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Case Report

Pyogenic brain abscess, ventriculitis and diffuse meningitis with fatal outcome in an adult: Radiologic–pathologic correlation☆,#

Abdelkader Mahammedi[a,*], *Suha Bachir*[a], *Jenna Purdy*[b], *Mykol Larvie*[a], *Mark Buehler*[b]

[a] *Cleveland Clinic, Department of Neuroradiology, Neuroradiology Room L10-407, 9500 Euclid Ave., Cleveland, OH 44195, USA*

[b] *University of Toledo, Department of Pathology and Neuroradiology, Toledo, OH, USA*

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ABSTRACT

Rupture of brain abscesses with evolution into ventriculitis with meningitis may result in sudden and dramatic worsening of the clinical situation. We present a 57-year-old man with such an event and fatal outcome. Multiple imaging modalities including computed tomography and advanced magnetic resonance imaging were correlated with gross specimen and histologic images. The differential diagnosis of multiple lesions with ring enhancement and prominent perifocal edema includes mainly infectious and neoplastic processes, such as brain abscess, metastasis, and multicentric glioblastoma. Pyogenic ventriculitis is an uncommon manifestation of severe intracranial infection that might be clinically obscure. We discuss the characteristic magnetic resonance findings of brain abscess and its complications, including meningitis and ventriculitis with emphasis on the role of diffusion-weighted and fluid-attenuated inversion recovery imaging.

1. Introduction

A 57-year-old Caucasian male with a past medical history of splenectomy after injury in 2013 was transferred from an outside facility and presented after being brought in by his sister for progressed confusion and a 1 day history of fever, random abnormal movements of his extremities. On admission, he was found to have blood pressure 50/40 mm Hg and heart rate in the 50s. He also had 6-7 mm nonreactive pupils. Initial brain computed tomography (CT) without IV contrast was performed and showed two hypodense left frontal and right parietal mass lesions with hyperdense rim and perifocal edema (Fig. 1).

☆ No disclosure.

During February, 2016 American Institute for Radiologic Pathology (AIRP) meeting (previously known as Armed Forces Institute of Pathology, AFIP), this case was selected as the best case in neuroradiology, as it perfectly illustrated strong radiologic pathologic correlation.

* Corresponding author.
E-mail address: abdelkm2@gmail.com (A. Mahammedi).

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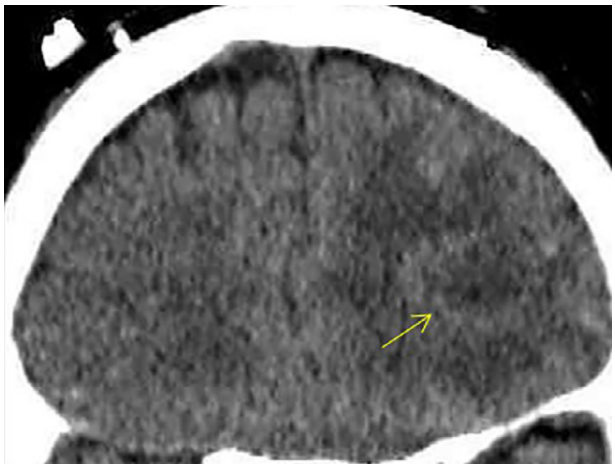

Fig. 1 – Coronal computed tomography without IV contrast shows left frontal lobe hypodense lesion.

Initially, there was concern that these lesions were metastasis versus abscess versus multicentric glioblastoma. The patient subsequently underwent magnetic resonance imaging (MRI) Siemens (Avanto 1.5T 1100g/cm Software B19) to further differentiate these masses, which showed left frontal and right parietal lobe ring-enhancing lesions with central increased diffusivity. The ring enhancement was incomplete medially toward the lateral ventricle (Figs. 2 E and F). The susceptibility weighted imaging (SWI) and T2/fluid-attenuated inversion recovery (FLAIR) showed a peripheral irregular low signal ring with typical dual rim sign on the FLAIR (Figs. 2 B, C, and D). The clinical context and image features (central diffusion restriction, dual rim sign, and the medially incomplete ring of enhancement) clearly favored abscesses over multicentric glioblastoma. Lumbar puncture showed many white blood cells but no organisms or yeast elements. Chest X-ray demonstrated left lower lobe pneumonia. Patient was empirically treated with broad spectrum antibiotics with vancomycin, ceftriaxone, and flagyl.

