Role of conventional magnetic resonance imaging in the screening of epilepsy with structural abnormalities: a pictorial essay

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Abstract: Epilepsy is a chronic neurological disease with serious impact on patients and society. The causes of epilepsy comprise a heterogeneous group of disorders, rendering epilepsy diagnoses rather difficult and challenging. The primary role of MRI is to locate and define the probable anatomic epileptogenic lesions. In the developing countries, where functional MRI (fMRI) is not popular, conventional MRI (cMRI) becomes especially important in epilepsy diagnoses. Apart from that, an experienced radiologist can increase the diagnostic yield of MRI to epileptogenic lesions. Thus, we present a pictorial review focusing on the role of cMRI in the screening of epilepsy with structural abnormalities and highlighting the key findings on cMRI to help radiologists to be familiar with the characteristic findings. Considering the complexity and diversity of the structural abnormalities, we propose a mnemonic “MAGIC TVs” approach to reduce false negative diagnosis and improve the diagnosis rate.

Keywords: Epilepsy, magnetic resonance imaging

Introduction

Epilepsy is a chronic neurological disease characterized by sudden, repeated and transient dysfunction of central nervous system due to abnormal, excessive neuronal activity [1-10]. Epilepsy affects more than 50 million patients worldwide and imposes substantial global disease burden [11, 12]. The situation is more serious in developing countries than in developed ones. It is reported that the incidence of epilepsy in low and middle-income countries is approximately twice that of high-income countries [13, 14]. In addition, the prevalence is higher in rural areas than in urban areas of low-income economies. It is a contradiction problem between the high incidence of epilepsy and the resource-constrained health services in developing countries. Epilepsy control is largely limited by relatively deficient of imaging and neurophysiological facilities, a large treatment gap, costly drugs, limited epilepsy surgery, etc [15].

The sophisticated technologies, taking magnetic resonance imaging (MRI) as an example, used in epilepsy diagnosis are highly accessible to most of the population in developed economies, whereas not or only available in big cities in some developing countries [15]. The International League Against Epilepsy (ILAE) suggests that everyone with epilepsy should have, in the ideal situation, a high quality MRI [16]. The National Institute of Health and Clinical Excellence (NICE) guidelines recommend that MRI of the brain should be the investigation of choice in children and adults with epilepsy to screen for structural abnormalities.

With the rapid development of magnetic resonance technology, especially functional MRI (fMRI), MRI is becoming more and more important in the diagnosis and management of patients with epilepsy. The primary role of MRI is to locate and define the probable anatomic epileptogenic lesions. However, the conventional MRI (cMRI) is not popularized in developing countries due to the various limitations as mentioned before, let alone the much more expensive fMRI. Under this condition, it would be particularly important for us to use the limited resources more effectively, that is to increase
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The diagnostic yield of MRI. Apart from some objective factors as the scanner and applied techniques, which are restricted by economic reasons, the experience of the radiologists who obtain and interpret the images is significant to the success of MRI in detecting abnormalities. It is reported that the diagnostic yield increases when an epilepsy dedicated MRI are performed and interpreted by an experienced radiologist [17, 18].

The causes of epilepsy comprise a heterogeneous group of disorders, rendering epilepsy diagnoses rather difficult and challenging. The primary role of a radiologist is to assess if there is a structural etiology for the patient’s epilepsy [19]. The present article focuses on the role of cMRI in the screening of epilepsy with structural abnormalities. Considering the complexity and diversity of the structural abnormalities, we propose a mnemonic “MAGIC TVs” approach to reduce false negative diagnosis and improve the diagnosis rate. Each capital letter of “MAGIC TVs” represent a kind of disease, “M” stands for mesial temporal sclerosis (MTS), “A” stands for atrophy/gliosis, “G” stands for hypothalamic hamartoma with gelastic seizures, “I” stands for infection, “C” stands for malformations of cortical development (MCDs), “T” stands for tumor, “V” stands for vascular malformations, “s” stands for Sturge-Weber syndrome (SWS). We will illustrate and depict the characteristic imaging features of “MAGIC TVs” on cMRI one by one.

