How Confusing Can an Acute Confusional State be?

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The approach to a patient presenting with an acute confusional state includes a neurologic workup. Space-occupying lesions (SOLs) of the central nervous system must be part of the differential diagnosis, even if focal neurologic deficits are not present. Different imaging techniques and biopsy methods can be used but their diagnostic accuracy and efficacy vary. We discuss the investigational process findings of a patient who presented to our department with an acute confusional state.

PATIENT DESCRIPTION

The patient was an 87 year old woman who arrived at the emergency department (ED) in an acute confusional state. Prior to her admission she had intact cognitive function and was entirely independent; she was able to live on her own and drive without assistance. After presenting to her general practitioner with a 3 day history of acute confusion and bizarre behavior, she was sent to the ED. On the day of admission, the patient was afebrile without any signs of infection, photophobia, phonophobia, neck rigidity or other focal neurologic signs. She denied antecedent weight loss, headache, nausea and vomiting. Her laboratory values were non-significant for her condition and her vital signs were normal. Apart from confusion and bizarre behavior, the physical examination showed no other significant findings. The patient was confused although cooperative and did not understand why she was admitted to the hospital. She was disoriented in time, place, and did not recognize her son.

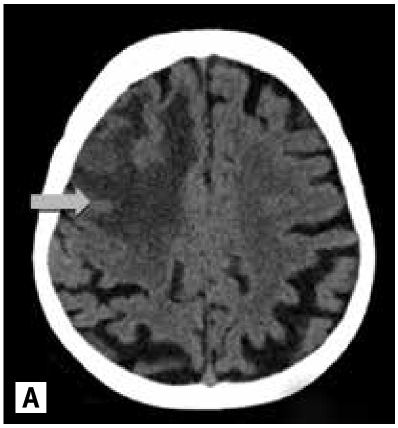


Figure 1. [A] CT without contrast shows the right frontal lobe with hypodense vasogenic edema, and mass effect on the right frontal lateral ventricle

[B] CT-contrast shows three focal ring-enhancing lesions of the frontotemporal area with edema

In light of this presentation a computed tomography (CT) scan was performed, showing hypodense vasogenic edema in the right frontal lobe, with a mass effect on the anterior horn of the right lateral ventricle without signs of intracranial hemorrhage [Figure 1A] With the injection of contrast material, three focal ring enhancing lesions of the frontotemporal area and edema were demonstrated [Figure 1B]. High dose dexamethasone was initiated due to the brain edema. Under that treatment the patient´s cognitive function improved over the next few days.

In order to further classify the tumor and to estimate the most approachable area for biopsy, we performed magnetic resonance imaging (MRI) that showed, at T1, three intra-axial space-occupying lesions in the right upper hemisphere. Another lesion was found caudally within the cortical supra-sylvian fissure that infiltrated the meninges. The lesions were ring-shaped with peripheral enhancement [Figure 2A]. At T2, there was also peri-tumoral vasogenic edema around the frontal lesions but with no significant mass effect [Figure 2B].

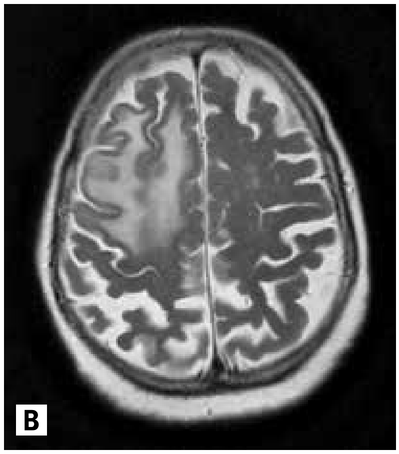
Our differential diagnosis centered on metastases versus multifocal glioma. In order to reach a final diagnosis a brain biopsy was scheduled and the patient was discharged from the hospital after resolution of her acute confessional state, with instruction to continue dexamethasone at the same dosage until the surgery.

