Journal of Neurology & Experimental Neuroscience

https://doi.org/10.17756/jnen.2019-062

Case Report

Open Access

Idiopathic Focal Cerebritis Mimicking a Neoplasm

Mohamad Ezzeldin[1*], Ahmed Yassin[2], Daniel Graf[3], Gerald Campbell[4], Narges Moghimi[3], Xiangping Li[3], Todd Masel[3] and Xiang Fang[3*]

[1]Department of Neurology, St Vincent Medical Center, Toledo, OH, USA
[2]Department of Neurology, Jordan University of Science and Technology, Irbid, Jordan
[3]Department of Neurology, University of Texas Medical Branch, Galveston, TX, USA
[4]Department of Pathology, University of Texas Medical Branch, Galveston, TX, USA

[*]Correspondence to:
Dr. Mohamad Ezzeldin, MD
Department of Neurology, St Vincent Medical Center, Toledo, OH 43608, USA
E-mail: mohamadezzeldin@hotmail.com

Xiang Fang, MD, PhD, FAAN, FANA,
Department of Neurology & The Mitchell Center for Neurodegenerative Diseases
University of Texas Medical Branch
Galveston, TX 77555, USA
E-mail: xiang.fang01@gmail.com

Received: September 19, 2019
Accepted: December 26, 2019
Published: December 28, 2019

Citation: Ezzeldin E, Yassin A, Graf D, Campbell G, Moghimi N, et al. 2019. Idiopathic Focal Cerebritis Mimicking a Neoplasm. *J Neurol Exp Neurosci* 5(2): 106-109.

Published by United Scientific Group

Abstract

Cerebritis is a local or diffuse inflammatory reaction within the brain, usually secondary to various local or systemic etiologies. We are reporting a challenging case of a focal brain lesion mimicking neoplasm that presented with a seizure caused by idiopathic focal cerebritis. A 35-year-old male presented with three episodes of generalized tonic clonic seizures. Neurological exam was non-focal. Cerebrospinal Fluid (CSF) showed 30 WBC with 75% lymphocytes. CSF studies including Bacterial culture, fungal culture and CMV/VZV/EBV/HSV PCR's, were negative. EEG was unremarkable. CT brain showed round cortical thickening in right posterior parietal lobe. Brain MRI revealed a non-enhancing right posterior parietal lesion. Magnetic Resonance Spectroscopy (MRS) showed increased choline activity with mildly increased N-acetylaspartate (NAA) and a lactate peak, suspicious for low grade glioma. Whole body imaging ruled out malignancy. Other infectious and inflammatory workup including urine and blood cultures, serum antibodies for HIV/syphilis/Hepatitis A, B, ESR, CRP and ANA were unremarkable. The lesion was surgically resected. The biopsy revealed inflammatory changes with predominantly perivascular (without arterial involvement) and diffuse parenchymal involvement. The inflammatory infiltrate was mainly mononuclear but was not granulomatous. Demyelination was not evident. Special staining ruled out the presence of mycobacteria, fungi, spirochetes and parasites. Immunohistochemical stains revealed the polyclonal (non-neoplastic) nature of the lymphoid and plasmacytic infiltrates, and negative viral antigens; HSVI & II, EBV, SV 40 and viral inclusions were not observed. The patient has been seizure free after levetiracetam treatment at 1-month follow-up. Although uncommon, a neoplasm-like mass lesion on MRI can actually be a focal cerebritis, which more rarely can be idiopathic. A full investigation in respect to the nature of such lesion is of paramount importance for the decisions related to treatment and prognosis.

Keywords

Focal cerebritis, Tumor mimic, Seizure, Treatment, Prognosis

Introduction

The differential diagnosis of a focal cortically based lesion may include infectious, neoplastic, demyelinating, granulomatous and vasculitic lesions. Some causes such as radionecrosis may be ruled out by history alone, while others need a full workup that may include a surgical biopsy. Differentiation

between the primary causes of lesions of the central nervous system is essential for management and prognosis. In reality, many tumor-like lesions including tumefactive MS plaques, abscesses, resolving hematomas, vascular malformations, and even giant Virchow–Robin spaces may have similar imaging features [1]. Functional MR imaging such as Magnetic Resonance Spectroscopy (MRS), and sequences such as Diffusion Tensor Imaging (DTI), Perfusion-Weighted Imaging (PWI), Susceptibility-Weighted Imaging (SWI) may facilitate the differentiation between a tumor and tumor-like lesions [1].

