Case Report

Primitive neuroectodermal tumor coexistent with anaplastic ganglioglioma

Rezzan Erguvan-Önal[1], Çağatay Önal[2], Metin Şener[2], Bülent Mızrak[3], Erol Duran[2], Nasuhi Engin Aydın[1]

[1] Inonu University School of Medicine Department of Pathology, Malatya, Turkey
[2] Inonu University School of Medicine Department of Neurosurgery, Malatya, Turkey
[3] Damla Hospital Department of Pathology, Elazığ, Turkey

Abstract

Primitive neuroectodermal tumors are among the most common tumors of childhood and the most frequent location of them is cerebellum. Supratentorial primitive neuroectodermal tumors are uncommon. These tumors, regardless of site of origin, may show differentiations towards different cell lines such as glial, neuronal, and mesenchymal. To our knowledge, there is only one case in the literature describing ganglioglial differentiation in a cerebellar medulloblastoma. The presented report discloses a supratentorial primitive neuroectodermal tumor coexistent with anaplastic ganglioglioma in a 46-year-old man. Both components of the tumor disappeared after radiotherapy, with a proceedent glioblastomatous differentiation in the follow-up period.

Key words: primitive neuroectodermal tumor, anaplastic ganglioglioma, glioblastoma multiforme, brain

Corresponding Address: Çağatay Önal, M.D., Inonu University School of Medicine Department of Neurosurgery, Malatya, Turkey.
E-mail: conal_tr@yahoo.com

Introduction

"Primitive neuroectodermal tumors" are among the most common tumors of childhood and are frequently located in cerebellum. These tumors, regardless of site of origin, may contain cells displaying features of neoplastic astrocytes, oligodendrocytes, ependymal cells, neuronal cells, melanocytes, or mesenchymal cells, such as smooth or striated muscle [1]. To our knowledge, there is only one case in the literature describing ganglioglial differentiation in a cerebellar medulloblastoma [2]. A supratentorial primitive neuroectodermal tumor (S-PNET) coexistent with anaplastic ganglioglioma in an adult which both components disappeared and a glioblastomatous differentiation occurred after radiotherapy is described for the first time in this report.

Case Report

A 46-year-old man with the major complaint of somnolence for twenty days was admitted to the neurosurgery department. History revealed alcohol addiction for twenty years. Physical examination did not reveal any data of interest except for cachectic appearance. Somnolence, loss of orientation, and poor plantar responses bilaterally were detected in neurologic examination. Laboratory findings were in normal ranges.

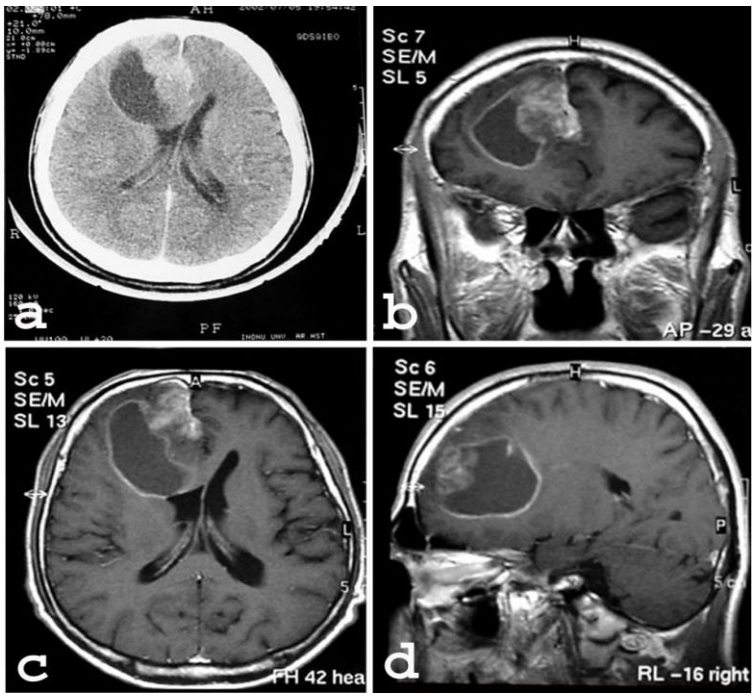

Fig. 1: a-Contrasted cranial axial CT showing cystic and solid tumor revealing enhancement in the solid area. **b-**T1-weighted contrasted coronal MRI showing solid-cystic lesion reaching the interhemispheric fissura in the right frontal region. **c-**T1-weighted contrasted axial MRI showing the enhanced tumor compressing the right frontal horn. **d-**T1-weighted contrasted sagittal MRI showing solid-cystic lesion in the frontal area.

