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The Interesting Link Between Neurocysticercosis and Glioblastoma in a 41-year-old Hispanic Female

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ABSTRACT

Neurocysticercosis (NC) is a common condition worldwide while glioblastoma is the most common brain cancer among adults but overall, a rare disease. NC is the most common cause of seizures in developing countries. Although no causal relationship is established, there have been an association previously reported between NC and glioblastoma. Here we present a case of a 41-year-old female who was diagnosed with NC, treated with antiparasitic medications who developed worsening neurologic deficits despite treatment, and was subsequently diagnosed with a large left frontotemporal mass consistent with glioblastoma. Patient then underwent treatment with concurrent radiation and temozolomide.

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Introduction

Neurocysticercosis (NC) is one of the most common causes of seizures in developing countries which is caused by ingesting eggs of helminth *Taenia solium*. It is estimated that over 1.7 to 3.0 million people worldwide acquire epilepsy due to NC. Even though *Taenia solium* is rare in the United States, cases of NC can be found in patients who have migrated from endemic regions. NC can be found in intra-parenchymal or extra-parenchymal spaces depending on the distribution of blood in the brain. The clinical presentations of NC are diverse and rely on location and severity of the disease. However, seizure remain the most common presenting symptom of NC which accounts for 78.8% of the cases.[1] The diagnosis of NC is established based on clinical manifestations and brain imaging. Serology testing and cerebrospinal fluid analysis are often also used. Biopsy may require in rare case of non-diagnostic neuroimaging findings to differentiate from other brain lesions like glioblastomas.[2]

Glioblastoma is the most common primary malignant brain tumor among adults with a high morbidity and mortality rate. The overall age-adjusted incidence of glioblastoma in the United States is 3.22/100,000 with a mean progression-free survival of approximately 6 months and overall survival of around 18 months depending on the molecular markers.[3] Most of the glioblastoma are sporadic. The most common risk factor is previous exposure to ionizing radiation. Although an association of brain cancers and NC with infection is not very well-known, there have been various case reports linking an association between NC and glioblastoma, with some cases reporting similarities in the microenvironment.[4-5] Although no causal relationship has been determined, further studies on their correlation could provide insight into the relationship between parasitic infections and certain malignancies. It is hypothesized that NC has been implicated in the pathogenesis of human cancer by chronic inflammation, parasite-induced immune-suppression, and transfer of genetic material from parasite to host.[6-7] This is a case of a 41-year-old female who was diagnosed with glioblastoma after diagnosis of NC. Our patient was treated with concurrent temozolomide and radiation therapy.

Case Presentation

A 41-year-old Hispanic female originally from Cuba presented to the emergency department (ED) in December 2018 with fever (39.5°C), headache, neck pain and vomiting. CT brain without contrast was performed in the ED showing no acute abnormalities. MRI was not ordered in the ED at the time. Patient underwent a lumbar puncture (LP) and was started on empiric treatment with ceftriaxone, vancomycin, steroids, and acyclovir for aseptic meningitis. Cerebrospinal fluid (CSF) gram stains and cultures as well as meningitis/encephalitis panel were negative at the time. Patient then presented to the ED in July 2019 with continued fever, frontal headache as well as sore throat and was discharged home on amoxicillin/clavulanic acid for possible pharyngitis. On December 2020, patient presented to the ED again after a seizure event. Patient was then admitted. Infectious disease was consulted as well as neurology. Patient underwent an enzyme-linked immunoassay for Cysticercus antibody (Ab) in serum which turned out to be negative. Repeat LP was performed which was positive for Cysticercus Ab in CSF: 5.8 (normal <0.75 meaning Ab not detected). Repeat brain CT in April 2020 showed at least 4 well defined hypodense lesions with partial cystic components throughout left cerebral hemisphere (one being in frontal lobe, and 3 lesions in left parietal lobe). MRI brain was performed for the first time in December 2020 showing a few well-defined hyper intense rim-enhancing lesions in left parietal lobe with the largest lesion measuring 1.2 x 0.7 cm. The patient was subsequently started on levetiracetam 1000 mg Q12hr and dexamethasone 6 mg Q6hr for cerebral edema

