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Case Report

Secondary oligodendroglioma after postoperative irradiation for medulloblastoma: a case report and review of the literature

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Abstract: Medulloblastoma, a malignant, invasive embryonal tumor of the cerebellum, occurs most often in children. It has high metastatic potential and is usually treated by aggressive multimodal therapy, including surgery, chemotherapy and craniospinal irradiation. Multiple secondary tumors have been reported following craniospinal irradiation. It is rare with the occurrence of oligodendroglioma after irradiation. In this report, we described a patient with secondary oligodendroglioma after postoperative craniospinal irradiation for medulloblastoma.

Keywords: Medulloblastoma, oligodendroglioma, radiation-induced glioma

Introduction

Medulloblastoma, an invasive embryonal tumor of the cerebellum, is the most common malignant brain tumor of childhood. It has an inherent tendency to metastasize via cerebrospinal fluid (CSF) pathway. Approximately 30% of patients are found with metastatic disease at diagnosis [1]. Medulloblastoma is now treated with aggressive multimodal therapy, including surgical resection, radiotherapy and chemotherapy [2]. However, significant treatment-related sequelae exist after craniospinal irradiation, including increased risks of secondary malignancies, loss of cognitive function and endocrine abnormalities. Multiple radiation-induced tumors in the head and neck region have been reported, including meningiomas, glioblastomas, gliosarcomas, astrocytomas and sarcomas [3]. It is rare with the occurrence of oligodendroglioma after irradiation. In this report, we present a patient with secondary oligodendroglioma after postoperative craniospinal irradiation for medulloblastoma.

Case report

The patient was a 32 year-old man who had cerebellar medulloblastoma at the age of 10. He received surgery, followed by radiotherapy (with a total dose of 5600 cGy) at that time. 18 years later, he had metastatic medulloblastoma in the right frontal area of cerebrum. He received tumor resection again followed by concurrent chemoradiotherapy (with a total dose of 5040 cGy). The patient underwent regular follow-up at the Department of Neurosurgery. 5 years later, Magnetic resonance imaging (MRI) of brain revealed a heterogeneous enhancing mass measuring 5.0 cm in diameter with perifocal edema in the right frontal lobe, suggestive of tumor recurrence (**Figure 1**). The location of this tumor was the same with the previous metastatic medulloblastoma. He underwent total resection of this tumor, and the specimen was sent for pathological examination.

Materials and methods

The specimen was fixed in 10% formalin solution and embedded in the paraffin block. Sections were cut and stained with hematoxylin and eosin for light microscopy. Immunohistochemical (IHC) stains were performed by using standard reagents and techniques on an BOND-MAX Automated Staining System (Leica Microsystems). Briefly, Sections were deparaffinized, hydrated, and subjected to heat-induced

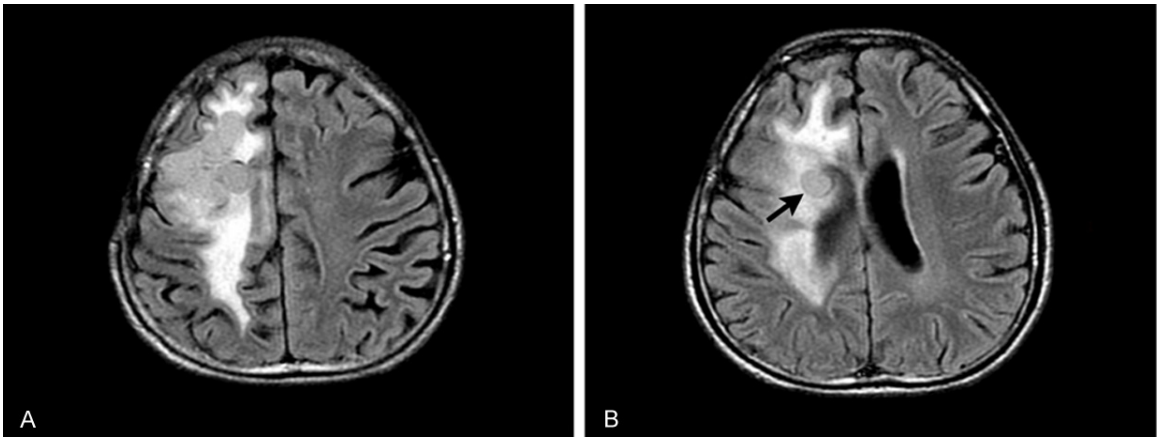

Figure 1. Magnetic resonance imaging (MRI) of brain revealed a heterogeneous enhancing mass (A) measuring 5.0 cm in diameter with perifocal edema (B, arrow) in the right frontal lobe.

antigen retrieval with Bond epitope retrieval (EDTA based pH 9.0 solution, Leica Microsystems). The primary antibodies, including synaptophysin (Clone 27G12, Leica, 1:200), S100 (Clone S1/61/69, Leica, 1:500), GFAP (Clone GA5, Leica, 1:300) and Ki-67 (Clone GM010, Genemed, 1:1000) were applied for 30 minutes at room temperature followed by application of Biotin-free bond polymer refine detection (Leica Microsystems). Positive and negative controls were done according to manufacture's instruction. It was defined as positive when at least 20% of the malignant cells in the slides revealed positive staining.