The cMRI is crucial in evaluating the structural abnormalities of hippocampus. The standard MRI protocol uses coronal slices perpendicular to the long hippocampal axis for evaluation of temporal lobe abnormalities. The typical cMRI features of HS include reduced hippocampal volume, increased signal intensity on T2WI, and disturbed internal architecture [20, 21, 24]. It is established that reduced hippocampal volume correlate with lower neuron cell counts and the increased T2 signal in the HS was mainly influenced by gliosis in the dentate gyrus [25, 26]. Internal architecture changes defined as blurring of the low signal intensity streak which pathologically considered being stratum radiatum. Associated findings include temporal lobe atrophy, amygdala atrophy, dilatation of the temporal horn, loss of the gray-white matter demarcation in the anterior temporal lobe, entorhinal cortex atrophy, atrophy of the ipsilateral fornix and mammillary body and atrophy of the parahippocampal gyrus due to degeneration of afferent or efferent projections of the hippocampus (Figure 1) [21, 27].

“Dual pathology”, refers to the coexistence of MTS with lesions located outside the hippocampus, is observed in 15% of patients with surgery TLE [28]. MCDs, early ischemic lesions, such as childhood febrile convulsions, central nervous system infections, head injury, etc. After a seizure-free interval of several years, refractory recurrent seizures would occur [20-23].

The characteristics of “MAGIC TVs” on cMRI

“M”: mesial temporal sclerosis (MTS)

MTS refers to the sclerosis of mesial temporal lobe structures, such as hippocampus, amygdala, uncus and so on, of which hippocampal sclerosis (HS) is the most common one. HS is pathologically identified by neuronal loss and chronic fibrillary gliosis and is the most common pathology underlying refractory mesial temporal lobe epilepsy (MTLE). Patients with MTLE often have a history of an early initial precipitating injury, such as childhood febrile convulsions, central nervous system infections, head injury, etc. After a seizure-free interval of several years, refractory recurrent seizures would occur [20-23].

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Figure 1. HS. A. T2FLAIR image shows atrophy and hyperintensity of the left hippocampus (arrow). B. Coronal T2FLAIR image of another patient shows atrophy and hyperintensity of the right hippocampus (arrow). Brain atrophy can be seen in both images, especially ipsilateral temporal lobe atrophy with the dilatation of the ipsilateral temporal horn and the ipsilateral Sylvian fissure.
low-grade tumors (such as dysembryoplastic neuroepithelial tumours (DNET), gangliogliomas (GG)), and vascular malformations can be associated with HS and are mostly ipsilateral [28, 29]. MCDs are the most common extrahippocampal lesions. Possibly the HS may have been “kindled” by this second pathology. Thus, an exhaustive search for additional epileptogenic lesions must be performed to avoid missing another possible lesion which plays important role in the course and prognosis. It is suggested that the best surgical approach of dual pathology is to remove both the lesion and the HS [30, 31].

It is important to pay attention to bilateral HS, which occurs in approximately 10-20% of cases and may be difficult to detect on cMRI [21, 22]. Under these conditions, quantitative methods and carefully view images are useful for the diagnoses of bilateral HS.

“A”: atrophy/gliosis

Atrophy is the final common pathway for many neurologic processes including trauma, infarctions, infections and so on, and the commonest focal atrophy associated with epilepsy is due to trauma. Atrophy appears as low signal intensity on T1WI, high intensity on T2WI, and low intensity on T2FLAIR, standing for the focal or diffuse volume loss of the brain, with high intensity on T2FLAIR around the lesion, standing for the gliosis of the peripheral tissues. The accompanying signs are negative mass effect, including the deeper of the neighboring sulci and fissures, the enlargement of the neighboring subarachnoid space, the dilation of the ipsilateral lateral ventricle and the shift of middle line structure sometimes. HS is a common appearance among chronic traumatic brain injury survivors, presumably because of diffuse injury mechanisms that lead to damage of vulnerable neurons or axons in mesial temporal structures. Other refractory epilepsies can occur from focal gliosis resulting from localized contusions and intracranial hemorrhages (Figure 2) [32].

“G”: hypothalamic hamartoma (HH) with gelastic seizures

HH is a congenital non-neoplastic lesions characterized by the typical symptoms as gelastic seizures and precocious puberty and the characteristic imaging findings. The typical appear-
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Figure 3. HH. (A) Sagittal T1WI; (B) Axial T1WI; (C) Axial T2WI; (D) Sagittal and (E) coronal enhancement scans show a small round nodule at the hypothalamus region (arrows), appearing as uniformly isointense to gray matter on T1WI, isointense on T2WI, and without contrast enhancement.