and anti-parasitic medications, which she completed. By this time, 2 years elapsed between initial presentation and now. Patient at the time exhibited no dysarthria or speech abnormality. Patient then was readmitted for worsening weakness for the past 2 to 3 weeks, difficulty ambulating, altered mental status, and worsening lesions on CT. Repeat CT brain in May 2021 revealed a left frontal mass, 4.1 x 4.6 x 5.5 cm and a left frontotemporal mass, 3.5 x 2.2 cm with vasogenic edema, mass effect over lateral ventricular system, subfalcine herniation along with right lateral ventricular compression. ICU was consulted, MRI stat ordered, and patient was started on dexamethasone and levetiracetam. Infectious disease was consulted and albendazole 15 mg/kg/day was started in 2 doses and praziquantel 50 mg/kg/day in 3 doses to complete a 14-day course. Empiric ceftriaxone 2 gm Q12hr, vancomycin 15 mg/kg Q8hr and metronidazole 500 mg Q8hr was also started. Further tests included: human immunodeficiency virus (HIV), antinuclear antibodies (ANA), and human T-cell lymphotropic virus (HTLV), all of which were negative.

Repeat brain MRI showed multiple intra-axial masses of the left cerebrum, abutting the ependymal surface of the left lateral ventricle without discrete interventricular extension. Patient then underwent brain biopsy which revealed high grade glioma, glioblastoma, isocitrate dehydrogenase (IDH) wild type, WHO grade IV, and negative for O^6- methylguanine-DNA methyltransferase (MGMT) gene promoter methylation.

Neurosurgery was consulted. Due to disease location, extent and neurological dysfunction, surgical resection was not recommended. Radiation and medical oncology were consulted for further review and management. Temozolomide and radiation therapy was then started. During follow up, patient continued to have refractory seizures after completion of treatment and palliative care was consulted.

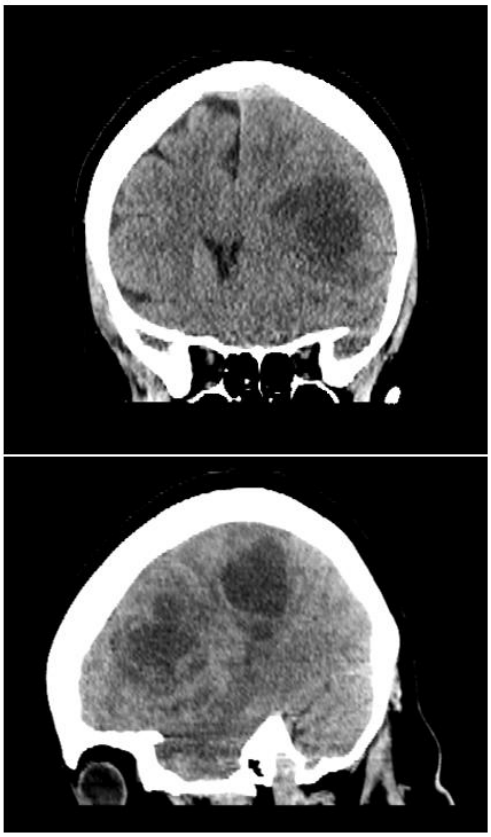

Figure 1 CT Brain without contrast showing large left cerebral hemispheric masses with vasogenic edema and midline shift.

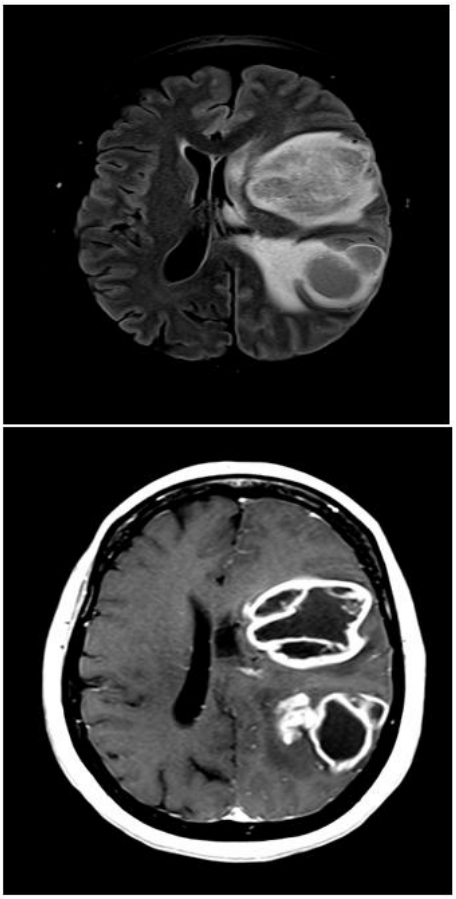

Figure 2 MRI Brain with/without contrast showing multiple intra-axial masses of left cerebrum abutting left lateral ventricle. Given history of NC findings may reflect changes of NC with cerebritis. Moreover, masses showing diffuse edema and 12 mm right midline shift with subfalcine and left uncal herniations.

