

# Intravascular Proliferation: A Case Report of Intravascular Large B Cell Lymphoma Arising within a Glioblastoma, IDH Wild Type

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## Abstract

A synchronous multiple primary tumors is a second tumor that occurs within two months of identification of the first primary cancer. Collision tumors is the definition given to two synchronous tumors in the same organ whereby distinct borders between the two primary tumors are maintained. The occurrence of collision tumors is a very rare phenomenon. Here, we describe a case of an 82-year-old woman who presented with approximately one month's duration of neurologic deficits. Magnetic resonance imaging (MRI) revealed a left parietal lobe lesion which was radiographically concerning for a high-grade glioma. Following surgical resection microscopic examination of the mass revealed high-grade glioma with synchronous malignant lymphoma involving tumor vasculature, consistent with a collision of glioblastoma, IDH-wildtype, and intravascular large B cell lymphoma. To our knowledge, this represents the first reported case of a collision tumor involving these two entities.

## Keywords

B cell lymphoma, Glioblastoma, Intravascular proliferation

## Introduction

A synchronous multiple primary tumors is a second tumor that occurs within two months of the first primary cancer identification [1]. Collision tumors are defined as the presence of two synchronous tumors in the same organ, without the presence of non-neoplastic tissue between the primary tumors [2]; distinct borders between the two primary tumors are maintained [3]. Collision tumors are very rare. A review of the literature [2] found that the most common non-Hodgkin lymphoma observed in synchronous tumors was diffuse large B cell lymphoma, most commonly with adenocarcinoma (when compared to other carcinomas) [2]. While meningiomas are the most common primary brain tumors to be identified in collision tumors involving the brain, meningiomas coexisting with glioblastomas have been rarely reported [4-6]. Here, we present a case of a collision tumor involving high-grade glioblastoma and concurrent intravascular large B cell lymphoma (IVLBCL).

## Case Report

An 82-year-old woman presented with word-finding and comprehension deficits of approximately one-month's duration. Review of systems was negative for fever, chills, weight loss, or other systemic symptoms. Her medical history was significant for melanoma, removed from her forearm the year prior. The MRI of the brain revealed a left posterior 4.4 x 4.2 x 4.1 cm temporal mass with nodular and peripheral enhancement and central non-enhancement (Figure 1).

