely for GFAP (Figure 5). A diagnosis of gliosarcoma was made. The patient received postoperative radiotherapy and was discharged without any neurological deficit.

Five months following surgery the patient was readmitted to hospital with severe headaches. MRI demonstrated recurrence (Figure 6). The patient underwent another operation and histopathological examination confirmed the diagnosis of gliosarcoma. The patient was discharged without any neurological deficit. At four months from his last operation the patient is still symptom free.

Discussion

Neurofibromatosis type I (NF I) is the most common hereditary syndrome predisposing to neoplasia[7,8]. This syndrome is an autosomal dominant disorder characterized by neurofibromas, malignant peripheral nerve sheath tumors, optic nerve gliomas and other astrocytomas associated with cutaneous findings such as café-au-lait spots, axillary and inguinal freckling, Lisch nodules and various osseous lesions[9].

The majority of gliomas in neurofibromatosis type I patients are pilocytic astrocytomas that are located within the optic nerve[10]. Other gliomas observed in these patients include diffuse astrocytomas and glioblastomas[7,9]. However, the occurrence of gliosarcoma in neurofibromatosis type I is extremely rare.

Our case having the association of NF I with gliosarcoma is the third one in the literature. The first case was reported in 1967 in England, a patient with gliosarcoma and pheochromocytoma associated with neurofibromatosis type I[5]. The second case was reported in 1992 in Japan[4]. Additionally, the existence of hereditary

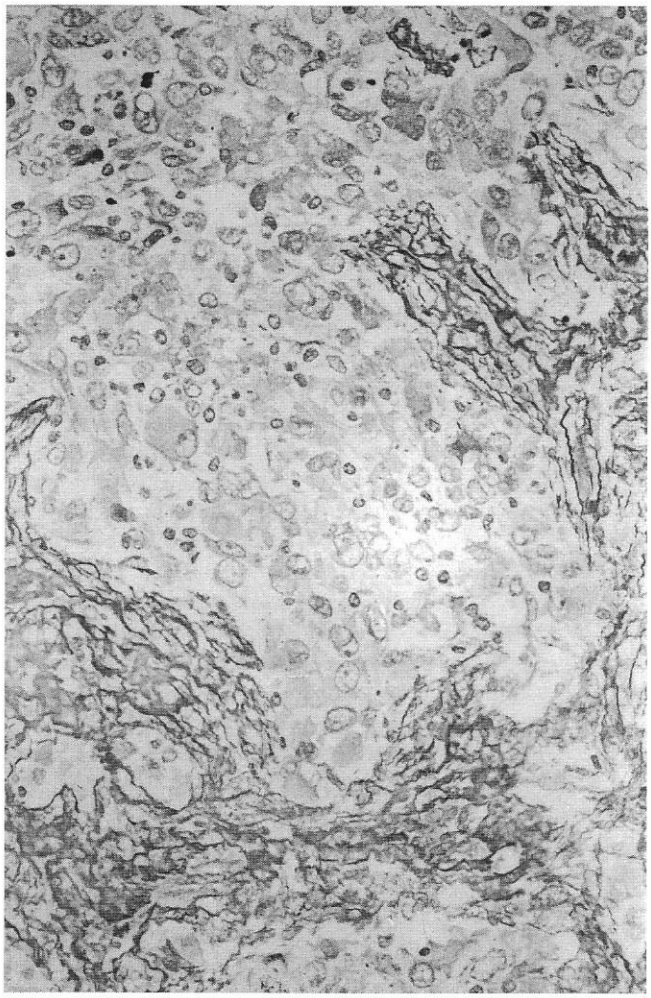

Figure 4 - The glial component of the tumor is free of reticulin while the mesenchymal component shows strong pericellular reticulogenesis.