Neurosurgery was rapidly involved. He was given: levophed, mannitol, IV fluid resuscitation, and stress dose steroids. His vital signs improved but his pupils became small at 2 mm bilaterally, though still sluggishly and minimally reactive. He also improved to have trace decerebrate posturing on the left side and had left corneal reflex, a gag, and cough. A repeat head CT 1 day after initial study showed significant interval ventriculomegaly with bilaterally dilated temporal horns. Bacteriologic tests showed the presence of *Streptococcus viridans*. Therefore, the patient underwent an emergency bilateral frontal ventriculostomy which drained cloudy fluid and purulent material. Subsequent neuropathologic and microbiological examination confirmed the presence of intracranial abscesses with meningitis and ventriculitis (Figs. 3 and 4).

Despite management of his sepsis, ventriculitis, respiratory failure, and brainstem herniation secondary to mass effect from brain abscesses, his neurologic status was very poor and continued to worsen throughout his stay. After review and consultation with neurology and neurosurgery, it was determined that his neurologic status and brain function status was not salvageable. On 5 DAA, with no additional treatment options, family decided to withdraw support. Patient expired shortly thereafter and postmortem examination was conducted.

2. Discussion

2.1. *Pyogenic abscess*

Brain abscesses are a potentially life threatening condition requiring rapid treatment, and prompt radiological identification [1]. The diagnosis of pyogenic brain abscesses remains challenging. The differential diagnosis of multiple ring enhancing with surrounding vasogenic edema includes mainly infectious and neoplastic processes, such as brain abscess, metastasis, or multicentric glioblastoma [1,2]. Fortunately MRI is usually able to convincingly make the diagnosis, distinguishing abscesses from other ring enhancing lesions [2]. The earliest MRI experiment involving an abscess was published in Radiology in 1985. With use of a 0.35-T MRI device, Kamra et al. [3] reported that MRI could help differentiate an infectious process from a purely cystic lesion on the basis of signal intensity changes related to the protein content of the fluid and capsule characteristics [4,5]. Advanced MRI techniques and multiple MR sequences complemented the role of conventional MRI and increased the sensitivity and specificity [6]. Currently, conventional nonenhanced and contrast-enhanced MRI with diffusion weighted imaging (DWI) and MRS are the workhorse sequences for diagnosis of brain abscess. The combined use of DWI and MRS to differentiate abscess from other pathologic processes has a sensitivity of 0.72–0.96 and a specificity of 0.86–0.96 [4,7].

2.1.1. *Diffusion-weighted imaging*

In 1986, Ebisu et al. [8] were the first to report reduced apparent diffusion coefficients (ADCs) in a pyogenic abscess at DWI. The high viscosity and cellularity of pus impede water mobility and result in reduced diffusion. DWI is based on the random Brownian motion of water molecules in a voxel of tissue; thus, it may provide information about the existing disease process according to the mobility of water within the lesion [9]. However, these findings were not always pathognomonic for abscess [7]. Stadnik et al. [10] reported that the clinical value of DWI in conventional MRI lies in the ability to readily differentiate these two entities on the basis of reduced diffusion and low ADCs in abscess and usually elevated ADCs in tumor. Additionally, DWI characteristics can be used to distinguish etiologic agents of abscess. Reduced diffusion is a fairly consistent finding among pyogenic and fungal abscesses. However, parasitic infection with *Toxoplasma gondii* demonstrates increased diffusivity related to the underlying acellular core in toxoplasmosis [11]. DWI can also be used for therapeutic response particularly after antibiotic therapy or surgical drainage. Decreased signal intensity of abscess fluid on DWI, implies reduction of purulent material, whereas, persistent or recurrent reduced diffusion in a treated abscess is a characteristic finding of treatment failure [12]. Although DWI