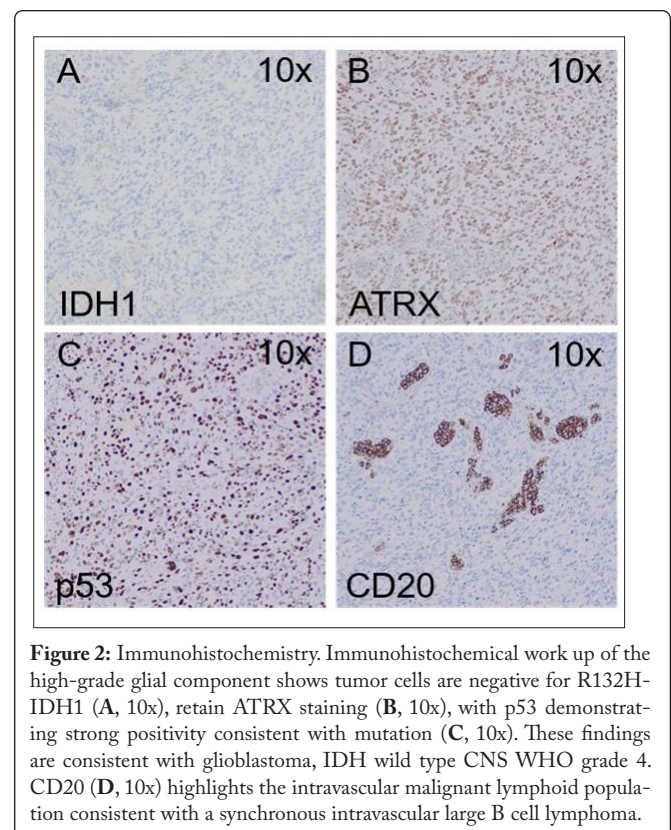
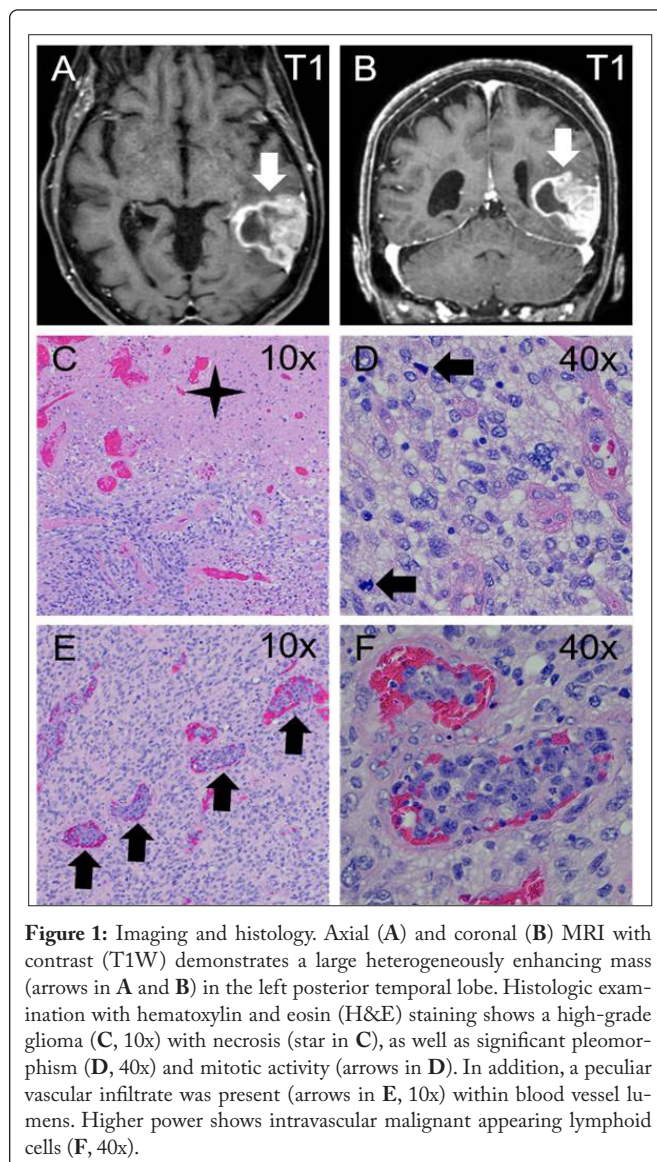
MRI also demonstrated a secondary T2/FLAIR hyperintense lesion in the left parietal lobe with cortical infiltration, which was favored to represent a high-grade glioma. Further work up with computed tomography of the chest, abdomen, and pelvis and positron emission tomography scan of the body revealed no primary malignancy or metastatic disease. She underwent surgical resection of the mass. Microscopic examination revealed a high-grade glioma with microvascular proliferation and necrosis, consistent with CNS WHO grade 4. In addition, a malignant appearing population of cells was observed focally within intra-tumoral blood vessel lumens.

Immunohistochemical stains were used to thoroughly characterize the lesion. The R132H-IDH1 staining pattern was negative, consistent with wild type (Figure 2A). ATRX demonstrated retained nuclear expression, consistent with wild type (Figure 2B). Strong staining was seen with p53, consistent with TP53 mutation (Figure 2C). These findings confirmed a diagnosis of glioblastoma, IDH wild type. Molecular testing was positive for MGMT promoter methylation. Additional immunohistochemical stains to characterize the observed malignant appearing intravascular population showed

positivity for both PAX5 and CD20, consistent with B cell origin (Figure 2D). Therefore, in the context of malignant cytology, the findings were consistent with a simultaneous diagnosis of intravascular large B cell lymphoma.

## Treatment

Following the diagnosis, the patient was treated with dexamethasone and radiation therapy, with a plan for 3000 cGy in 10 fractions to the resection cavity and residual tumor, due to advanced age and frailty. Aside from steroids and radiation therapy, specific treatment for lymphoma was not pursued due to clinical prioritization to treat the symptomatic tumor, which was assumed to be the glioblastoma based on symptom location and MRI finding, as well as patient preference to avoid intravenous and inpatient chemotherapy regimens, and physician concern about toxicity and tolerability of chemotherapy. The patient completed 7 of 10 planned fractions of radiation (2100 cGy) and then was hospitalized due to seizures and unable to complete radiation due to need for inpatient rehabilitation. She was subsequently treated with three cycles of adjuvant temozolomide (150 - 200 mg/m<sup>2</sup> for 5 days q28 days), until first progression and then one cycle of lomustine. The treatment course was complicated by recurrent lower extremity cellulitis with a hospitalization for secondary osteomyelitis and bacteremia. After one lomustine cycle, the patient experienced both clinical and radiographic disease progression, characterized by worsening aphasia and increased enhancement on the MRI, and made the decision to transition to home hospice care. She passed away 10 months after the initial diagnosis.



