BACKGROUND: Radiation-induced gliomas (RIG) can occur in 3% of patients receiving cranial radiation. Often, these gliomas are high-grade, treatment refractory, and share common molecular profiles like PDGFRA amplification, regardless of their previous malignant origin. Despite similar genetic alterations, the clinical course of these tumors is varied and not well-studied. Herein, we describe three patients with a PDGFRA-amplified RIG with a particular focus on their contrasting disease course.

CASE DESCRIPTION:
Our first patient is a now-deceased male diagnosed with medulloblastoma at 5 years of age, treated with surgical resection and craniospinal radiation followed by chemotherapy per COG ACNS0332. Ten years later, he was diagnosed with diffuse pediatric type high-grade-glioma (HGG) in the pons with PDGFRA, KIT, MTAP amplification, and CDKN2A/B loss. His condition deteriorated quickly, and he succumbed to his disease in 8 weeks after family decided against further therapies. Our second patient is a now 20-year-old female, initially diagnosed with a craniopharyngioma at 6 years of age and treated with surgical resection and adjuvant radiation therapy. Eleven years later, she developed a diffuse pediatric type HGG in the pons with PDGFRA, MDM2, and MYCN amplification. She was treated with radiation therapy and has had stable disease on serial imaging for 3 years. Our third patient is a now-deceased male diagnosed with a right temporal melanotic neuroectodermal tumor at 5 years of age, treated with surgical resection and craniospinal radiation followed by chemotherapy per POG99701. Fifteen years later, he developed a diffuse pediatric-type HGG in the cerebellum/pons with PDGRFA amplification. He was treated with proton radiation and concurrent oral Temozolomide per COG ACNS0423.
His disease progressed on treatment, and he died prior to initiation of a PDGFRA kinase inhibitor (avapritinib), CONCLUSIONS: Further investigation into the underlying factors that drive the differing disease course in patients with RIG is needed.