Case Description

A 35 years old right-handed Caucasian male with past medical history significant for narcotic abuse, presented to the neurology clinic with new onset generalized tonic seizure for which he was placed on Levetiracetam and an outpatient Magnetic Resonance Imaging (MRI) was requested. Ten days later, he presented to the emergency department with three episodes of generalized tonic clonic seizures. His neurological exam was non-focal. Initial metabolic and infectious workup was unrevealing. Computed Tomography (CT) scan of the brain showed round cortical thickening in right posterior parietal lobe (Figure 1). Patient was admitted to the hospital, and MRI of the brain with/without contrast was done that revealed a right posterior parietal non-enhancing lesion and hyper vascularity of the sulci surrounding the mass with no evidence of restricted diffusion nor significant mass effect (Figure 2). Magnetic Resonance Spectroscopy (MRS) of the brain showed findings concerning for low-grade tumors (Figure 3).

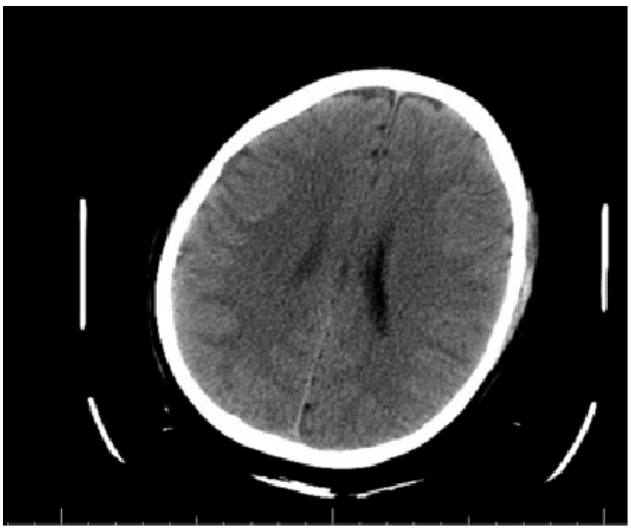

Figure 1: CT brain: focal cortical thickening in right posterior parietal lobe

Lumbar puncture was performed on admission day, and Cerebrospinal Fluid (CSF) showed 30 WBC with 75% lymphocytes, glucose 78, and protein 60 MG/DL. CSF studies were initially concerning for viral meningitis for which he received two days course of Acyclovir that was discontinued subsequently after viral workup (CMV, VZV, EBV, HSV) came back negative. Further work up including CSF

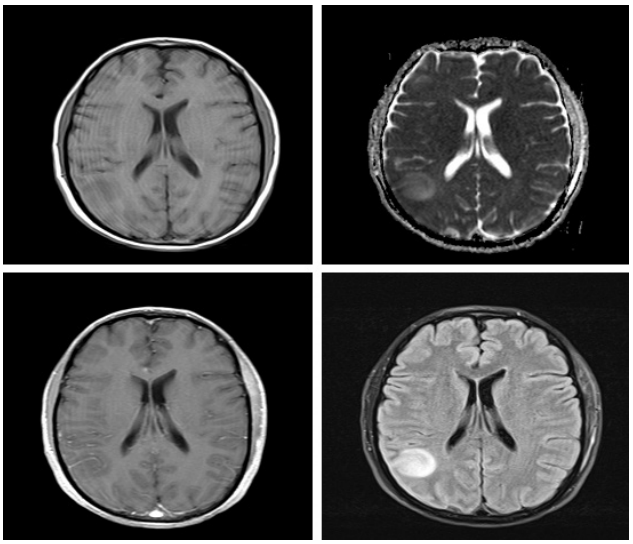

Figure 2: MRI brain **A.** T1 without contrast **B.** T1 with contrast **C.** ADC **D.** FLAIR.

Right parietal lesion, T1 isointense/FLAIR hyperintense located in cortical/subcortical region, without enhancement or restricted diffusion.