Computed tomography (CT) of the brain revealed a 5x4x3 cm, partially hypo and partially iso-hyperdense lesion which was interpreted as solid and cystic components with contrast enhancement and right frontal horn compression. Magnetic Resonance Imaging (MRI) confirmed the CT appearance (Fig.1a-1d). The patient underwent surgery with the suspected diagnoses of high grade glial tumor, abscess or metastasis. A microsurgical gross total excision was performed.

Macroscopically the specimen was composed of multiple fragments of tissue of 30 cc volume. They were soft and greyish white to brown colored. Histologically it was a tumor partially composed of glial cells with hyperchromatic and pleomorphic nuclei showing hypercellularity with accompanying gemistocytes and atypical neuronal cells (Fig.2a). The other component was a tumor composed of closely packed cells with hyperchromatic, oval and carrot-shaped nuclei and indistinct cytoplasm. Cells formed rosettes in these areas (Fig.2b). The stroma in both components of the tumor was fibrillary. Wide necrotic areas were also detected. Both components were mitotically active.

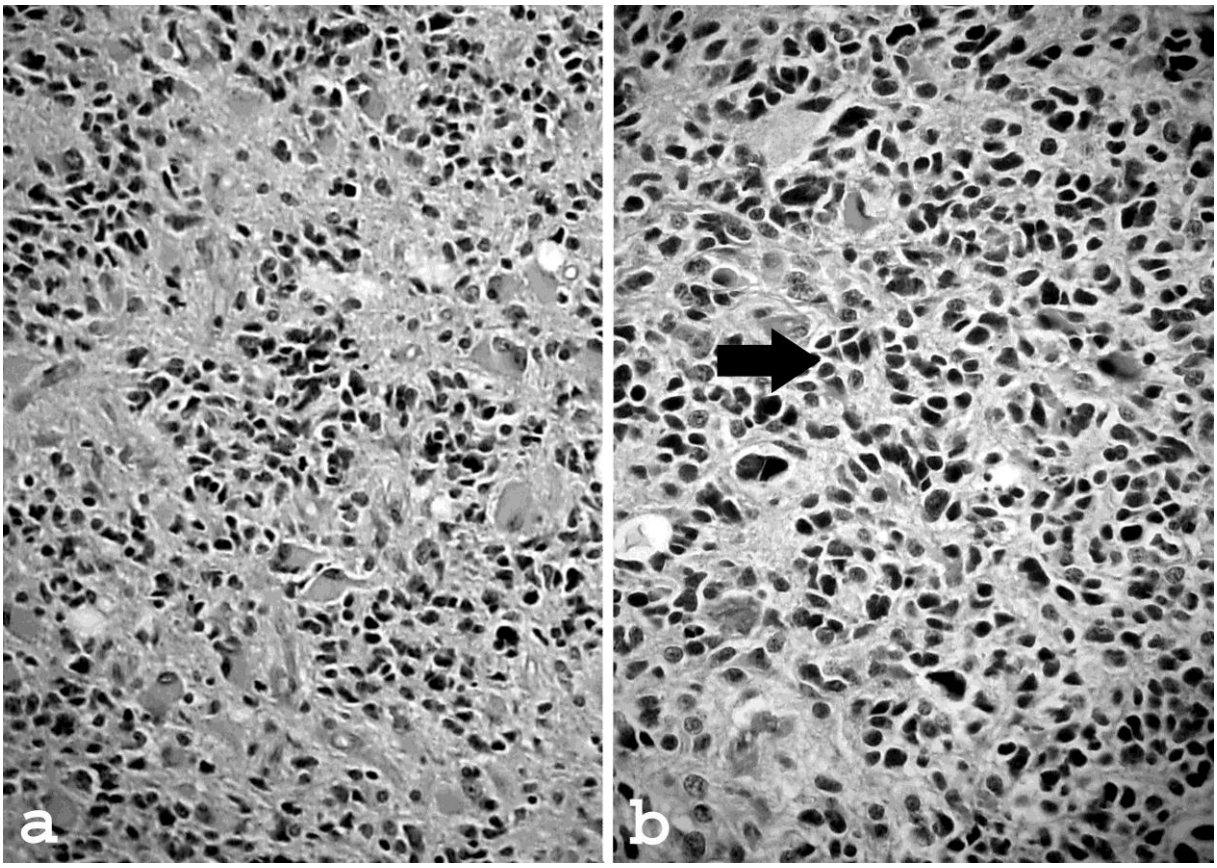

Fig. 2: a-Pleomorphic glial cells with hyperchromatic nuclei and atypical neuronal cells (H.E. x 100). **b**-The rosette formations (arrow) made by cells with hyperchromatic, ovoid-carrot shaped nuclei and indistinct cytoplasm on the fibrillary ground (H.E. x 200).

Immunohistochemically the anaplastic ganglioglial component of the tumor was positive for glial fibrillary acidic protein (GFAP) (Fig.3a), S-100 protein, and vimentin. The atypical neuronal cells were positive for chromogranin A (Fig.3b) and neurofilament (Fig.3c). The second component of the tumor was negative for all these markers, but positive for neuron specific enolase (NSE).