Discussion

Neurocysticercosis (NC) is one of the most common causes of seizures in developing countries with improper slaughterhouse services and poor sanitation. However, NC has become more prevalent in developed countries. Humans obtain the infection through ingestion of Taenia solium eggs, a tapeworm found in pigs. Clinical manifestations can range from seizures, which is the most common, to headache, depression, and focal weakness, blindness, meningitis, or dementia.[2] Humans are colonized by the larval stage, the cysticercus, which then penetrates the intestinal mucosa. It is diagnosed by a combination of clinical symptoms, imaging, and serologic testing. Revised diagnostic criteria are as follows. Absolute criteria are histologic confirmation from brain biopsy, visualization of subretinal cysticercus or visualized scolex within cystic lesions on neuroimaging studies. Confirmative neuroimaging criteria is resolution after treatment or migration of cysts on imaging. Minor neuroimaging criteria includes abnormal enhancement of basal leptomeninges or obstructive hydrocephalus. Major imaging criteria include ring enhancing lesions, cystic lesions with scolex, brain calcifications, or multilobulated cysts in basal subarachnoid cisterns. Major clinical criteria are antibodies detected by immunodiagnostic tests, evidence of household contact or cysticercosis outside of CNS. Minor criteria include symptoms suggestive of NC or areas that are endemic with NC. Definitive diagnosis includes one absolute criterion or two major and one minor clinical/exposure criteria, one major and one confirming neuroimaging criteria with exposure/clinical criteria, or one major imaging

and 2 minor clinical/exposure criteria. Probable diagnosis includes one major neuroimaging criteria plus any two clinical/exposure criteria, or one minor neuroimaging criteria and one major clinical/exposure criteria.[8] Treatment involves albendazole and/or praziquantel with or without steroids.

Glioblastomas carry a bad prognosis, with median overall survival less than 2 years. Current treatment involves optimal surgical resection with radiation and treatment with temozolomide. High grade gliomas can have a wide range of symptoms depending on the location in which they present. Symptoms include headache in 50 to 60%, seizures in 20 to 50 % or focal neurologic deficits. Preferred imaging modality includes MRI. They appear as rim enhancing with central necrosis. They are classified based on histology and molecular patterns. Grade IV is defined by necrosis and vascular proliferation. Molecular testing for IDH and MGMT is important for prognostic value as MGMT unmethylated tumors carry a worse prognosis. MGMT repairs DNA damage by alkylating agents, and methylation of MGMT, which reduces expression, allows for effectiveness of treatment with alkylating agents such as temozolomide. [13]

The association between NC and gliomas was reported in a study conducted in 1997 in Ecuador. Eight (16.8%) of 43 patients with a glioma and 5 (2.9%) of 172 controls had NC (P<.001). The odds ratio for this association was 7.63 (95% confidence interval, 2.03-31.09) [6]. However, more studies are needed in order to determine if there is a casual relationship between the two. Perhaps the answer lies in the similarities in the microenvironment of gliomas and the environment seen in NC.

It is known that NC is associated with a strong inflammatory effect, with secretion of interleukin (IL)-1B, IL-6, tumor necrosis factor alpha (TNFa) with an increased regulatory T cells (Tregs) response in the periphery. [7] T regs play a role as a compensatory mechanism to downregulate the immune response by secreting IL-10. It is known immune evasion is one of the critical steps in tumorigenesis. It is also known that many non- central nervous system cancers in which there are high levels of Tregs in the microenvironment, there is a worse prognosis. Some studies have shown that there is an increase in the T reg population within the microenvironment of many cancers, including glioblastoma multiforme, especially with Tregs expressing receptors to the CCL2 chemokine that leads them towards the location of the glioma and allow for tumorigenesis.[8-9] There are some studies attempting to target this pathway in human gliomas and these studies state that as the glioma grade increases so does the number of Tregs which could be a prognostic factor. [9] Moreover, STAT3 tends to be overexpressed in gliomas, and it is a key regulator of immunosuppression. Il-6 plays a role in the STAT3 pathway for oncogenesis and as previously mentioned and NC has been shown to increase IL-6 and other inflammatory cytokines. Hence, there may be a relationship between NC and gliomas that needs further investigation.

