Title: The Impact of Social Determinants of Health on the Diagnosis of Anaplastic Oligodendroglioma: A Case Report

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Highlights:

- Anaplastic oligodendroglioma is a rare CNS neoplasm characterized by elusive clinical manifestations that may lead to delays in diagnosis
- A careful evaluation needs to be performed particularly in bilingual patients presenting with expressive aphasia, since it can be mistaken for limited English proficiency
- Patients with expressive aphasia have difficulty producing words in any language, while patients with limited English proficiency have difficulty producing words in a specific language

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ABSTRACT

Background:

Anaplastic oligodendroglioma is a rare central nervous system neoplasm, accounting for 0.5% of all primary brain tumors. It is derived from oligodendrocytes and is typically located in the frontal lobes of the brain. Since its clinical manifestations are non-specific, many patients present with months to years of symptoms before receiving a diagnosis. Identifying expressive aphasia can be especially challenging in bilingual patients, as it is often misidentified as limited English proficiency, leading to delays in diagnosis. Thus, it is critical for health care providers to recognize social determinants of health (SDOH) to establish a diagnosis of anaplastic oligodendroglioma and avoid delays in care.

The Case:

A 75-year-old bilingual woman presented to a routine Cardiology appointment and reported word finding difficulties that worsened over the past 6 months. Five months later at her visit with Geriatrics, she reported more recent issues with expressive aphasia in both English and Spanish and difficulty speaking that started 1-2 years prior. A brain MRI revealed a left frontal lobe mass extending into the genu and body of the corpus callosum. Patient underwent a brain biopsy, which identified an IDH-mutant, 1p/19p co-deleted WHO-III anaplastic oligodendroglioma.

Conclusion:

Assessing social determinants of health such as language can help physicians diagnose medical conditions presenting with non-specific symptoms. In this case, the diagnosis of expressive aphasia was delayed likely because patient's symptoms were attributed to limited English proficiency. After careful examination and identifying her symptoms as aphasia in a bilingual patient, a work-up led to the diagnosis of anaplastic oligodendroglioma. Physicians should be aware of the social determinants of health and how they affect individual patients to avoid diagnostic biases, as delays in care such as this one have been shown to result in worsened outcomes, including increased length of hospital stay and mortality.

Keywords: oligodendroglioma, social determinants of health, SDOH in healthcare, diagnosis, multilingualism, aphasia, geriatrics, bilingual patient, brain tumor diagnosis

TEXT

Introduction

Oligodendrogliomas (OD) are brain tumors originating from the white matter of the brain.[1] According to the World Health Organization (WHO), they are classified as diffuse gliomas characterized by a mutation in isocitrate dehydrogenase type 1 (IDH1) or type 2 (IDH2). It is estimated that 1000 new cases of oligodendroglioma are diagnosed in the United States annually. These neuroepithelial tumors can be divided between low grade (about 75% of cases) and anaplastic oligodendrogliomas.[2] Approximately 55% of all cases occur in individuals aged 40 to 64 .[3] Notably, older adults have a markedly decreased relative 5-year survival rate.[4] Among its manifestations, aphasia can be elusive, particularly in bilingual patients. As delays in diagnosis and missed signs and symptoms such as expressive aphasia can lead to tumor identification at a later stage, prompt diagnosis is critical to achieve the best clinical outcomes. As studies have shown that SDOH such as race, sex, education, and economic status have been associated with significantly increased hospital length of stay ($p = 0.0036$) and 90-day mortality (OR 2.82) in neuro-oncology patients, early identification of these factors is essential to reducing morbidity and mortality.[5] This case underscores the importance of identifying social determinants of health (SDOH) disparities to establish a proper diagnosis and start the recommended treatment.

The Case

A 75-year-old woman with relevant past medical history of insulin-dependent type 2 diabetes, coronary artery disease, generalized anxiety disorder, and essential hypertension came to the Geriatric Clinic to establish care and complaining about speech difficulties (Figure 1). The patient first noticed symptoms 1-2 years before her visit, with significant worsening in the last 6 months. Spanish was her primary language, but she spoke both Spanish and English and was having trouble with naming and forming words in both languages. Other associated symptoms included mild writing difficulties and mild headaches. She denied any problems with reading and any cognitive changes. She noted that she experienced significant social isolation as she lived alone, her closest family member lived one hour away, and her closest friend passed away recently. This social isolation worsened around the start of the COVID-19 pandemic. She had reported these symptoms to previous health care providers. Her last appointment with a primary care provider was thirty days before coming to the Geriatric Clinic. Her mother was diagnosed with Alzheimer's disease in her 60s.