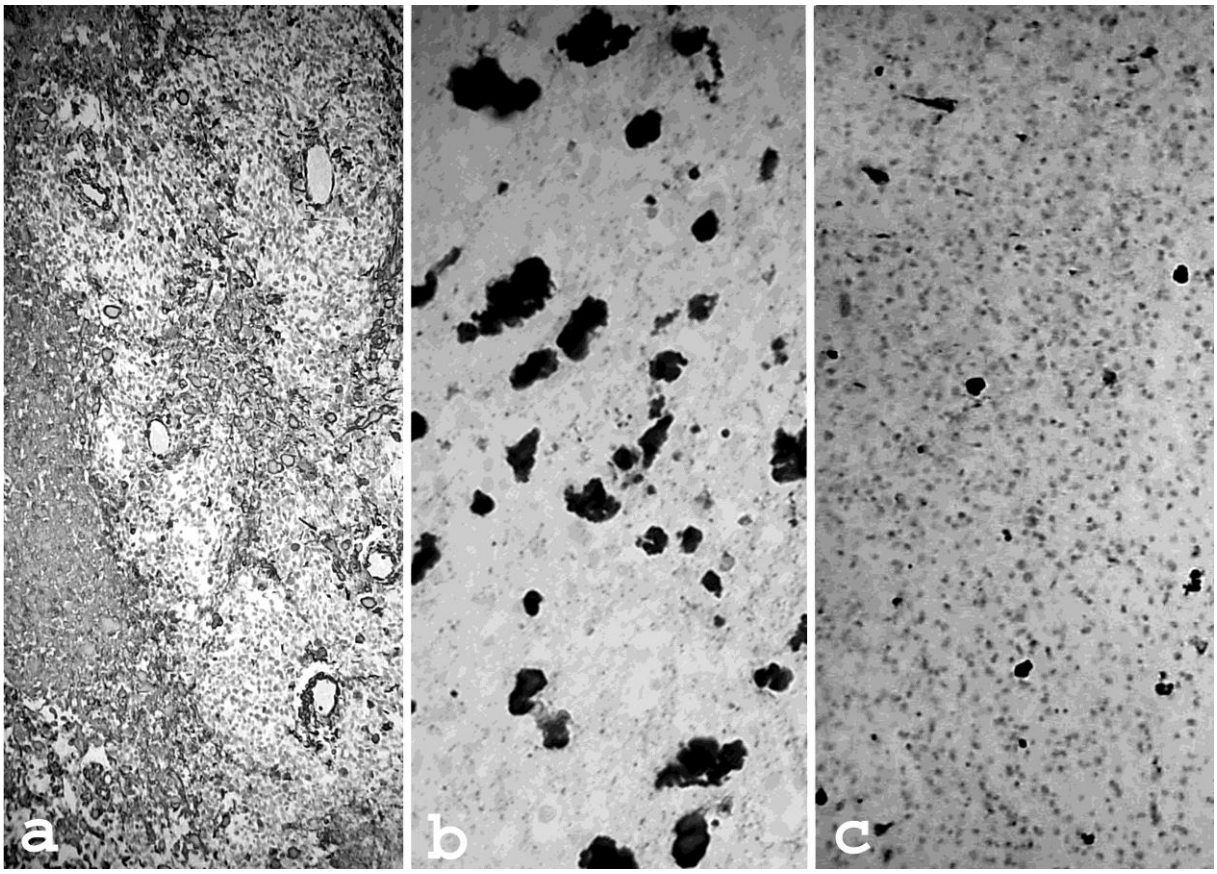

Fig.3: a-Anaplastic ganglioglial component showing GFAP positivity. Note that PNET component is negative for GFAP (GFAP x 100). **b**-Chromogranin positivity in atypical neuronal cells (Chromogranin A x 200). **c**- Atypical neuronal cells showing neurofilament positivity (Neurofilament x 150).

In the light of all these findings 'a composite tumor including anaplastic ganglioglioma and S-PNET' was diagnosed. Radiotherapy was instituted and control CT of the brain six months after the surgery showed a lesion with heterogenous contrast enhancement in the right frontal region which suggested a recurrent tumor. Cranial T1-weighted axial and sagittal contrasted MRI revealed a lesion with heterogenous conrast enhancement disclosing dural invasion and mass effect. The patient was subsequently re-operated on and gross total mass excision was performed. Macroscopically the specimen was composed of soft, greyish white to brown colored tissue fragments with 23 cc volume. Histologically a tumor composed of pleomorphic cells showing distinct microvascular proliferation and necrosis was detected (Fig.4). The

tumor was positive for GFAP immunohistochemically. The final diagnosis was glioblastoma multiforme. The patient was discharged without any complication and chemotherapy was proposed. The patient denied chemotherapeutic regimen. His follow-up examination twenty-two months after the first operation was within normal limits. The patient referred to the emergency department two months later with a recurrent intracranial mass. Further therapy was rejected and the patient expired within a month.