Results

Histologic examination of the metastatic lesion in the right frontal lobe revealed multiple fragments of tumor tissue composed of densely packed cells with oval or carrot-shaped hyperchromatic nuclei surrounded by scanty cytoplasm (**Figure 2A** and **2B**). The tumor cells were positive for synaptophysin, compatible with a medulloblastoma. 5 years later, in the same location, there was a recurrent tumor. It was composed of infiltrative uniform neoplastic cells with round nuclei and perinuclear halos, separated by dense network of branching capillaries (**Figure 2C-E**). In the immunohistochemical study, these cells were positive for S100 and GFAP. There was no expression of synaptophysin. The MIB-1/Ki-67 labeling index was about 10% (**Figure 2F**).

Discussion

Secondary malignancies are an uncommon, but critical post-irradiation complication in long-term survivors of medulloblastoma. Although irradiation destroys cancer cells, it can induce mutations, most often the deletion of DNA segments in surrounding normal cells. Passage through subsequent generations of genetic abnormalities is a key element in tumorigenesis and plays an important role in the development of chemo- or radio-resistance. Ionizing radiation induces genomic instability, which is transmitted over many generations after irradiation through the progeny of surviving cells. Induced genomic instability can be caused by the following delayed effects, including delayed reproductive death or lethal mutation, chromosomal instability, and mutagenesis [4]. No clinical, radiological or pathological characteristics are capable of differentiating between radiation-induced tumors and so called "spontaneous" ones.

Meningiomas, gliomas, and sarcomas are the most common secondary tumors that arise after cranial irradiation. Among secondary gliomas, glioblastomas and anaplastic astrocytomas have the highest incidence rate [3, 5]. It is rare in the occurrence of oligodendroglioma after irradiation for medulloblastoma. In 1987, Huang et al. reported a 38 year old man developing an oligodendroglioma of the left medial temporal lobe and parasellar region 12 years after radiotherapy with 6600 cGy for pituitary adenoma [6]. In 2008, Doskaliyev et al. presented a 48-year-old man who developed an anaplastic oligodendroglioma 38 years after receiving 5000 cGy of cranial irradiation to a pineal tumor [7]. In this report, they also reviewed another seven patients with second-