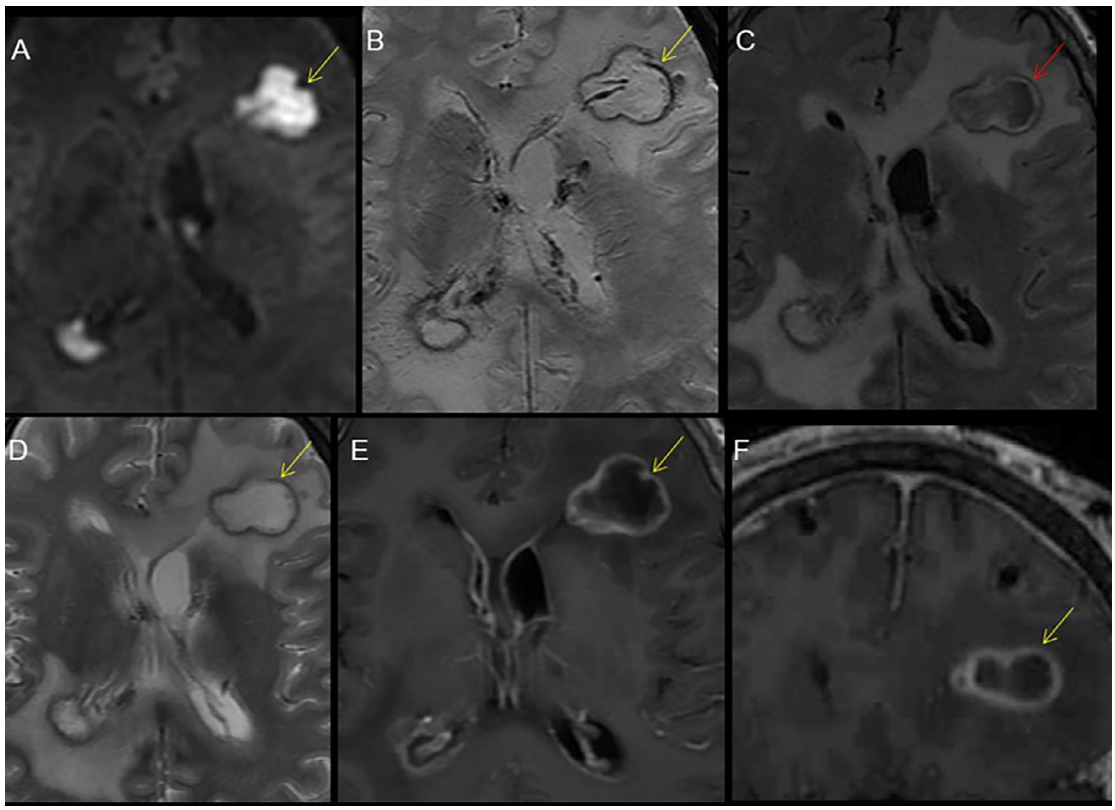

Fig. 2 – Axial diffusion-weighted imaging (A), susceptibility weighted imaging (B), fluid-attenuated inversion recovery (C), T2 (D) and T1 postcontrast (E, F) shows two ring enhancing lesions in the left frontal lobe and right parietal lobe, greater in the left (E) with diffusion restriction (A) and the characteristic appearance of "dual rim sign" on the susceptibility weighted imaging and fluid-attenuated inversion recovery images (red arrow in [C]) which is a specific feature of brain abscesses. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

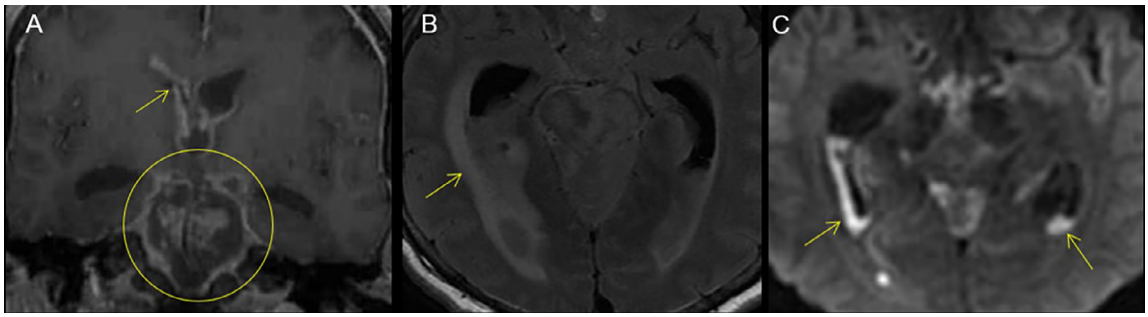

Fig. 3 – Coronal T1 postcontrast showing ventriculitis and brainstem leptomeningeal enhancement (yellow arrow and circle in [A]). Axial fluid-attenuated inversion recovery shows left pons and ependymal hyperintense signal along the perioccipital/temporal horns of the ventricles (B). Axial diffusion-weighted imaging showing diffusion restriction in the brainstem and along the occipital/temporal horns consistent with ventriculitis and meningitis (yellow arrows in [C]). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

has been proposed as the method of choice, it does not solve the diagnostic dilemma or obviate the need for biopsy [13]. In unclear cases, additional information can be gathered from proton magnetic resonance spectroscopy (PMRS). This method is not routinely available, but some authors have found the results promising [14,15].