## Discussion

Intravascular large B cell lymphoma is a rare, aggressive type of diffuse large B cell lymphoma, characterized by nearly exclusive growth within most types of blood vessels [7]; no or only a few neoplastic cells circulate in the peripheral blood [8]. Blood vessel lumina are the main site of replication as well as the means of spread [7]. The malignant cells express adhesion molecules that allow adhesion of cells to the endothelium but lack the adhesion molecules involved in extravasation [7], an important trait that differentiates IVBCL from diffuse large B cell lymphoma (DLBCL). The lymphoma cells may become entrapped within thrombi or organized fibrin, leading to tissue infarction or hemorrhage [8]. The median age of patients affected is 70 years [7, 8], with the presenting symptoms varying, but often neurologic in nature, including sensory and motor deficits or neuropathies, aphasia, dysarthria, and seizures, among others [7]. Many of these symptoms may be a result of occlusion of the vasculature by the lymphoma cells [8]. While most intravascular lymphoma is treated with systemic chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), there is also consideration for use of high dose methotrexate in cases where primary or secondary CNS involvement is likely [9]. Rarely, cases of IVBCL involving only cerebral vessels have been reported [10, 11]. In our patient's case, B cells were visualized in the intracranial vessels on brain biopsy and the co-occurring glioblastoma disrupted the integrity of the blood brain barrier. As such, we felt that if we were going to treat the lymphoma with chemotherapy, high dose methotrexate should be considered in the regimen. Ultimately this did not align with the patient's goals of care and as such the treatment regimen focused primarily on glioblastoma with supportive use of steroids and radiation therapy.

Glioblastoma is an aggressive, infiltrating, astrocytic glioma that most commonly affects adults over 55 years of age [12, 13]. The only known risk factor, thus far, is exposure to high dose ionizing radiation, particularly of the head and neck [12]. Though survival has improved in fit patients to a median of 20 months [14], prognosis in elderly patients remains poor with a median survival of less than a year [15]. Co-occurring glioblastoma and lymphoma in the same patient are rare. One case involving glioblastoma as a second primary tumor has been previously reported. In this case, a 50-year-old man was diagnosed with a glioblastoma approximately five years after achieving remission of DLBCL. The occurrence of glioblastoma was partly attributed to the treatment effects for the lymphoma. In another case, DLBCL occurred after temozolomide and radiotherapy for glioblastoma, with the glioblastoma treatment suspected as the underlying etiology [16].

Another rare phenomenon involving two primary brain tumors is that of tumor-to-tumor metastasis, by which a metastasis occurs from a primary cancer to a secondary pre-established malignancy [17]. A recent case was reported, in which an 83-year-old man with a history of lentigo maligna melanoma of the forehead and upper back was incidentally found on a staging brain MRI to have a suspected low-grade intraparenchymal neoplasm that was managed by observation [17]. Four years thereafter, an abrupt deficit in neurolog-

ic function occurred over a two-week period [17]. Pathology identified two histologically distinct neoplastic cell types co-existing within the same tumor, a metastatic malignant melanoma within an oligodendroglioma [17]. The patient received radiation and systemic treatment, but imaging demonstrated disease progression, prompting transition to hospice care and the patient passing away five months post operatively [17].

## Conclusion

To date, our case is the first case, to our knowledge, of a collision tumor involving intravascular large B cell lymphoma and high-grade glioma. Given the rarity of the co-occurrence of these two entities, little is known regarding the underlying etiology, effective treatment measures, or prognosis in this rare clinical scenario. Continued documentation of similar cases is necessary to better understand the factors that may give rise to synchronous CNS malignancies such as that described here and treat them more effectively.

## Acknowledgement

None.

## Conflict of Interest

Dr. Thomas is the PI for two industry studies: one supported by ONO and one by Novocure, which are for CNS lymphoma and glioblastoma, respectively. She is also a consultant for Roon.

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