Figure 4. Multiple brain abscesses. (A) Axial T1WI; (B) Axial T2WI; (C) Axial T2FLAIR and (D) axial enhancement scan show three abscesses in the frontal and parietal lobes (arrows). They appear as low intensity on T1WI, high intensity on T2WI and ring enhancement of the lesions in the right frontal and parietal lobes while the one in the left parietal lobe shows patchy enhancement. There are enormous edema areas around the lesions. The arrow heads show the typical ring sign with multiple concentric rims. The lesions with ring enhancement show high signal intensity on DWI (E). The (F) and (G) show the other three lesions with high signal intensity on DWI (arrows). (H) Shows the follow-up examination 5 months later. The lesions are smaller with focal atrophy and gliosis after effective treatment.

ances on cMRI are uniformly isointense to gray matter on T1WI, slightly hyperintense or isointense on T2WI, and without contrast enhancement (Figure 3). Atypical findings of HH on cMRI include the large size and cystic change [33].

“I”: infection

The most common cause of epilepsy worldwide is infection. An infectious etiology refers to a patient with epilepsy, rather than with seizures occurring in the acute period of infection such as meningitis or encephalitis [19]. In most situations, infectious epilepsy occurs in the aftermath of the acute infection, due to gliosis or atrophy which has been mentioned above.

Atypical organisms such as parasitic infection as neurocysticercosis, sparganum can be epileptogenic in all disease phases (Figure 4) [22, 23].

“C”: malformations of cortical development (MCDs)

MCDs, which were recognized as a major cause of drug-resistant epilepsy and developmental delay, are a heterogeneous group of abnormalities that result from the interruption of the major cerebral cortical developmental steps. MCDs can be classified into three major groups: Group I, malformations due to abnormal neuronal and glial proliferation or apoptosis, e.g.
focal cortical dysplasia (FCD) type II, tuberous sclerosis (TS), neoplastic; Group II, malformations due to abnormal neuronal migration, e.g., heterotopia; and Group III, malformations due to abnormal late neuronal migration and cortical organization, e.g., polymicrogyria (PMG) and schizencephaly [34-38].

**MCDs: FCD**

FCD are the most common group of MCDs in patients presenting with medically intractable epilepsy [34, 36]. It comprises a broad range of architectural and cytoarchitectural disorders which were divided into several subtypes reflecting the degree of severity: mMCD type I and type II, FCD type IA and IB, FCD type IIA and IIB [39, 40]. FCD type II, first described as a distinctive disturbance of cortical structure by Taylor and his colleagues in 1971 [41], was subsequently divided into two subtypes based on the presence or absence of balloon cell (type IIA and type IIB). The characteristic findings of FCD type II on cMRI include: focal thickening of the cortex, blurring of the gray/white matter junction, increased subcortical white matter signal intensity on T2WI and T2FLAIR and decreased signal intensity on T1WI. The transmantle sign, appearing as white matter signal abnormalities tapering towards the ventricle, is a radiological marker of FCD type II (Figure 5) [34, 40, 42]. Besides, abnormal cortical gyration and sulcation, focal enlargement of the subarachnoid spaces may assist in the diagnosis of FCD type II [34]. Apart from FCD type II, the other type of FCDs such as mFCD and FCD type I may be completely cryptic or may be revealed by atrophy of the dysplastic cortex and by mild blurring of the gray/white matter demarcation on cMRI [34]. FCD type I most frequently occur in the temporal lobe associated with ipsilateral HS, representing the so called “dual pathology” [43, 44]. On the contrary, FCD type II is most commonly found in extratemporal locations, especially the frontal lobe. FCDs, particularly type I, sometimes can occur accompanying with developmental tumors, such as DNET and GG [34].

**MCDs: TS**

TS is an autosomal dominant, neurocutaneous syndrome that results in multi organ hamartomas. Mental retardation, epilepsy, and adeno-ma sebaceum are characteristic features of TS. Classically, the central nervous system involve-
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ment of TS is characterized by multiple cortical and subcortical tubers and subependymal nodules along the lateral ventricles [16, 22, 45]. Tubers, most commonly located in the frontal lobes, expand the gyri they originate and are hyperintense on T2WI and iso- or hypointense on T1WI [45]. The lesions typically have a triangular configuration with the apex pointing toward the ventricle [46]. When there is calcification, the signal can differ, i.e., a lower T2 signal and a higher T1 signal. Subependymal nodules usually are calcified and seen as T1 hyper- and T2 hypointense nodules (Figure 6). T1WI is a most valuable sequence in the detection of tubers among babies who are younger than 6 months old. Tubers appear as obvious hyper-intensity on T1WI, whereas can be difficult to recognize on T2WI or FLAIR sequences due to the native high T2 signal of the unmyelinated white matter [16, 45].

