

# Primitive neuroectodermal tumor after radiation therapy for craniopharyngioma

## Case report

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The authors report a case of primitive neuroectodermal tumor induced by radiation therapy of craniopharyngioma. This African-American male patient originally presented with craniopharyngioma, for which he underwent resection and whole-brain radiation therapy. Eight years later, at the age of 20 years, he returned with a left facial droop and left hemiparesis. A right basal ganglia mass was identified and resected. Histopathological examination identified the lesion as primitive neuroectodermal tumor.

Although radiation therapy has shown to be beneficial in decreasing the recurrence rate in subtotally resected craniopharyngioma, the risks of radiation treatment should be clearly communicated to the patients, their families, and neurosurgeons before starting such treatment. This report expands the spectrum of reported radiation-induced neoplasms in the CNS. (DOI: 10.3171/2010.11.FOCUS10224)

**KEY WORDS** • craniopharyngioma • radiation-induced neoplasm •  
whole-brain radiation therapy • primitive neuroectodermal tumor

**W**HOLE-brain radiation therapy is part of the treatment for craniopharyngioma. One of the rare side effects of radiation therapy is the evolution of tumors, including malignancies such as sarcomas, gliomas, and benign neoplasms such as meningiomas and schwannomas. Few cases of postradiotherapy PNET have been described in the literature. The majority of these rare cases occurred in patients who undergone WBRT for the treatment of acute leukemia, lymphoma, or astrocytoma. This paper is the first description of the development of a postradiotherapy PNET after resection of craniopharyngioma.

### Case Report

*History and Presentation.* This young African-American man was initially treated in our institution in 1994 (at the age of 12 years) for craniopharyngioma (Fig. 1). At that time, he presented with left hemiparesis and a

history of similar, transient episodes during the previous few months with deterioration during the last week. The patient denied having headache, nausea, vomiting, ataxia, or seizures. He underwent resection of the mass and was treated with 6 weeks of WBRT. During that time, he suffered from panhypopituitarism and blindness.

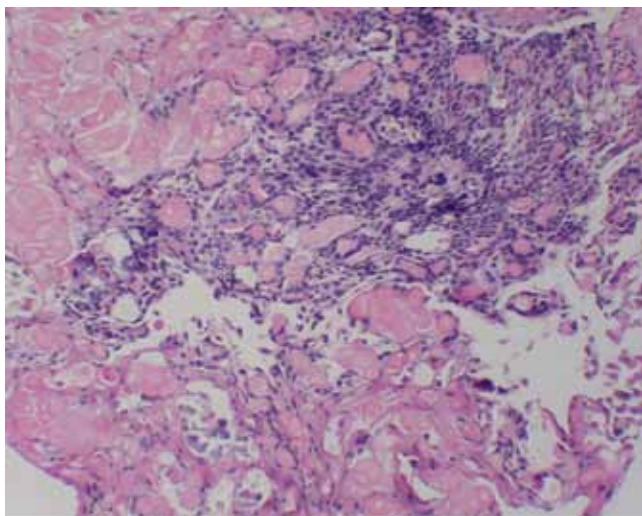
He returned in 2002, at the age of 20 years, with new-onset left facial droop and left hemiparesis.

*Neuroimaging.* An MR imaging study of the brain demonstrated a 2.5-cm enhancing lesion that was hypointense on T1-weighted images and hyperintense on T2-weighted images. The lesion involved the right basal ganglia, the genu of the internal capsule, and the posterior internal capsule (Fig. 2 left). The mass was not noted to involve the sellar region (Fig. 2 right). The tumor was noted to exert mass effect on the right lateral ventricle.

*Operation and Postoperative Course.* A brown-grayish necrotic tumor was subtotally resected via a right frontotemporo-pterional craniotomy.