2.1.2. Proton MRS proton

MRS and DWI were used in clinical practice about the same time. MRS provides a means to probe tissue metabolism. Typically, the spectral signature of abscess includes elevated acetate, succinate, lactate, and alanine signals [4,16]. Amino acids from neutrophil-driven protein breakdown are specific

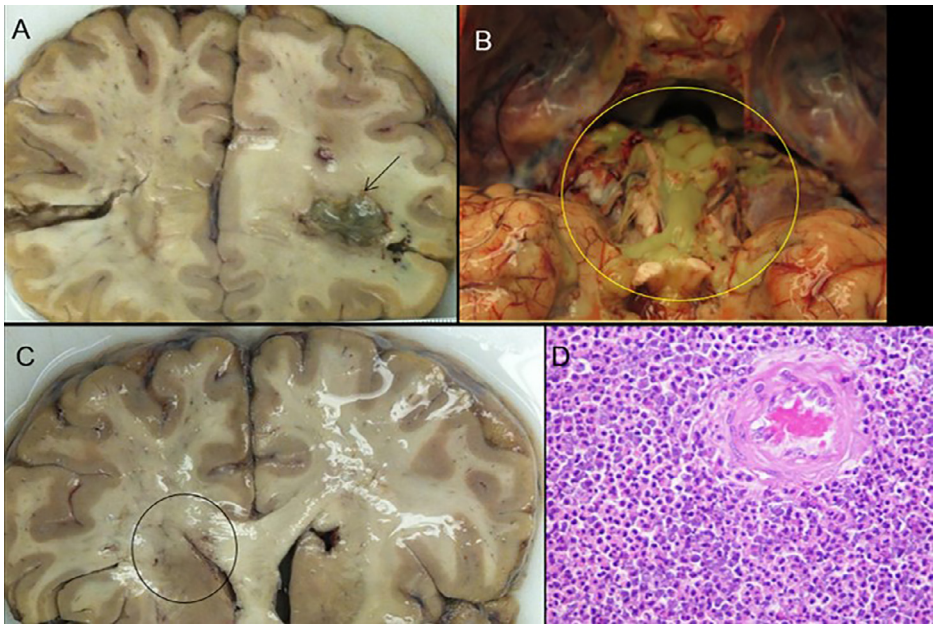

Fig. 4 – Gross: A coronal gross section demonstrates a 2.5 x 1.5 x 1.1 cm purulent lesion in the left frontal lobe white matter at a level 1 cm anterior to the genu of the corpus callosum. This lesion appears to have ruptured into the lateral ventricle in the inferior lateral frontal lobe (A). Large amount of purulent material in the subdural space surrounding the brainstem, the cerebellum, and throughout the ventricular system (yellow circle in [B]). A coronal gross section demonstrates some purulent material in the right lateral ventricle with minimal periventricular extension (black arrow in [C]). Tissue section from hippocampus, high power view (Hemotoxylin and Eosin x 40) shows the dense inflammatory infiltrate within the meninges consists mostly of neutrophils (D). These findings are consistent with meningitis. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

for pyogenic abscess [16]. MRS can be used to further differentiate anaerobic from aerobic metabolism on the basis of elevated succinate and acetate peaks observed only in anaerobic infections due to glycolysis and subsequent fermentation. Lactate peaks are lowest in strict anaerobes owing to metabolic lactate consumption [16]. MRS is also useful to differentiate bacteria from viral or fungal infection. For example, a lipid peak in the absence of amino acids suggests mycobacterial infection, and α,α-trehalose signals may be seen in fungal infection at correlative MRS (Fig. 5) [4]. The presence of an elevated choline peak in the enhancing wall suggests cystic or necrotic tumor rather than infection [7].

