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Case Reports & Case Series

Case of cerebral toxoplasmosis masquerading as high-grade glioma

Kathleen P. McKenzie[a], Winnifred M. Wong[b], Shane B. Patterson[c], Joseph H. McDermott[d], Narayana K. Swamy[e], Claire L. Hiles[f,*]

[a] David Grant Medical Center (DGMC), Dept Family Medicine, United States of America
[b] DGMC, Dept Radiation-Oncology, United States of America
[c] DGMC, Dept Infectious Disease, United States of America
[d] DGMC, Dept Pathology, United States of America
[e] DGMC, Dept Neurosurgery, United States of America
[f] DGMC, Dept Hematology/Oncology, United States of America

A B S T R A C T

A 72-year-old female status post renal transplant presenting with right hemiparesis, expressive aphasia, and weight loss was found to have a left frontal ring-enhancing lesion with associated vasogenic edema. Imaging was most concerning for high-grade glioma, gliomatosis cerebri with anaplastic transformation, vs solitary metastasis and less concerning for evolving intraparenchymal hemorrhage, abscess, tuberculoma, or fungal granuloma. Maximal safe resection was not feasible. Awaiting stereotactic biopsy results, plans for palliative chemoradiotherapy for presumed glioblastoma were initiated. Frozen pathology review suggested high-grade glioma but ultimate diagnosis of cerebral toxoplasmosis was made. Patient started sulfadiazine, pyrimethamine, and leucovorin. This case identifies an uncommon presentation of cerebral toxoplasmosis whose definitive pathological diagnosis was indispensable to preservation of life. It serves as a critical example of the importance of maintaining a wide differential, as a patient with presumed aggressive terminal cancer was diagnosed with a treatable parasitic infection. We share perspectives from neurosurgery, medical-oncology, radiation-oncology, and infectious disease specialists regarding diagnosis and management. We highlight atypical presentations of cerebral toxoplasmosis, emphasize differential diagnoses, and promote obtaining tissue diagnosis in guiding medical decision making of ring enhancing lesions.

1. Case report

A 72-year-old female, two years status post renal transplant for end-stage renal disease on mycophenolate and tacrolimus, was brought in by family for acute right-sided hemiparesis and expressive aphasia. Review of systems was notable for 20 lb. weight loss over the prior 6 months but no overt evidence of systemic infection or acute cerebrovascular accident. Imaging revealed a left frontal ring-enhancing lesion and vasogenic edema highly concerning for primary brain tumor (Fig. 1).

Systemic imaging was negative for malignancy. The patient was started on intravenous steroids with slight improvement. Maximal safe resection of this eloquent brain area was not feasible. Frozen section of stereotactic biopsy revealed gliosis and necrosis, and a high-grade glial neoplasm was favored (Fig. 2C).

Neurologic functioning regressed following biopsy. Plans were made for palliative chemoradiotherapy for presumed glioblastoma. The permanent section tissue revealed tachyzoites and bradyzoites, which stained positive for toxoplasmosis by immunohistochemistry, yielding a final diagnosis of toxoplasmosis (Fig. 2A, B, D). Further interrogation revealed three cats in her house. Patient started sulfadiazine, pyrimethamine, and leucovorin with subsequent gradual recovery of verbal and motor function and regression of edema on follow-up imaging (Fig. 3).

2. Discussion

Diagnosing toxoplasmosis is a complicated task requiring combined clinical, radiological, and microbiologic assessments; often made more difficult in an immunocompromised patient whose differential is extensive. Toxoplasmosis in the immunocompromised may present with encephalitis, meningitis, pneumonitis, or dissemination and treatment may be required before diagnosis is confirmed. The ring-enhancing lesion, despite being a classic finding in toxoplasmic encephalitis, is a relatively non-specific finding with its own differential. Infections including cryptococcosis, histoplasmosis, neurocysticercosis, tuberculoma, toxoplasmosis, and brain abscess must be considered along with non-infectious causes including primary brain tumors such as

* Corresponding author at: DGMC, Dept Hematology/Oncology, 101 Bodin Cir, Travis AFB, CA 94534, United States of America.
E-mail addresses: kathleen.p.mckenzie.mil@mail.mil (K.P. McKenzie), winnifred.m.wong.mil@mail.mil (W.M. Wong), shane.b.patterson.mil@mail.mil (S.B. Patterson), joseph.h.mcdermott.mil@mail.mil (J.H. McDermott), narayana.k.swamy.civ@mail.mil (N.K. Swamy), claire.l.hiles.mil@mail.mil (C.L. Hiles).