The patient recovered from surgery with some improvement of motor strength. Histopathological examination of the tumor demonstrated a highly cellular neoplasm

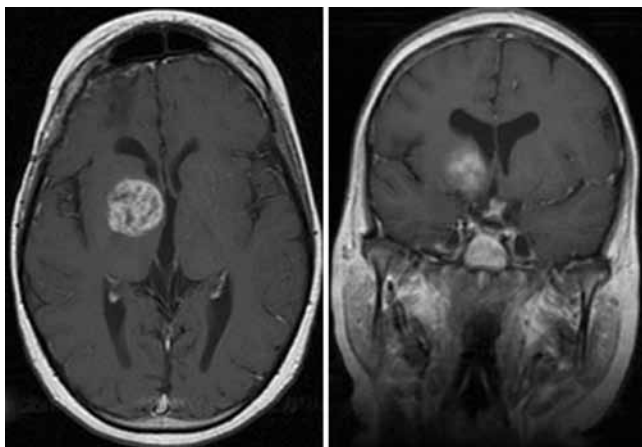
*Abbreviations used in this paper:* GFAP = glial fibrillary acidic protein; PNET = primitive neuroectodermal tumor; WBRT = whole-brain radiation therapy.



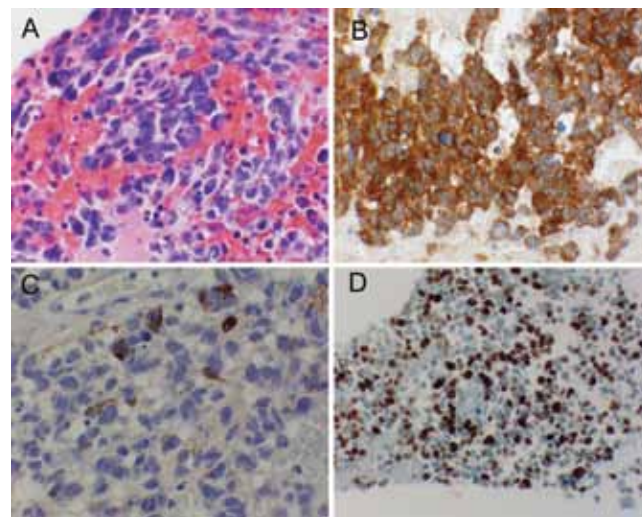
**FIG. 1.** Photomicrograph of an H & E-stained section of the initial pathological specimen demonstrating craniopharyngioma. Original magnification  $\times 400$ .

composed of cells with round-to-oval nuclei and scanty cytoplasm (Fig. 3A). Tumor cells showed widespread immunoreactivity for vimentin, neuron-specific enolase, and synaptophysin (Fig. 3B), and focal immunoreactivity for GFAP (Fig. 3C) and neurofilament protein. The results of immunohistochemical evaluation for keratin markers (AE1/AE3, CK7, CK20), carcinoembryonic antigen, Melan-A, epithelial membrane antigen, desmin, leukocyte common antigen, and smooth muscle-specific actin were negative. Mucicarmine staining was also negative. The Ki 67 proliferation marker stained over 30% of the tumor cells (Fig. 3D). The final diagnosis was a WHO Grade IV PNET. Postoperative imaging showed no residual mass (Fig. 4A).

Two months later, follow-up MR imaging of the brain demonstrated that the mass in the right basal ganglia was now 3.5 cm (Fig. 4B). Another follow-up MR imaging study 3 weeks later revealed that the mass was larger still, at  $5.2 \times 4.4 \times 5.8$  cm (Fig. 4C).



**FIG. 2.** Preoperative contrast-enhanced T1-weighted MR images. **Left:** Axial image showing a right enhancing lesion measuring 2.5 cm in diameter. **Right:** Coronal view demonstrating the lack of sellar involvement.