Here we present a case of a patient diagnosed with glioblastoma IDH wildtype, WHO grade IV, MGMT negative after a probable diagnosis of NC. Our patient satisfied the following criteria for probable diagnosis of NC: one major imaging criteria (ring enhancing lesions on imaging), one major clinical criterion (Ab in CSF), and minor clinical criteria of symptoms consistent with NC (seizures). She underwent brain biopsy which confirmed glioblastoma IDH wildtype, WHO grade IV. The patient received treatment with steroids and anti-parasitics but developed right hemiparesis, lethargy, global aphasia secondary to the new left cerebral masses with associated midline shift/edema. She was treated with radiation and temozolamide as she was not a surgical candidate. After completion of treatment, patient continued experiencing refractory seizures, right-sided hemiparesis and palliative care was consulted in the end.

This case is important in that it brings to light the possibility of an association between glioblastoma and NC, which prompts further clinical research into preventing the development of glioblastoma in patients with NC. Moreover, further investigation into the microenvironment of the tumor and the similarities between NC microenvironment could enable targeted treatment in the future. This case also brings awareness about the salient nature of parasitic infections and predisposition to certain cancers, which merits further studies to evaluate for a causal relationship.

Ethics approval

Institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

References:

[1]. Carabin H, Ndimubanzi P, Budke C, Nguyen H, Qian Y, Cowan L et al. Clinical Manifestations Associated with Neurocysticercosis: A Systematic Review. *PLoS Neglected Tropical Diseases.* 2011;5(5):e1152.

[2]. Carabin H, Ndimubanzi P, Budke C, Nguyen H, Qian Y, Cowan L et al. Clinical Manifestations Associated with Neurocysticercosis: A Systematic Review. *PLoS Neglected Tropical Diseases.* 2011;5(5):e1152.

[3]. Wen P, Weller M, Lee E, Alexander B, Barnholtz-Sloan J, Barthel F et al. Glioblastoma in adults: a Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) consensus review on current management and future directions. *Neuro-Oncology.* 2020;22(8):1073-1113.

[4]. Gonzales I, Rivera J, Garcia H. Pathogenesis ofTaenia soliumtaeniasis and cysticercosis. *Parasite Immunology.* 2016;38(3):136-146.

[5]. Chang A, Miska J, Wainwright D, Dey M, Rivetta C, Yu D et al. CCL2 Produced by the Glioma Microenvironment Is Essential for the Recruitment of Regulatory T Cells and Myeloid-Derived Suppressor Cells. *Cancer Research.* 2016;76(19):5671-5682.

[6]. Alibek K, Kakpenova A, Baiken Y. Role of infectious agents in the carcinogenesis of brain and head and neck cancers. *Infectious Agents and Cancer.* 2013;8(1).

[7]. Del Brutto O, Dolezal M, Castillo P, García H. Neurocysticercosis and Oncogenesis. *Archives of Medical Research.* 2000;31(2):151-155.

[8]. Del Brutto O, Nash T, White A, Rajshekhar V, Wilkins P, Singh G et al. Revised diagnostic criteria for neurocysticercosis. *Journal of the Neurological Sciences.* 2017;372:202-210.

[9]. Kumar N, Bhattacharya T, Kumar R, Radotra B, Mukherjee K, Kapoor R et al. Is neurocysticercosis a risk factor for glioblastoma multiforme or a mere coincidence: A case report with review of literature. *Journal of Neurosciences in Rural Practice.* 2013;04(01):67-69.

[10]. Abou-Ghazal M, Kong L, Reina-Ortiz C, Yang D, Wei J, Qiao W et al. The Role of Tregs in Human Glioma Patients and their Inhibition with a Novel STAT-3 Inhibitor. *Neurosurgery.* 2008;62(6): 1423.