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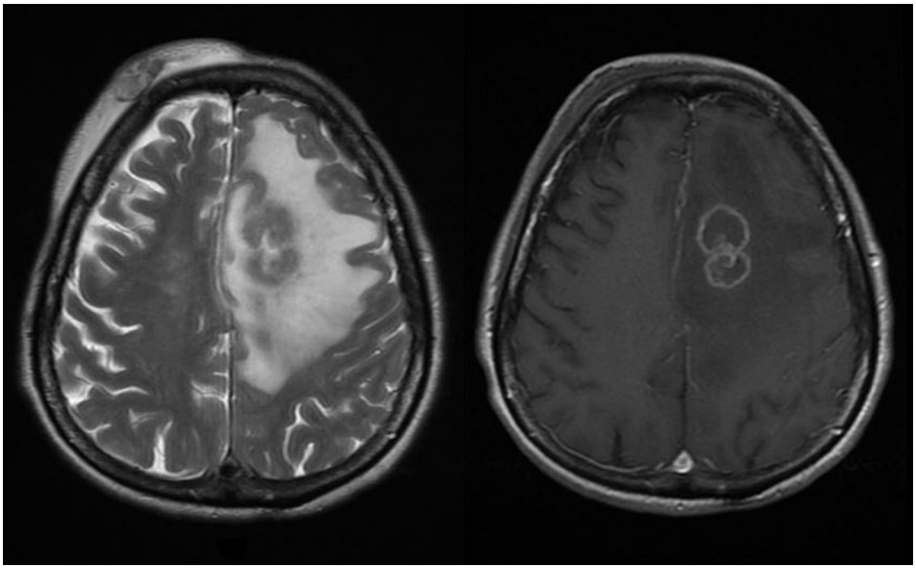

Fig. 1. Presenting images.
MRI brain at presentation (left: axial T2 without contrast, right: axial T1 with contrast) demonstrating 3.1 cm ring-enhancing lesion within left frontal cortex with surrounding vasogenic edema associated mild rightward midline shift and right frontal cephalhematoma.

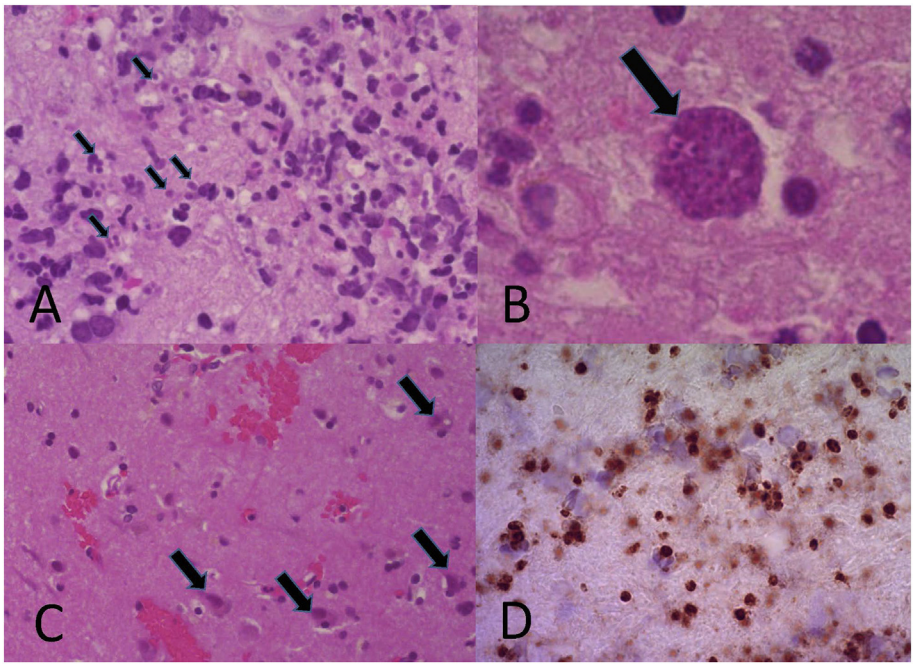

Fig. 2. Brain biopsy pathology.
In box A, arrows point to tachyzoites, some of which are in pairs and tetrads due to recent division (40×). In B, the arrow points to a cyst containing bradyzoites (100×). In C, arrows point to reactive appearing astrocytes, indicating reactive gliosis, which resembles a glial neoplasm and can lead to a wrong diagnosis (40×). In D, immunostain for toxoplasmosis stains the organisms (all tachyzoites) brown (100×). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

glioblastoma, metastases, infarcts, and resolving hematomas [1,2].