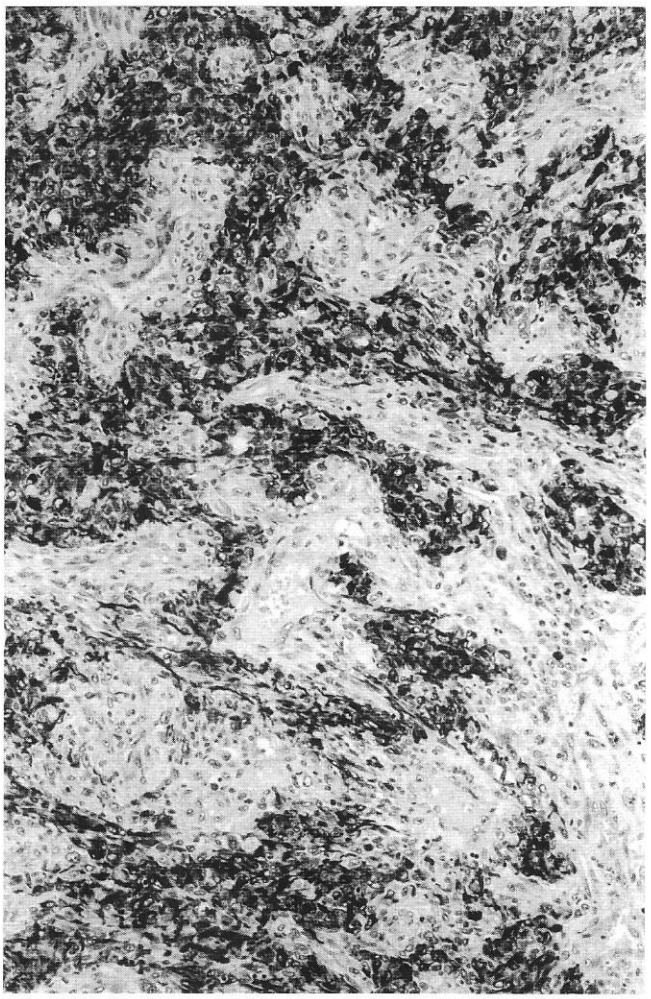

Figure 5 - The islands that were free of reticulin stain darkly for GFAP (BioGenex).

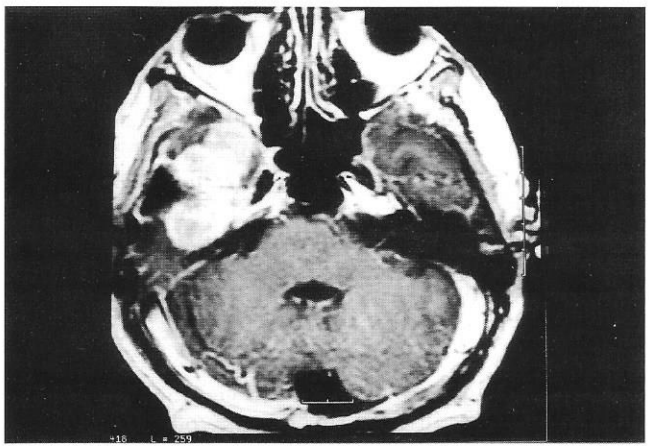

Figure 6 - Magnetic resonance image showing tumor recurrence.

glioma such as this in patient, whose son was known to have both NF I and PXA, is rare and deserves attention. These data may show a similar underlying molecular-genetic disturbance with different severity for PXA and gliosarcoma.

The NF I gene, which is located on chromosome 17, is a tumor suppressor gene[11]. The protein product of the NF I gene has been termed neurofibromin. Its loss is associated with NF I. Neurofibromin acts in signal transduction in ras-dependent mitogenic pathway presumably in two different roles: as a negative controller of p21ras-mediated signaling pathway for proliferation, and as a downstream effector of p21ras possibly in differentiation[12,13]. Neurofibromin may act to inhibit the oncogenic potential of a tyrosine kinase, which is p21ras. People with NF I are at increased risk of the development of both anaplastic astrocytoma and glioblastoma, although astrocytic tumors of lower histologic grade predominate. This report may represent possible clinical evidence of a common alteration with different severity in NF I gene functions, presumably the ras-dependent mitogenic pathway, in neurofibromatosis I, gliosarcoma and PXA.

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