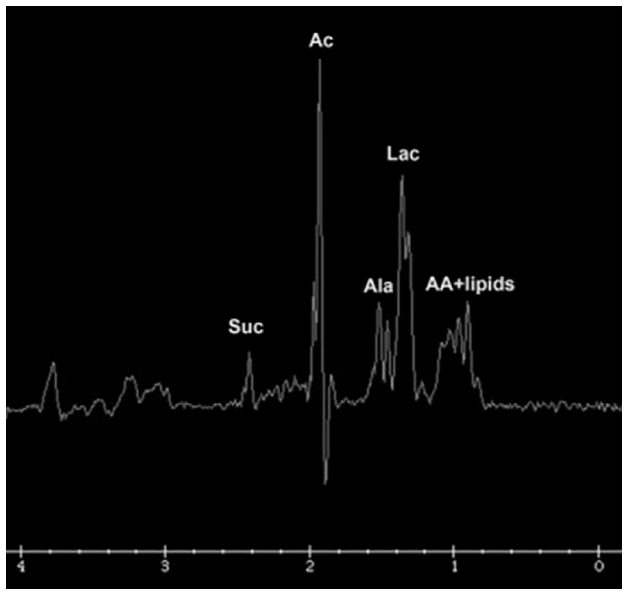

Fig. 5 – Magnetic resonance spectrography showing typical findings of bacterial cause: Spectrum from short-echo magnetic resonance spectrography shows multiple picks of amino acids and lipids (AA+lipids), lactate (Lac), alanine (Ala), acetate (Ac), and succinate (Suc). There is no N-acetylaspartate and choline peaks.

2.1.3. *Susceptibility weighted imaging*

It utilizes the susceptibility differences between tissues to obtain an intrinsic imaging contrast by combining the gradient echo data of phase and magnitude [17]. SWI is sensitive to the differences between paramagnetic substances which have positive susceptibility, such as iron and blood products, and diamagnetic substances which have negative susceptibility, such as calcium, water, and other tissue contents [17]. SWI is helpful in detecting blood products associated with the pathologic process, such as angiogenesis in glioblastoma [18]. The random deposition of hemorrhagic products in glioblastoma results in a hypointense rim surrounding the necrotic center, which is usually irregular and incomplete, in contrast

to the hypointense rim present in brain abscess, which is usually smooth and complete [19]. Pyogenic brain abscess, and not glioblastoma, has a characteristic appearance of a concentric hypointense rim surrounding a hyperintense rim. This appearance is called a "dual rim sign" and is found in the SWI due to its sensitivity to both paramagnetic and diamagnetic substances (Fig. 2B) [19]. The end products by macrophages of paramagnetic free radicals have been proposed to be responsible for the hypointense rim, and the granulation tissues between the necrotic center and fibrocollagenous capsule are most likely responsible for the hyperintense signal [14,19]. The dual rim sign has been reported to be the most specific feature in differentiating brain abscess from glioblastoma on SWI [19]. The signal intensity on the SWI is dependent on magnetic strength [14].

2.1.4. *Diffusion-tensor imaging*

Diffusion Tensor Imaging (DTI) is a refinement of DWI. It depicts three-dimensional diffusivity and is most commonly used to evaluate white matter tracts in and around a brain mass. Fractional anisotropy is a quantitative variable derived at diffusion-tensor imaging that reflects the degree of tissue organization. Abscess shows a high fractional anisotropy, in contrast to cystic or necrotic tumor, this is related to the organized leukocytes in the abscess cavity. Low fractional anisotropy corresponds to the acellular collagen capsule in the region of rim enhancement. Higher fractional anisotropy is present in the perilesional edema of tumor compared with abscess, a relatively specific finding that is thought to represent the increased organization of chronic gliosis associated with brain tumors [4,19].

2.1.5. *Perfusion imaging*

Two techniques are used in MRI perfusion imaging. The commonest used technique is the dynamic susceptibility contrast imaging [20]. It uses the signal intensity loss in T2* gradient recalled echo. The role of perfusion imaging, particularly the calculated relative cerebral blood volume (rCBV), is an estimation of the angiogenesis, which is a marker for aggressive tumors, in which the enhancing rim contains viable tumors and demonstrates an increased rCBV. The enhancing rim in brain abscess has markedly lower microvascular density than in glioblastoma due to the lack of neovascularization, and thus, it demonstrates lower rCBV values on the enhancing rim compared to glioblastoma [19]. The corrected rCBV demonstrates different values between neoplastic and infectious processes, but the K2 values are the same. However, perfusion measurement is a complex process in which many factors may lead to abnormal findings, including the specific technique used [4,21].