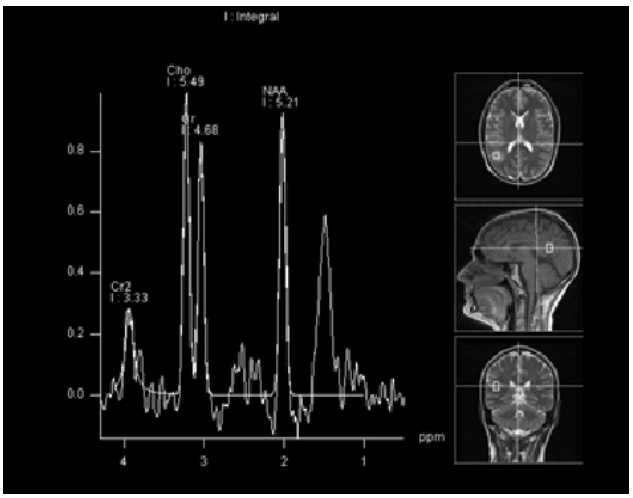

Figure 3: MRS: increased choline activity with mildly increased NAA and a lactate peak

cultures (bacterial and fungal), urine and blood cultures, serum HIV, syphilis, hepatitis A/B/C, Erythrocyte, ESR, CRP, and ANA were negative. CT scan of the thorax/abdomen/pelvis ruled out malignancy.

Due to high suspicious of low-grade tumor, 25 days after the first seizure event, he underwent an elective right parietal craniotomy using neuronavigation. The lesion was found to be well demarcated, firm, and non-suckable. A total excision of the lesion was performed. Histopathological analysis was consistent with inflammatory infiltrate, non-neoplastic, non-vasculitic, non-granulomatous, non-demyelinating, predominantly perivenular and lymphoplasmacytic, and negative for all available histologic tests for organisms (mycobacteria, fungi, spirochetes, parasites). Immunohistochemical (IHC) stains for viral antigens (HSVI & II, EBV, SV 40) were negative. Microscopic examination of the resected brain tissue revealed intense lymphoplasmacytic non-granulomatous infiltrates,

predominantly perivenular but with a less prominent diffuse parenchymal component (Figures 4A and 4B). There is minimal evidence of necrosis or thrombosis of small vessels, but muscular arteries are not involved, and arteritis is not a component of this process (Figure 4C). Likewise, primary demyelination is not evident in involved white matter areas by myelin staining, and macrophages present in the sections do not contain stainable myelin debris (Figure 4D). Astrogliosis and microglial activation are evident on the areas of inflammation. Immunohistochemical stains for lymphocytic markers (CD3, CD20, lambda and kappa light chains) demonstrate the polyclonal nature of the infiltrate, and stains for viral antigens (Herpes simplex I and II, Epstein-Barr virus and SV40 polyomavirus, which is cross-reactive with the JC virus) are negative. Likewise, negative are special stains for acid fast bacteria (Ziehl Neelsen and Fite), fungi (Grocott-Gomori methenamine silver), spirochetes (Warthin-Starry) and Giemsa for bacteria and parasitic organisms.

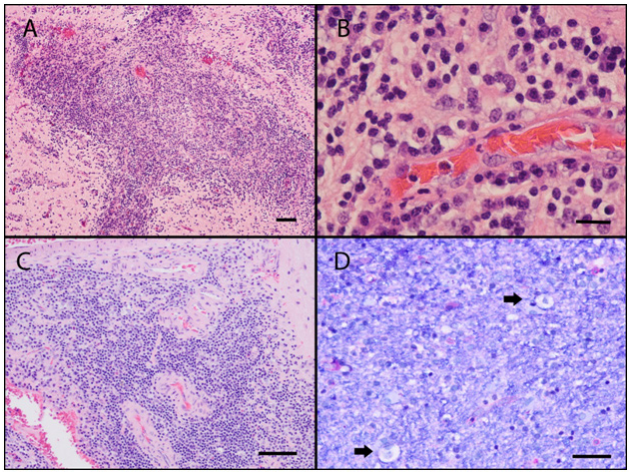

Figure 4: A. Intense inflammatory infiltrate in resected brain tissue (hematoxylin and eosin - H&E, scale bar = 100 microns), seen at higher magnification in panel. **B.** to be composed of lymphocytes and plasma cells with a few included macrophages (H&E, scale bar = 20 microns). **C.** Small muscular arteries are negative for arteritis (H&E, scale bar = 100 microns). **D.** Myelin staining reveals relatively intact white matter. The sparse macrophages (arrows) do not contain stainable myelin debris (PAS/Luxol fast blue, scale bar = 50 microns).