The physical exam showed a blood pressure of 114/62, heart rate of 96, respiratory rate of 15, oxygen saturation of 97%, and body mass index of 30.5. The patient was right-handed and had a hand grip of 21kg on both hands. The neurological exam was characterized by word finding difficulties, mild dysarthria and halting on prolonged speech, and 5/5 strength in both the upper and lower extremities. She was able to obey complex commands correctly and successfully perform finger to nose testing. Her gait was slow and hesitant, and she was unable to perform heel-toe testing. Cranial nerves I-XII were intact, and she had a negative Romberg sign. Laboratory studies were unremarkable. Geriatric assessment included a mini-cog score of 4/5 (normal), patient health questionnaire (PHQ-2) of 0 (normal), Katz index of independence in activities of daily living of 6 (fully independent), and Lawton-Brody scale for instrumental activities of daily living of 8 (high function, independent).

Magnetic Resonance Imaging (MRI) performed 1 month after her visit with Geriatrics showed a T2/FLAIR signal abnormality in the left frontal lobe, involving the white matter and extending into the genu and body of the corpus

callosum, concerning for a primary brain tumor (Figure 2). A stereotactic biopsy was performed, and the diagnosis of Grade 3 Anaplastic Oligodendroglioma, IDH1 mutant R132H, 1p/19q co-deleted was made (Figure 3). Due to the tumor's location and extent as well as the patient's baseline health and shared decision-making, surgery was not performed. Instead, the patient received temozolomide because it is standard of care, easy to administer, and usually has better patient tolerance than alternatives.[7] However, temozolomide was stopped after 4 weeks due to the adverse effect of severe thrombocytopenia. She then received radiation therapy, consisting of six weeks of treatment to 59.4 Gy in 33 fractions, which is again standard of care.[6] The patient reported that her expressive aphasia improved to some degree after treatment. Unfortunately, the patient passed away 2.5 years after the diagnosis due to worsening extensive vasogenic edema and worsening mass effect.

Discussion

The clinical manifestations of oligodendrogliomas (OD) are diverse and largely depend on the tumor's location and grade, with symptoms ranging from focal seizures to cognitive dysfunction. Frontal, parietal, and temporal lobe OD present with focal or generalized seizures. Frontal tumors tend to cause executive dysfunction, hemiparesis, or personality changes. Parietal tumors can lead to visuospatial impairment or hemisensory loss. On the other hand, occipital tumors may present with visual field deficits. On rare occasions, OD manifests as cerebellar ataxia and increased intracranial pressure. Low-grade OD generally present with seizures. In contrast, high-grade OD may present with increased intracranial pressure, focal deficits, and cognitive deficits.[1] Cognitive symptoms are a prominent clinical feature in central nervous system (CNS) tumors, such as lymphoma or gliomatosis cerebri, and are not seen as frequently with OD.[7] These symptoms include changes in memory, attention, orientation, personality, executive function, language, and activities of daily living. Tumors originating in dominant hemispheres are more likely to be associated with cognitive dysfunction.[8]

While cognitive symptoms such as those seen in oligodendrogliomas (OD) can complicate diagnosis, aphasia—particularly in bilingual patients—adds an additional layer of complexity, often leading to misinterpretation of symptoms and delays in care. It is estimated that 41% of Hispanic individuals have low health literacy in their second language.[9] In this case, expressive aphasia was initially misinterpreted as limited English language proficiency. Even though there is strong evidence to assess language proficiency in bilingual individuals with post-stroke aphasia, very few standardized approaches have been developed to evaluate patients with aphasia due to oncologic conditions.[10] This may be related to the fact that aphasic patients speaking multiple languages exhibit a variety of patterns of impairment across their languages.[11] At present, the best way to assess for bilingual aphasia is perhaps the Bilingual Aphasic Test (BAT), which was created for the purpose of assessing the language skills of multilingual individuals with aphasia in an equivalent way. Yet not all physicians are aware of its existence, and it is not always utilized in the appropriate clinical contexts.[12]

Several SDOH disparities were identified in this patient, including limited English proficiency, comorbidities, and access to bilingual physicians. Those factors have also been identified in Hispanic bilinguals with aphasia prior to stroke.[9] There are numerous studies showing the impact of having these disparities and the outcomes in patients with brain tumors.[13] A large study including 99,665 patients who underwent craniotomies secondary to

a tumor showed that African American patients had a higher mortality and were less likely to be discharged directly to home compared to patients of other ethnicities in all types of tumors.[14] Similar outcomes were obtained from a study including non-black minority race. A more recent study involving 2,519 brain tumor patients who underwent resection and had at least one SDOH disparity, including race and socioeconomic status, predicted a prolonged hospital length of stay, greater odds of a nonroutine discharge, and increased 90-day mortality.[5] These and many other studies make it clear that patients with SDOH disparities often have worse outcomes than their peers without the same SDOH disparities. In the present case, the patient's bilingualism and lack of access to providers who could parse out differences between language proficiency and expressive contributed to delays in diagnosis, possibly limiting the quality and amount of care that she was able to receive.