MCDs: gray matter heterotopia

Gray matter heterotopia are accumulations of normal appearing neurons in abnormal locations anywhere from the subependymal region of the lateral ventricles to the cerebral cortex secondary to arrest of radial migration of neurons [42, 47]. Heterotopia is divided into periventricular (subependymal) heterotopias (PVH), subcortical heterotopias (SCH), and band (laminar) heterotopias (BH) on the basis of the location and configuration of the ectopic gray matter tissue [48]. PVH are frequently bilateral and located in close proximity to the ventricular wall, commonly in the region of the trigone and occipital horns. The typical appearances of PVH are small, round or oval nodules isointense to the normal gray matter on all MRI sequences, located in the ventricle wall or project into the ventricular lumen or lie within the periventricular white matter, and without contrast enhancement (Figure 7) [42, 47, 48]. PVH is often associated with other malformations such as cerebellar dysgenesis, corpus callosum anomalies, etc [49]. SCH are located within the subcortical or deep white matter between the ventricular ependymal surface and the cerebral cortex with various forms including nodular, curvilinear or mixed. Thin overlying cortex and shallow sulci are typical findings for SCH. BH is a rare developmental malformation seen primarily in female and may be familial with X-linked dominant inheritance. The characteristic appearance of BH is a 3-layer cake, that

Figure 7. Heterotopia. The (A-C) show PVH, (A) Axial T1WI; (B) Axial T2WI and (C) coronal T2FLAIR show bilateral PVH (arrows) in the trigone of the lateral ventricles which are isointense to the normal gray matter. The figures (D and E) show band heterotopia, (D) Axial T1WI and (E) axial T2WI show bilateral, symmetric, smooth, thick bands of gray mater outlined by thin layers of white matter and seem like a 3-layer cake.

Figure 8. PMG. (A) Saggital T1WI; (B) Axial T1WI; (C) Axial T2WI and (D) axial T2FLAIR show the excessive number of abnormally small prominent convolutions separated by shallow sulci with an irregular appearance of the cortical surface and cortical-white matter junction in the frontoparietal region (arrows).
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PMG is characterized by an excessive number of abnormally small prominent convolutions separated by shallow sulci with an irregular appearance of the cortical surface and cortical-white matter junction. The anomaly can be unilateral or bilateral; focal, multifocal or diffuse, symmetric or asymmetric. The most frequent anatomic localization (about 60%-70%) is in regions adjacent to the Sylvian fissures, particularly the posterior perisylvian area [42, 47, 50, 51]. It may be associated with other malformations such as corpus callosum agenesis or hypogenesis, cerebellar hypoplasia, periventricular or subcortical heterotopias [41, 42]. The combination of three characteristics on MR images has been used to identify PMG: abnormal gyral pattern; increased cortical thickness; and irregularity of the cortical-white matter junction due to packing of microgyri (Figure 8) [52]. Anomalous venous drainage is common in areas of dysplastic cortex, seen in up to 51% of patients with PMG [42, 51, 53].

MCDs: schizencephaly

Schizencephaly appears as a cleft filled with cerebrospinal fluid (CSF) from the subarachnoid space to the lateral ventricle. The wall of the cleft is lined with dysmorphic gray matter. The cleft most frequently locates in the frontal and parietal lobes, particularly in the areas adjacent to the central fissure, and may be small or large, unilateral or bilateral. The anomaly may be of the open-lip type, which has separated lips and a cleft of CSF extending to the underlying ventricles, or closed-lip type, in which the walls of the cleft are in contact with each other [42, 54]. Closed- and open-lip clefts are equally frequent in the unilateral cases, while open-lip clefts are commoner in bilateral schizencephaly [54]. The associated brain malformations include PMG, agenesis of the septum pellucidum, atrophy of the optic nerve, agenesis or thinning of the corpus callosum, hippocampal malformations, etc (Figure 9) [42, 54, 55].