In summary, the lesion is inflammatory non-neoplastic, non-vasculitic, non-granulomatous, predominantly perivenular and lymphoplasmacytic, and negative for all available histologic tests for organisms. Patient postoperatively did well and with no neurological deficits upon discharge. He continued to be seizure free on an increased dose of Levetiracetam, and repeated brain MRI 2-months after surgical resection showed post-surgical changes of right parietal lobe lesion with thin enhancement at the surgical cavity walls (data not shown).

Discussion

Radiological differential diagnosis of the cortically based lesions can be challenging. This may include: neoplasm, abscess, focal cortical dysplasia, and less commonly solitary vasculitic lesions, demyelinating lesions and focal cerebritis [2]. Histopathologically, focal cerebritis could be secondary to vasculitis, infectious, demyelinating, or granulomatous diseases. In the early stages of a brain abscess formation, an area of un-encapsulated inflammation develops. In this stage, astrocyte and microglial response to the infecting microbe results in neutrophil accumulation, focal inflammation and edema. Following that, a necrotic center develops, and macrophages and lymphocytes predominate in the infiltrate. In the later stages, a capsule form in an attempt to isolate the infection.

Because it is unusual for patients to present in early stages of cerebral infection, imaging of early cerebritis has not been reported widely. On T1-weighted MR images, an ill-defined area of isointensity or hypointensity and subtle mass effect may be seen, and contrast enhancement is absent or minimal. On FLAIR and T2-weighted images, the infected tissue is hyperintense [3, 4]. In our case, CSF studies were initially concerning for viral meningitis for which the patient received only two days of Acyclovir. The negative CSF viral workup for CMV, VZV, EBV and HSV in addition to the negative IHC stains for HSVI & II, EBV, SV 40 antigens argue against the viral etiology of this brain lesion. In addition, CSF cultures (bacterial and fungal), urine and blood cultures, serum HIV, syphilis, hepatitis A/B/C, were negative. Histopathological analysis was also negative for organisms (mycobacteria, fungi, spirochetes, parasites). These negative results argue against other infectious etiologies for this brain lesion. Metagenomic next generation sequencing (mNGS) technique for other potential underlying infection was not performed.

Tumor-like mass lesions have also been reported in patients with systemic vasculitis such as Systemic Lupus Erythematosus (SLE) and Primary Angitis of the CNS (PACNS). Huang et al., reported a 14-year old boy with SLE with a large tumor-like temporal mass lesion. Brain biopsy showed extensive perivasculitis with no tumor was detected [5]. Molloy et al., described a subset of PACNS who presented with solitary tumor-like mass lesion with edema and contrast enhancement [6]. In our case, the normal ESR, CRP and ANA, the lack of involvement of arteries and the non-granulomatous nature of the process makes vasculitis less likely. It should be noted that patient has history of narcotic drug abuse that can cause vasculitis and cerebral vascular accident, but to our knowledge that the tumor-like mass lesion associated with drug abuse has not reported.

Other important radiological differential diagnosis in our case include Oligodendroglioma, Ganglioglioma (GG), Dysembryonic Neuroepithelial Tumor (DNET) and focal cortical dysplasia [2]. Seizure is the presenting clinical sign of 30–50% of patients with brain tumours [7]. Seizures are mostly the first and the only clinical manifestation of certain low grade (WHO grade II) cortically based Glial tumors [8]. Oligodendroglioma are typically have well-defined margins, most commonly arise in the frontal lobe, and frequently contain calcifications (up to 90%). On MRI, tumor is usually hypointense on T1-weighted images and hyperintense compared to gray matter on T2-weighted images. Heterogeneity of this signal intensity is the rule.