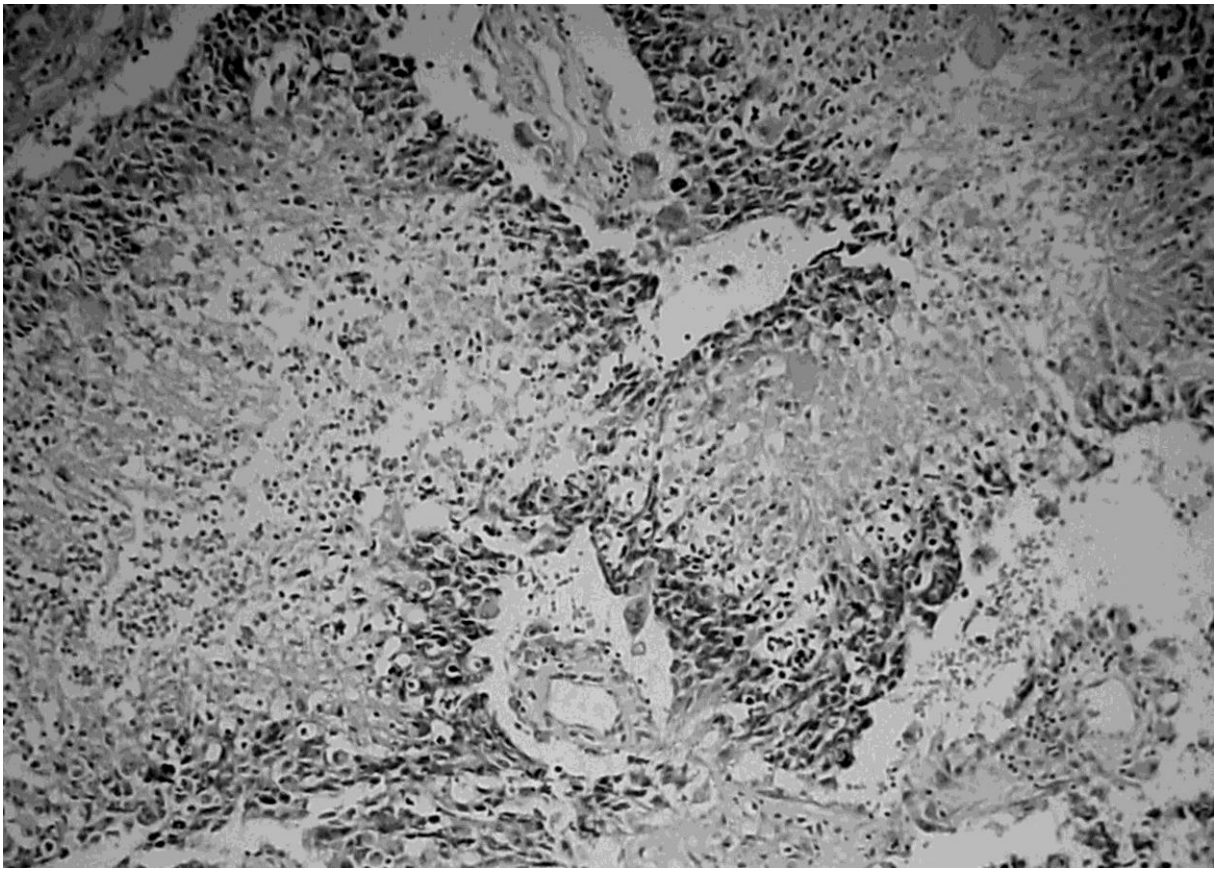

Fig. 4: Atypical glial cells and wide necrotic areas (H.E. x 40).

Discussion

S-PNET is an uncommon embryonal tumor of cerebral hemispheres or suprasellar region composed of undifferentiated or poorly differentiated neuroepithelial cells which have the capacity for or display divergent differentiation along neuronal, astrocytic, ependymal, muscular or melanocytic lines, as defined by the World Health Organization (WHO). It corresponds histologically to WHO grade IV [3]. The term PNET which was first described by Hart and Earle in 1973 has been widely used for a group of morphologically similar tumors in both the central and peripheral nervous systems [4,5]. S-PNETs primarily occur in children [4,6,7], ranging between the ages of 4 weeks to 10 years, with a mean of 5.5 years

[3]. They are most commonly located in the hemispheres [4]. They are highly malignant tumors with a rapid course to death and their survivals range between 7-24 months [4]. Light microscopic features of S-PNETs are basically similar to cerebellar medulloblastoma [1,3,6,7]. It is stated that tumors identical in appearance to medulloblastoma might arise in retina, pineal gland, cerebrum, or spinal cord, and their biologic behaviour is similar [1,8]. So they are indistinguishable by histology alone if their location is unknown, and named under the name of PNET. Rorke et al commented that a simple description of the recognizable types within these tumors (e.g. PNET *with astrocytes*) would be more acceptable than an interpretive diagnosis such as "PNET *with astrocytic differentiation*" [1].

Evidence of divergent differentiation in cells is most reliably identified by use of various antibodies such as GFAP, neurofilament protein and desmin [3]. The histogenesis of PNETs as a group is still controversial [3,6,7], and the only issue upon which consensus has been achieved is that these embryonal tumors arise from primitive neuroepithelial cells regardless of their location [3].

Pearl et al reported a supratentorial glioblastoma that occurred 13 years after radiation therapy for a cerebellar medulloblastoma. They commented that the diverse ultrastructural features of the glioblastoma might reflect the multipotentiality of the cells in medulloblastoma, or alternatively, the glioblastoma represented a radiation-induced neoplasm after therapy for a medulloblastoma [9]. Though Bhangui et al reported a synchronous occurrence of optic nerve glioma, a pilocytic astrocytoma, a ganglioglioma and a medulloblastoma in a 12-year-old girl, the tumors in their case were located in different sites of the brain. So, they were multiple primary tumors, but not a composite tumor [10].