Conclusions

The diagnosis and treatment of rare conditions like OD can be delayed, particularly in bilingual patients presenting with aphasia. Incorporating the consideration of SDOH, such as language, into diagnostic workflows for aphasia may help clinicians avoid diagnostic biases and ensure accurate identification of underlying conditions. This case highlights the importance of recognizing SDOH as a valuable tool in enhancing the quality of care for older adults who are non-native English speakers.

Abbreviations

OD Oligodendroglioma(s)

CNS Central nervous system

IDH isocitrate dehydrogenase

MRI Magnetic resonance imaging

SDOH Social determinants of health

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FIGURES AND TABLES

Comentado [PI1]: Please delete the word chemotherapy in temozolamide chemotherapy

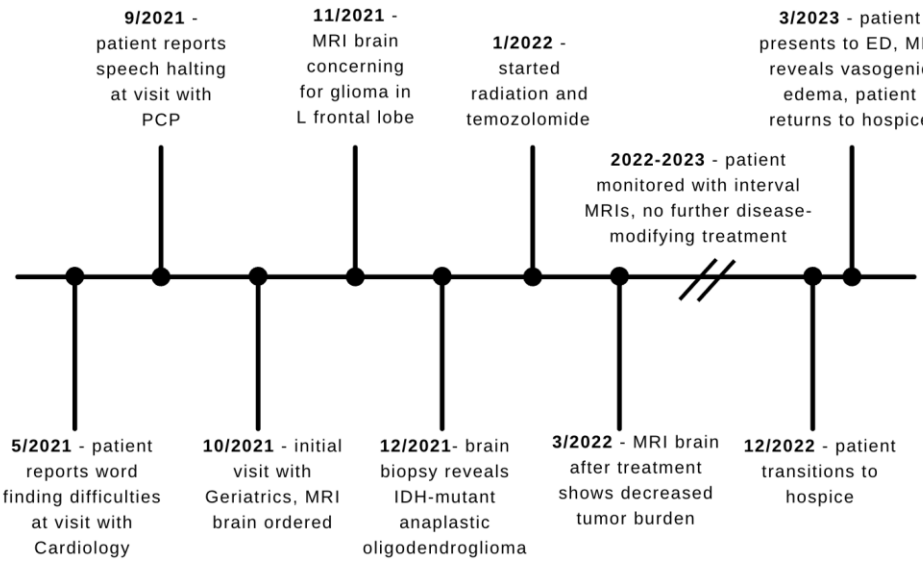

Figure 1: Timeline of key events in the case's disease course.

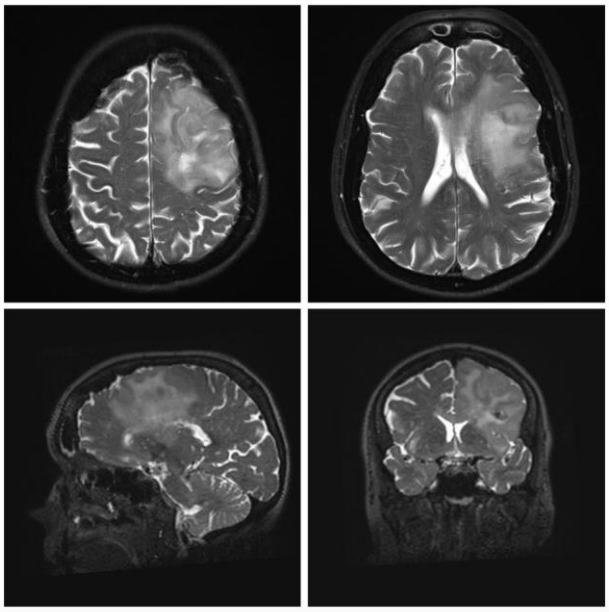

Figure 2: Brain MRI with contrast, showing mildly expansile white matter on T2 sequence in the left frontal lobe with extension into genu and corpus callosum.

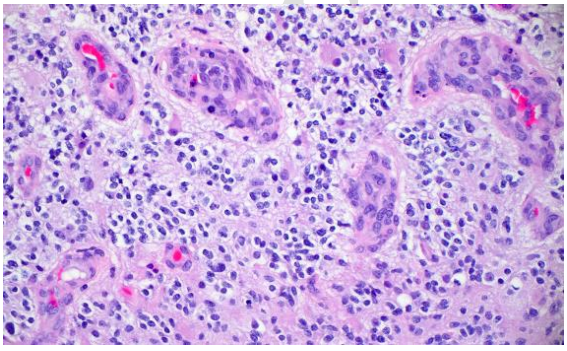

Figure 3**:** Brain biopsy on H&E stain, showing an infiltrating glioma with an oligodendroglial morphology. Focal necrosis and microvascular proliferation are also present.