Impaired cell mediated immunity following solid organ transplant raises susceptibly to opportunistic central nervous system infections and de novo malignancy. This patient's presentation was not initially concerning for an infectious etiology without fever, leukocytosis, or ill-appearance on chronic stable doses of immunosuppressives. She did not present with meningitis, encephalitis, or hemorrhagic involvement of cerebral lesion which would have raised suspicion for an infectious etiology [3]. A more gradual neurologic decline may have suggested a diagnosis of progressive multifocal leukoencephalopathy. The acute onset of hemiparesis was more suspect of stroke or mass lesion. Lack of ocular symptoms or robust response to steroids lowered suspicion for lymphoma. Given the acute onset of symptoms, her age, the size of the lesion with mass effect and extensive edema, lack of systemic signs or symptoms of infection, and minimal response to initial steroid therapy, glioblastoma was highest on the list of suspected etiologies. This was further supported by gliosis and necrosis on the initial frozen biopsy specimen.

When patient presentation and imaging suggest glioblastoma, three of the most important factors to determine best treatment course are resectability, age, and performance status [4]. Per neurosurgical consultation, biopsy was favored over subtotal resection in this elderly patient with poor presenting Karnofsky performance status less than 60 and dubious location of the left frontal lesion in an eloquent area limiting radical resection. Given the high probability of glioblastoma and above risk factors, the initial treatment options included hypofractionated brain radiation alone, temozolamide alone, or palliative/best supportive care.

Historic radiation studies show that for patients with advanced age and poor performance status the addition of abbreviated brain radiation

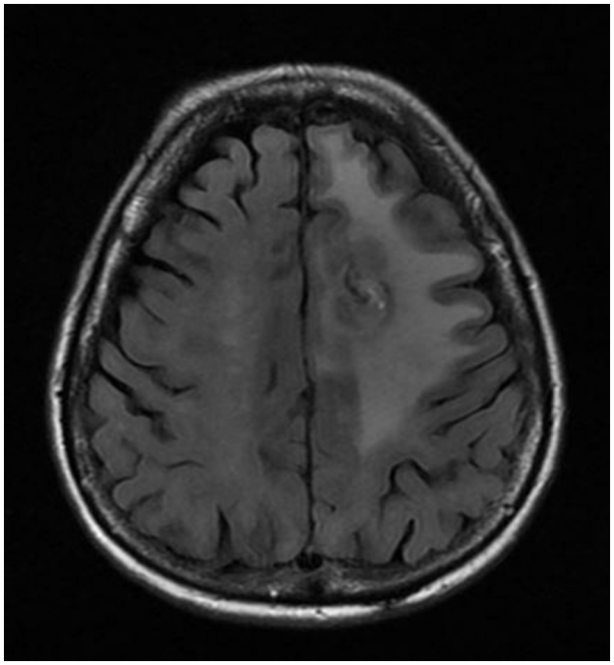

Fig. 3. Post-treatment image.
1-month follow-up MRI brain (axial T2 without contrast due to poor renal function) after starting antibiotics demonstrating decreased edema but stable cyst.

can decrease steroid and improve median survival from 1 month to 7–10 months [5–7]. While awaiting final pathology, her performance status further declined along with the potential benefit for radiation. Fortunately, final pathology returned within 8 days revealing toxoplasmosis alone. Literature review lacks data on brain radiation and toxoplasmosis, however, it may be assumed that brain radiation would have worsened this disease process, potentially even causing cyst hemorrhage and further dissemination.

Upon suspected diagnosis of toxoplasmosis, prompt initiation of antimicrobial therapy is warranted due to the high mortality rate of up to 65% [8]. Most treatment paradigms for toxoplasma encephalitis come from HIV/AIDS literature with limited data in the transplant population. A pyrimethamine, sulfadiazine, and folinic acid regimen is standard, though trimethoprim-sulfamethoxazole is often administered initially until pyrimethamine becomes available. Treatment is continued for 6 weeks following improvement in symptoms before transition to a maintenance regimen depending on the patient's immune status.

Infection with toxoplasmosis as a complication of solid organ transplant can occur via graft transmission, reactivation, or de novo. Most often, infection within the first 3 months posttransplant is secondary to graft transmission; however, disease occurring after 3–6 months tends to be reactivation or de novo acquisition [9]. Additionally, therapy with mycophenolate mofetil has been noted to increase the risk of toxoplasmic encephalitis [10]. In the case of this patient, who had mycophenolate mofetil as part of her anti-rejection regimen, it was felt that she acquired her infection after transplant based on the timing posttransplant and close physical proximity of the patient's sleeping area to her cat's litter box.

3. Conclusion

This case identifies an uncommon presentation of cerebral toxoplasmosis whose definitive pathological diagnosis was indispensable to preservation of life. From a radiation therapy standpoint, this serves as a cautionary tale on the need for final pathology, even while trying to balance patient decline and potential benefit from therapy. It emphasizes the critical importance of maintaining a wide differential, as a patient with presumed aggressive terminal cancer was diagnosed with treatable parasitic infection.

Conflict of interest

The authors have no conflicts of interest to disclose.

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