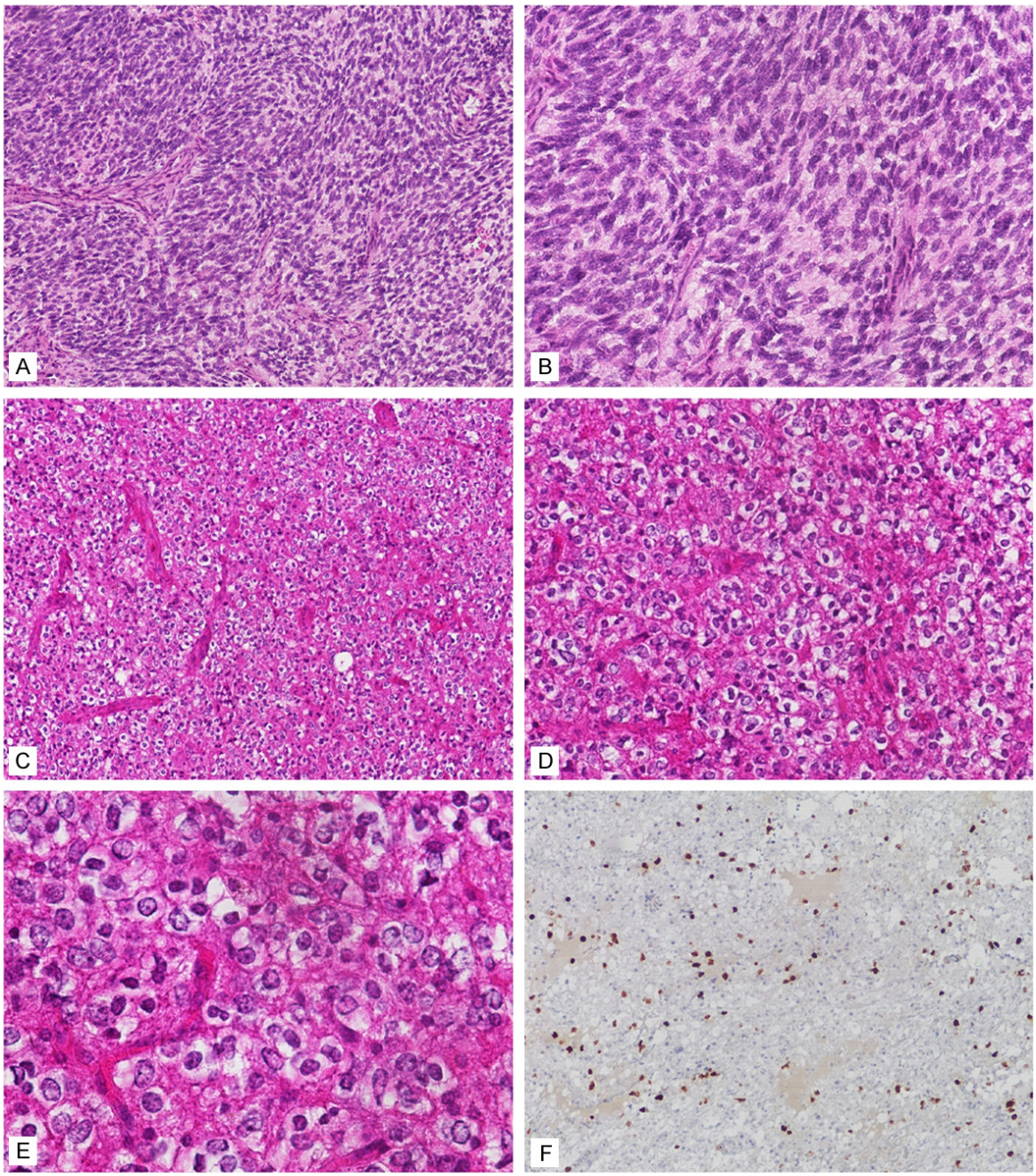

Figure 2. On hematoxylin and eosin-stained sections, there were densely packed cells with oval or carrot-shaped hyperchromatic nuclei surrounded by scanty lightly eosinophilic cytoplasm, compatible with a medulloblastoma (A and B: ×100 and ×200, respectively). In the recurrent tumor occurred 5 years later, there was increased cellularity of infiltrating uniform cells separated by chicken-wire vasculature (C: ×100). The tumor cells had uniform round nuclei, perinuclear halos and well-defined cell membrane (D and E: ×200 and ×400, respectively). The MIB-1/Ki-67 labeling index was about 10% (F: ×100).

ary oligodendroglial tumors after cranial irradiation. Six of them were associated with high-grade gliomas, including combined glioblastoma/oligodendroglioma, anaplastic oligodendroglioma and anaplastic oligoastrocytoma [6, 8-12]. Only one case had low-grade oligoastrocytoma [13]. Pure secondary oligodendroglioma is extremely rare after cranial irradiation. Doskaliyev et al. also proposed that secondary oligodendroglial tumors tend to develop after low-dose irradiation or in the immediate vicinity of a field exposed to high-dose radiation treatment. However, this phenomenon not occurred in our case.

It is important to differentiate local tumor recurrence from radiation-induced brain changes. Radiation typically causes necrosis accompanied by severe vascular changes in chronic stage. Endothelial cells may become plump, swollen and sometimes vacuolated. The blood vessels, particularly small arteries and arterioles reveal fibrinoid necrosis of the vessel wall with perivasculitis, accumulation of collagen fibers and various degrees of thrombosis. The common appearance of brain tissue after radiation is vacuolated with myelin breakdown. Eventually various degrees of reactive astrogliosis follow that may culminate in cavitation and dense fibrillary gliosis. It is very important to keep in mind that reactive glial elements may become very pleomorphic with marked anisonucleosis and hyperchromasia [14]. It is sometimes hard to differentiate bizarre reactive gliosis from metastatic tumors or high-grade astrocytic tumors without the aids of immunohistochemical study. In our case, the discrimination between recurrent tumors and reactive gliosis was not difficult because of distinct morphologic features in oligodendroglioma.

In summary, we described a patient with a secondary oligodendroglioma that developed after cranial irradiation. Among the secondary gliomas after cranial irradiation, most of them are high-grade tumors. More studies are needed for further clarifying the role of irradiation in the carcinogenesis in low-grade oligodendroglial tumors. It is also important to differentiate tumor recurrence from radiation-induced brain changes.

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Disclosure of conflict of interest

None.

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