Surrounding vasogenic edema is not common. Enhancement is seen in 15%–20%. Lower Apparent diffusion coefficient (ADC) values differentiate them from high- grade tumors [2]. Gangligliomas can have inhomogeneous appearance due to the presence of a combination of solid, cystic and calcified components. DNET are multicystic, hypointense on T1-weighted images and hyperintense on T2-weighted images with minimal or without mass effect and surrounding vasogenic edema. Contrast enhancement could be found in about 30% of cases [8]. Focal cortical dysplasia Type I has later onset, more often seen in adults, with changes present in the temporal lobe. Type 2 is usually seen in children, more common in the frontal lobes with more severe clinical symptoms. MRI imaging shows abnormalities in the majority of type II dysplasias and in only some of type I cortical dysplasias. MRI imaging would show focal cortical thickening or thinning and increased signal on T2- and FLAIR-weighted images in the gray and subcortical white matter often tapering toward the ventricle [9]. Although in our patient the MRI and the MRS were concerning for low grade tumor, this was ruled out by histopathological study.

Solitary lesions of various demyelinating diseases, including multiple sclerosis (MS), Progressive Multifocal Leukoencephalopathy (PML) and Acute Disseminated Encephalomyelitis (ADEM) may mimic tumor. Pathologic studies typically report large areas of confluent demyelination with an inflammatory response associated with peri-lesional edema and mass effect. This was not the histopathological finding in our patient's biopsy. In addition, though MS lesions can occur juxta-cortically, they are more classically located in the perventricular region, brain stem, cerebellum, and spinal cord. Paraneoplastic etiology was also less likely given the young age of the patient, the lack of cancer risk factors, the lack of systemic symptoms and signs and the negative CT scan of the thorax/abdomen/pelvis for malignancy. Rarely, ischemic arterial or venous strokes may mimic tumors on neuroimaging. The acute onset of symptoms with matching clinical history will be suggestive. If a focal lesion crosses arterial vascular territory, a venous infarction should be considered. Lack of vascular risk factors, age, clinical history and MRI brain findings made this differential diagnosis less likely.

Conclusion

Focal cerebritis can look like a neoplasm or other lesions on brain imaging. More rarely, focal cerebritis can be idiopathic. Proper diagnosis is essential for decisions related to treatment and prognosis. The neurologist and radiologist should be aware of all the tumor mimics.

Disclosure

All authors have no disclosure.

References

1. Huisman TA. 2009. Tumor-like lesions of the brain. *Cancer Imaging* Spec No A: S10-S13. https://doi.org/10.1102/1470-7330.2009.9003
2. Koeller KK, Henry JM. 2001. From the archives of the AFIP: superficial gliomas: radiologic-pathologic correlation. Armed Forces Institute of Pathology. *Radiographics* 21(6): 1533-1556. https://doi.org/10.1148/radiographics.21.6.g01nv051533
3. Isada CM. 2010. Brain abscess.
4. Tung GA, Evangelista P, Rogg JM, Duncan JA 3rd. 2001. Diffusion-weighted MR imaging of rim-enhancing brain masses: is markedly decreased water diffusion specific for brain abscess? *AJR Am J Roentgenol* 177(3): 709-712. https://doi.org/10.2214/ajr.177.3.1770709
5. Huang CH, Hung CH, Chu YT, Hua YM. 2008. Tumor-like cerebral perivasculitis in a pediatric patient with systemic lupus erythematosus. *Kaohsiung J Med Sci* 24(4): 218-222. https://doi.org/10.1016/S1607-551X(08)70121-9
6. Molloy ES, Singhal AB, Calabrese LH. 2008. Tumour-like mass lesion: an under-recognised presentation of primary angiitis of the central nervous system. *Ann Rheum Dis* 67(12): 1732-1735. https://doi.org/10.1136/ard.2008.096800
7. van Breemen MS, Wilms EB, Vecht CJ. 2007. Epilepsy in patients with brain tumours: epidemiology, mechanisms, and management. *Lancet Neurol* 6(5): 421-430. https://doi.org/10.1016/S1474-4422(07)70103-5
8. Giulioni M, Marucci G, Martinoni M, Marliani AF, Toni F, et al. 2014. Epilepsy associated tumors: review article. *World J Clin Cases* 2(11): 623-641. https://doi.org/10.12998/wjcc.v2.i11.623
9. Kabat J, Król P. 2012. Focal cortical dysplasia - review. *Pol J Radiol* 77(2): 35-43. https://doi.org/10.12659/pjr.882968