COMMENT

According to the Monro-Kellie hypothesis, due to the skull being rigid and fixed, any increase in volume must be compensated by a decrease in volume of some other medium within the cranium: brain tissue,

Figure 2. [A] MRI at T1 shows three intra-axial space-occupying lesions (SOLs) in the right upper hemisphere and one caudal SOL within the cortical supra-sylvian fissure, with meningeal involvement. All lesions were ring-shaped with peripheral enhancement

[B] MRI at T2 shows peri-tumoral vasogenic edema around frontal lesions with no mass effect. The area was restricted in diffusion and did not include leptomeningeal enhancement



blood and/or cerebrospinal fluid (CSF) [1]. Space-occupying lesions of the central nervous system (CNS) can have a serious clinical course. The differential diagnosis of intracranial masses can be divided into five main categories, presented here in order of decreasing probability. They include:

- metastatic brain tumors
- infection (abscess, granulomatous disease, AIDS and associated conditions)
- primary brain tumors, vascular disease (aneurysms, atriovenous malformations, cerebral hemorrhage, cerebral infarct)
- inflammatory disease
- cysts.

Additional factors such as location, multiplicity, heterogeneity and enhancement should also be considered. Studies have shown a higher incidence of males with neoplastic SOLs when compared to females, and the highest number patients with SOLs were found in the fourth and fifth decades of life [2].

Radiologic modalities are the only means of assessing a SOL prior to surgical biopsy. Tissue biopsy with histopathologic investigation remains the gold standard for diagnosis. In the primary assessment of SOL, radiologic modalities include CT, MRI, MRI with contrast, MR spectroscopy (MRS), diffusion-weighted imaging (DWI), perfusion-weighted imaging (PWI), etc. These modalities help to determine whether the SOL is solid or has a cystic or vascular pattern, and whether necrosis is present or absent [2]. A neuroradiologist may be able to narrow the differential diagnosis using different image modalities, providing preoperative views of the lesion [3]. The lack of accuracy of CT scanning and conventional MRI limits their ability to localize CNS lesions and provide a preliminary diagnosis [2]. MRIs alone were found to be 39% accurate in diagnosis, since it is difficult to differentiate between necrotic glioblastomas, cystic metastases and abscesses [2,5]. When using multimodal imaging methods, such as MRS in combination with PWI, the collective diagnostic accuracy rises to 93%. In comparison, MRI in combination with CT showed a diagnostic efficacy of 68% [2]. For differentiation of circumscribed brain lesions to histologically infiltrating processes, MRI improves diagnostic accuracy, especially when compared to conventional morphologic methods. This is of clinical importance due to the differences in treatment between circumscribed lesions where surgery may be curative, and infiltrating lesions where treatment focuses on radiotherapy as well as chemotherapy [4]. By these means the probable diagnosis, prognosis and further behavior of the SOL can be estimated.

According to the literature, when performing endoscopic tumor biopsy, the diagnostic yield of the tumor ranges from 52% to 96%. It has been found that when histologic studies are used alone as a diagnostic tool there is 77.4% accuracy compared to cytohistologic methods that provide a diagnostic efficacy of 93.5%. The use of tumor irrigation fluid (TIF) provides more tumor tissue during biopsy. TIF is used during endoscopic procedures to clear the biopsy site and consists of Ringer's solution. If the tumor washings are kept and centrifuged, tumor fragments can be collected. These can be used for squash smears, enabling the original biopsy to be used for histology only. Squash smear evaluation is a diagnostic procedure with a high accuracy and high sensitivity, 75–90%. It requires less tissue and is useful in intraoperative diagnosis of intracranial masses. Squash smears have been shown to increase the diagnostic accuracy of histologic samples by 77.4% and of cytohistologic samples by 93.5%. A method that helps preserve tumor tissue is the addition of eosin prior to processing; this colors the tissue, giving the pathologist a more precise guide when cutting [3].

Due to the serious clinical course of SOLs in the CNS and its broad differential diagnosis, it is imperative to establish the location of the lesion before biopsy [4]. Multimodal imaging methods such as MRS with PWI have significantly increased rates of accuracy when compared to single imaging methods [2]. After localizing the biopsy, using TIF in addition to the biopsy increases the diagnostic yield of the tumor and provides greater diagnostic efficacy [3].

In conclusion, SOLs of the central nervous system must be included in the differential diagnosis of acute confusional state, even if other focal neurologic deficits are not present. Different imaging techniques and biopsy methods can be used to identify SOLs of the central nervous system but their diagnostic accuracy and efficacy differ. Multimodal imaging methods have significantly increased rates of accuracy whereas TIF increases the diagnostic yield of the tumor with higher sensitivity and specificity [2,3].

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