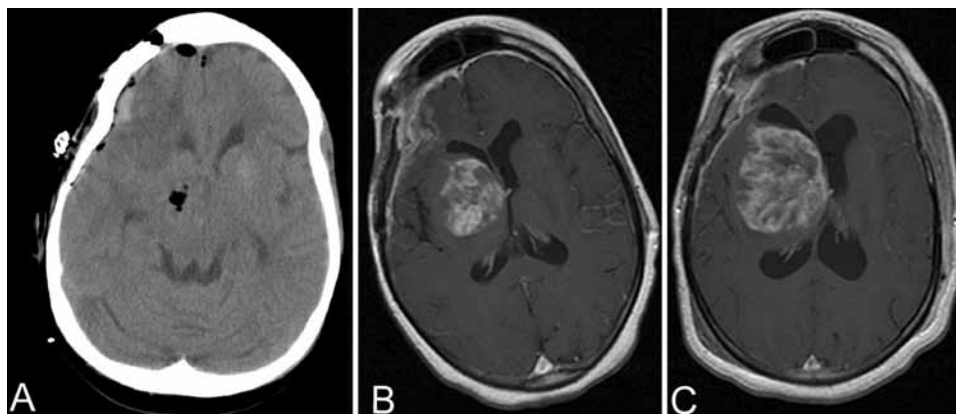


**FIG. 3.** Photomicrographs of sections of the second specimen (PNET) obtained 8 years after radiotherapy. **A:** An H & E-stained section demonstrating a highly cellular neoplasm composed of cells featuring round-to-oval nuclei and scanty cytoplasm, with significant pleomorphism. **B:** Synaptophysin immunoreactive staining of the PNET specimen demonstrating widespread immunoreactivity of tumor cells. **C:** Staining for GFAP showing focal immunoreactivity. **D:** Results of staining with Ki 67 proliferation marker showing staining in over 30% of tumor cells in the PNET specimen. Original magnifications  $\times 400$  (A–C) and  $\times 200$  (D).

The patient's records are incomplete, but the reports indicate that he received a full regimen of radiotherapy in 1994 for his craniopharyngioma; thus he was no longer a candidate for radiation therapy. A chemotherapy regimen consisting of vincristine, lomustine, and prednisone treatment was initiated. The patient was subsequently lost to follow-up.

## Discussion

Primitive neuroectodermal tumor is a rare type of tumor in the adult population, and cases of radiation-induced PNET are especially rare.<sup>7,11</sup> Possible risk factors for these tumors include young age at time of irradiation, genetic predisposition to malignancies, and genetic polymorphism in certain metabolic enzymes.<sup>12</sup> The case presented here meets all the requirements for a radiation-induced neoplasm as described by Cahan et al. in 1948.<sup>3,5</sup> These criteria are: 1) tumor originating from areas that were previously irradiated; 2) elapsed time between radiation treatment and the appearance of the radiation-induced lesion; 3) no other pathological conditions that will predispose to tumor development; and 4) the histological characteristics must be different from those of the primary lesion that prompted the radiation treatment.<sup>3,5</sup> In our patient, the PNET was found in the field of irradiation almost 9 years after the initial treatment, and showed histopathological characteristics that were markedly different from those of the initial tumor. Eleven of the 12 reports of radiation-induced PNET involved pediatric patients who had undergone combination treatment with methotrexate and whole-neuraxis irradiation. A supratentorial PNET was reported 12 years after irradiation for a Grade II



**FIG. 4.** Postoperative neuroimages. **A:** Noncontrast head CT obtained immediately after resection of the PNET, demonstrating no residual tumor. **B:** Axial contrast-enhanced T1-weighted MR image obtained 1 month postoperatively demonstrating a recurrent lesion measuring 3.5 cm in diameter. **C:** Axial contrast-enhanced T1-weighted MR image obtained 2 months postoperatively showing interval enlargement of the lesion, which is 5.8 cm in diameter in this image.

astrocytoma.<sup>4</sup> Multiple cases of postradiotherapy PNET were reported following initial diagnoses of pilocystic astrocytoma, ependymoma, and low-grade astrocytoma.<sup>5,6,9</sup> This is the first reported case of PNET after radiation therapy for the treatment of craniopharyngioma.

In the past, an association was found between mutation in the *K-ras* protooncogene and the development of PNET, implicating the combination of methotrexate and radiation therapy.<sup>1,2,6</sup> The current case report indicates that acute lymphocytic leukemia, lymphoma, and the combination of methotrexate and radiation therapy are not necessary for PNET development, but rather radiation alone can induce PNET. Even though radiotherapy is clearly beneficial in decreasing the recurrence rate in cases of subtotally resected craniopharyngiomas, the risks should be clearly articulated to the families and neurosurgeons before starting such treatment.<sup>10,13</sup> In the past, WBRT and proton beam therapy were used for the treatment of craniopharyngiomas.<sup>8</sup> In the modern era, single- or multifraction stereotactic radiosurgery would probably be employed.<sup>14</sup>

**Disclosure**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Chan. Drafting the article: Chan, Herrera, Wallace. Critically revising the article: Neckrysh, Valyi-Nagy, Charbel. Reviewed final version of the manuscript and approved it for submission: Valyi-Nagy, Charbel.

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