The classification of primary brain tumors poses many challenges. Glioblastoma multiforme (GBM), the most common primary adult primary brain tumor, is composed of cells of astrocytic origin exclusively and is characterized by infiltration of the brain parenchyma which makes surgical cure impossible. Though local radiation and chemotherapy are routinely employed to treat these aggressive tumors, they invariably progress with survival on the order of two years or less. Supratentorial primitive neuroectodermal tumors (sPNET) are histologically similar to medulloblastoma, composed of poorly differentiated neuroepithelial cells, and are typically found in children. Their response to chemotherapy is variable, but often better than GBM but poorer than medulloblastoma and CSF dissemination is common. Rarely, tumors with features of both malignant glioma and PNET occur which may arise from expansion of stem cell populations located within GBM. These mixed tumors pose not only a diagnostic challenge, but also a therapeutic challenge as GBM is typically treated with alkylating agents, such as Temozolomide, while PNETs are known to respond to platinum-based chemotherapy. We report a series of 5 patients with this rare mixed tumor. All patients underwent craniotomy and their clinical courses varied. CSF dissemination was seen in one patient. Their histologic features, radiographic presentation, and response to chemotherapy and to the Novocure-Tumor-Treating Fields is discussed.