“T”: epilepsy associated tumors

Epilepsy associated tumors constitute a distinct group of tumors that are often revealed by seizures in young patients. These neoplasms are located in the cortex (typically in the temporal lobe), slow-growing, well-defined, non-necrotic lesions and can be difficult to differentiate from MCDs [47, 48]. The common image features of these tumors include a cortical well-defined lesion, a cystic component, no peritumoral edema, no mass effect, no necrosis, and a scalloped adjacent bone [16]. Tumors can have associated FCD. Reversed triangle sign may show sometimes. The spectrum of epilepsy associated tumors comprises gangliocytoma, DNET (Figure 10), GG, pleomorphic xanthoastrocytoma (PXA), pilocytic astrocytoma and oligodendroglioma [16, 22, 23, 56].

“V”: vascular malformations

Cavernomas and arteriovenous malformations (AVMs) are the most frequent intracranial vascular malformations associated with epilepsy [57-59].
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Cavernomas are encountered more commonly in the fourth and fifth decades of life, and found most frequently in the white matter of supratentorial compartment. Cavernomas is typically a small mulberry or “popcorn-like” lesion consisting of intertwined clusters of sinusoidal vascular channels. On cMRI, cavernomas appears as a combination of high and low T1 and T2 signals with surrounding hemosiderin (Figure 11) [58].

About 22.7% patients harboring AVMs present with focal or generalized seizures. The lack of prior hemorrhage, large nidus diameter, cortical location of AVMs are particularly prone to seizure presentation [60]. The typical findings of AVMs on cMRI include flow voids, hemosiderin deposition, tangle of vessels, feeding arteries and draining veins, and accompanying aneurysm [58]. Surgical resection is recommended to AVMs patients with seizures because epilepsy control is typically excellent after surgical resection [58].

“s”: SWS

SWS is characterized by facial port wine stains in the trigeminal nerve distribution, leptomenin-
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gleal angiomatosis, glaucoma, epilepsy and mental retardation. The typical finding is the leptomeningeal enhancement on T1WI, showing the extension of the pial capillary malformation. Other classic features include enlargement of the choroid plexus, cortical calcifications, and cerebral atrophy [61, 62]. Abnormal signals in the white matter and the blurred gray and white matter interface can be observed on T2WI [62]. The characteristic findings appears as a linear low signal on MRI associated with atrophy of the involved hemisphere (Figure 12) [22].

Discussion

This article focuses on the structural etiology of epilepsy for the following reasons. From the moment that the patient presents with a first epileptic seizure, the clinician should be aiming to determine the etiology, with emphasis on those that have implication for treatment, among which structural etiology is the most important one. A structural etiology refers to structural abnormalities visible on structural neuroimaging that has a substantially increased risk of epilepsy. The imaging abnormalities assessed together with the electroclinical features could lead to a reasonable inference that the imaging findings are the likely cause of the patient’s seizures. It’s very important to detect the structural abnormalities of epilepsy by cMRI when the patient undergoes the MR scan for the first time, especially for intractable epilepsy. To analyze the structural abnormality together with electroclinical features can tell clinician whether the structural abnormality is the epileptogenic lesion or not. If it is the responsible focus, indicates the patient may be a candidate for surgery, because the majority of epileptic patients with structural abnormalities are refractory to medical therapy, rendering surgery the most effective method for controlling seizures in this subset of patients.

Structural etiologies may be acquired such as trauma, infection, or genetic such as many MCDs. Thus, they comprise a heterogeneous group of disorders, rendering the diagnoses rather difficult and challenging. Besides, the diagnoses sensitivity of structural abnormalities associated epilepsy might be low when we do not read the images systematically, especially when the lesions are subtle, the existence of dual pathology, or the radiologists are inexperienced [63]. Thus, we propose the “MAGIC TVs” approach, hoping that these “MAGIC TVs” can teach us how to assess the MR images of epileptic patients systematically so as to reduce false negative diagnosis and improve the diagnosis rate. Follow this stepwise “MAGIC TVs” approach, we can read the images comprehensively and logically to reduce omission. For example, when we assess the images of an epileptic patient, we should not be satisfied by the signs of HS, for the remainder “AGIC TVs” also should be scrutinized carefully. However, it does not mean that we should treat every “letter” equally without discrimination. We can focus on one or two diseases according to the electroclinical appearances, at the meantime, not omit other structural abnormalities that might coexist.

Conclusion

The role of cMRI in the screening of epilepsy with structural abnormalities is very important. Due to the kinds of causes and large variety of presentation, the subtle precise characterization of these images is important for the correct diagnosis and management of these patients with epilepsy. The “MAGIC TVs” approach might be helpful in reducing false negative diagnosis and improving the diagnosis rate.

Disclosure of conflict of interest

None.

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