To our knowledge, the presented case is the first composite tumor including anaplastic ganglioglioma and S-PNET recurring as glioblastoma in the literature. Ganglioglial differentiation in a medulloblastoma was reported by Kudo et al, but the ganglioglial component was benign and its localization was cerebellum in their case [2]. It is also a rare occurrence that the patient presented here is in his fifth decade for PNETs most commonly occur in children [3,6,7].

The prognosis is poorer in infants with PNET who are less than two years old at the time of diagnosis. While 5-year survival rate for the patients with S-PNETs is 34%, it is reported to be as high as 85% for the ones with a PNET arising in the posterior fossa [3]. Neither the GFAP-positivity nor the neuronal differentiation has been shown to correlate with prognosis or biological behaviour in medulloblastomas. However, Provias and Becker commented that further progression of neuronal differentiation within the tumor might reduce the malignant

potential [11]. On the other hand, the 4-year survival rates reported by Packer et al for PNETs showing no evidence of cellular differentiation and PNETs with differentiation were reported to be 70% and 32%, respectively [12].

The exact mechanism of the extensive neuronal and glial maturation of medulloblastoma cells is unclear, but the repetitive surgical interventions, radiation and chemotherapy might have had certain cytostatic effects on rapidly dividing medulloblastoma cells, giving them a chance to mature into postmitotic cells with potential for neuronal and glial differentiation [2].

In the light of all this scarce knowledge, it can be concluded that the glioblastoma presented in this report might be either a radiotherapy induced tumor or it may be derived from the S-PNET or anaplastic ganglioglioma. Whatever the case, the existence of this dual pathology deserves further interest.

References

1. Rorke LB, Gilles FH, Davis RL, Becker LE. Revision of the World Health Organization Classification of Brain Tumors for Childhood Brain Tumors. Cancer 1985; 56:1869-86.
2. Kudo M, Shimizu M, Akutsu Y, Imaya H, Chen MN, Miura M. Ganglioglial differentiation in medulloblastoma. Acta Pathol Jpn 1990; 40(1):50-6.
3. Rorke LB, Hart MN, McLendon RE. Supratentorial primitive neuroectodermal tumour (PNET). In: Kleihues P, Cavenee WK (eds). World Health Organization Classification of Tumours, Pathology & Genetics, Tumours of the Nervous System. Lyon: IARC Press; 2000: 141-4.
4. Becker LE, Hinton D. Primitive neuroectodermal tumors of the central nervous system. Hum Pathol 1983; 14: 538-50.
5. Jay V, Pienkowska M, Becker L, Zielenska M. Primitive neuroectodermal tumors of the cerebrum and cerebellum: abscence of t(11;22) translocation by RT-PCR analysis. Mod Pathol 1995; 8(5): 488-91.
6. Gyure KA, Prayson RA, Estes ML. Extracerebellar primitive neuroectodermal tumors: A clinicopathologic study with bcl-2 and CD99 immunohistochemistry. Ann Diagn Pathol 1999; 3(5):276-80.
7. Holl T, Kleihues P, Yasargil MG, Wiestler OD. Cerebellar medullomyoblastoma with advanced neuronal differentiation and hamartomatous component; Acta Neuropathol (Berl) 1991;82(5):408-13.
8. Greenberg MS. Handbook of Neurosurgery. 5th ed. Ontario, Canada: Webcome Limited; 2001: 451.
9. Pearl GS, Mirra SS, Miles ML. Glioblastoma multiforme occurring 13 years after treatment of a medulloblastoma. Neurosurgery 1980; 6(5):546-51.
10. Bhangui GR, Roy S, Tandon PN. Multiple primary tumors of the brain including a medulloblastoma in the cerebellum. Cancer 1977; 39(1):293-7.
11. Provias JP, Becker LE. Cellular and Molecular Pathology of Medulloblastoma. J Neurooncol 1996; 29:35-43.

12. Packer RJ, Sutton LN, Rorke LB, Littman PA, Sposto R, Rosenstock JG, Bruce DA, Schut L. Prognostic importance of cellular differentiation in medulloblastoma of childhood. J Neurosurg 1984; 61(2):296-301.