The clinical presentation of brain abscess is nonspecific with many cases having no convincing inflammatory or septic symptoms. Symptoms of raised intracranial pressure, seizures, and focal neurologic deficits are most common forms of presentation [7,9]. Eventually many abscesses rupture into ventricular system, which results in a sudden and dramatic worsening of the clinical presentation and often heralds a poor outcome [19].

The mainstay of treatment for cerebral abscesses is neurosurgical drainage which can be performed either by stereotactic aspiration or craniotomy. Broad spectrum intravenous antibiotics are also needed and can later be changed to agents tailored to the specific organisms [1,2,7].

3. Pyogenic ventriculitis

Pyogenic ventriculitis is an uncommon but very severe intracranial infection related to meningitis (both pyogenic and viral), ruptured brain abscess, ventricular catheter, or trauma [22]. Ventriculitis has been described using a variety of terms which reflect various facets of the disease's pathologic process. This includes ependymitis, intraventricular abscess, ventricular empyema, and pyocephalus [22]. It requires rapid diagnosis and therapy because of its high mortality. Bacterial ventriculitis may occur in healthy individuals after trauma or neurosurgical procedure [23]. Fungal or viral ventriculitis occurs most commonly in immunosuppressed patients. Ventriculitis occurs in 30% of meningitis patients; up to 80%-90% in neonates/infants [23–25]. *Staphylococcus* and *Enterobacter* are the 2 most common microorganisms causing ventriculitis [22,25]

The clinical features of ventriculitis are often obscure and nonspecific. Neuroimaging is the only tool to reliably diagnose this life-threatening condition [22]. Previously reported characteristic MRI findings of ventriculitis include intraventricular debris and pus, abnormal periventricular and subependymal signal intensity, and enhancement of the ventricular lining on conventional MRI sequences [22,25]. Ependymal thickening and enhancement with T2 prolongation surrounding the ventricles are often seen. Hydrocephalus and debris within the dependent aspect of the ventricles usually demonstrating decreased diffusion and high signal on T2-FLAIR can be seen [22]. Presence of irregular ventricular debris is especially characteristic of ventriculitis (Figs. 3 and 4). Choroid plexitis suggested by poorly defined margin of a swollen and enhancing choroid plexus is another finding associated with ventriculitis [26]. Viral infections, unlike pyogenic ventriculitis, result in periventricular calcifications in the chronic stage [26].

In 2005, Fujikawa et al. [27] reported that diffusion-weighted imaging are particularly useful for recognizing intraventricular debris and pus because of the conspicuity of the lesions, drawing attention to the existence of ventriculitis [26]. FLAIR imaging were more valuable than contrast-enhanced T1-weighted imaging for depicting periventricular abnormalities, the second most common MRI feature of ventriculitis (Figs. 3 and 4) (85% on FLAIR images and 60% on contrast-enhanced T1-weighted images) [27]. These results are in agreement with those of a previous study by Fukui et al. [22] and Pezzullo et al [26]. The number of lesions detected in bilateral ventricles was higher on the diffusion-weighted images than on the FLAIR images. This discrepancy was likely caused by a difference in lesion conspicuity between the sequences. Hyperintense intraventricular debris and pus were more conspicuous on the diffusion-weighted images than on the FLAIR images [27].

4. Image findings

Imaging: Multiple CT scans with and without IV contrast. MRI with IV contrast.

*Pathology: High power views (Hemotoxylin and Eosin × 40) tissue sections. Gross specimen and histologic images correlated to multiple imaging modalities.

5. Teaching point

Ventriculitis may be an indolent and lethal infection and is a potential source of persistent infection, even when meningitis is treated. Early diagnosis is essential for the appropriate treatment of ventriculitis. The finding of irregular ventricular debris with restricted diffusion is especially characteristic of ventriculitis; additional findings include ventriculomegaly with debris level, abnormal ependymal enhancement, and periventricular T2/FLAIR hyperintensity. Aggressive therapy is required. In cases where the abscess cavity does not completely obliterate, follow-up with MRI including DWI is useful and lack of restricted diffusion is reassuring. Demonstration of ongoing restricted diffusion in a cavity suggests persistent infection.

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