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Role of magnetic resonance imaging for preoperative evaluation of patients with refractory epilepsy

磁共振成像對難治的癲癇症術前評估的作用

Objective. To investigate the magnetic resonance imaging characteristics of patients with refractory epilepsy and the relationship to progression to surgery.
Design. Prospective observational study.
Setting. University teaching hospital, Hong Kong.
Patients. Patients undergoing preoperative evaluation for epilepsy surgery.
Main outcome measure. Cranial magnetic resonance imaging findings, correlation with electroencephalographic results, and percentage of patients who were considered suitable candidates for surgery.
Results. Structural abnormalities associated with refractory epilepsy in 100 consecutive patients were mesial temporal sclerosis (30%), neocortical sclerosis (23%), vascular malformation (7%), neuronal migration disorders (7%), and tumours (5%). Normal brain scans were found for 28% of patients. Fourteen of 30 (46%) patients with medial temporal lobe lesions at magnetic resonance imaging were suitable candidates for surgery compared with 8/42 (19%) patients with extrahippocampal lesions (odds ratio=3.7; 95% confidence interval, 1.3-10.6; P<0.012).
Conclusion. Mesial temporal sclerosis was the most common pathology in patients with refractory epilepsy. At the Prince of Wales Hospital, for patients who have undergone a basic magnetic resonance imaging protocol and surface electroencephalography, the result of cranial magnetic resonance imaging is an important determinant for whether patients will undergo surgery.

目的：研究患上難治的癲癇症患者磁共振成像的特徵，及其與是否適合進行手術的關係。
設計：預期觀察研究。
安排：大學教學醫院，香港。
患者：進行癲癇症術前評估的患者。
主要結果測量：腦磁共振成像的結果與腦電描記術結果的關聯，以及適合進行手術的病人的百分比。
結果：在連續100名患者中，與難治的癲癇症有關的結構異常為中顳硬化(30%)、新皮質硬化(23%)、血管畸形(7%)、神經元移動紊亂(7%)和腫瘤(5%)。28%的患者腦掃描屬正常。30名在磁共振成像上有中顳突出損傷的患者中，14名(46%)適合進行手術；與之相比，42名在磁共振成像上有外海馬損傷的患者中，有8名(19%)適合進行手術(比數比 =3.7；95% 置信區間， 1.3-10.6；P<0.012)。
結論：在難治的癲癇症患者中，中顳硬化是最普遍的病理。在威爾斯親王醫院中，對於那些已進行基本磁共振成像和表面腦電描記的病人，腦磁共振成像的結果是對患者應否進行手術的重要指標。

Key words:
Epilepsy;
Magnetic resonance imaging;
Surgery

關鍵詞：
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Introduction

In Hong Kong, 20% of patients attending neurological clinics have pharmacoresistant seizures but there is limited local information about epilepsy surgery.[1] Apart from the physical effects of seizures, patients with refractory epilepsy may experience social isolation, lost educational opportunities, loss of independence, and discrimination in employment. Surgery is an established treatment for

patients with partial epilepsies refractory to drug treatment—approximately 60% of patients become free of seizures after surgery, with even higher success rates reported for certain subgroups.[2-4]

In addition to radiological abnormalities, the identification of a surgical candidate requires concordant clinical, psychological, and electroencephalographic (EEG) confirmation. Magnetic resonance imaging (MRI) allows preoperative targeting of the epileptogenic substrate.[5-10] Magnetic resonance imaging is more sensitive than computed tomography (CT) in detecting structural abnormalities because of its superior soft tissue contrast multi-planar imaging capability and lack of beam hardening artefacts.[11,12] While the mechanisms by which structural lesions induce seizures are unclear in most instances, MRI implicates a particular region as the source of seizures. The epileptogenic zone is most commonly located in the medial temporal lobe and the structures involved include the hippocampus, amygdala, dentate, and parahippocampal gyri. Although, historically, MRI protocols were designed to detect the presence of structural pathology in this region, lesions beyond these mesial structures can also give rise to refractory epilepsy. The objective of this study was to determine the MRI features in Chinese patients with refractory epilepsy undergoing assessment for surgical management. The association between the neuroradiological lesion and likelihood of the patient progressing to surgery was also studied.

Methods

Clinical information and brain MRI scans of patients referred to the epilepsy surgery programme of the Prince of Wales Hospital in Hong Kong—a regional centre that accepts referrals from other hospitals—were prospectively collected. Patients were considered potential candidates if they had refractory and disabling seizures despite adequate trials of two appropriate anti-epileptic drugs. International League Against Epilepsy classification of epilepsies and epileptic syndromes was used for determining the clinical diagnosis.[13]

The following exclusion criteria applied:
(1) presence of generalised epilepsy syndrome;
(2) presence of systemic illness such as neoplasm, or renal or liver failure;
(3) coexisting moderate-to-severe mental retardation; and
(4) active mental illness requiring treatment with psychoactive drugs.

Magnetic resonance imaging results were reviewed by two experienced neuroradiologists. Magnetic resonance protocols consisted of axial T1-weighted and T2-weighted images (high resolution, 2 mm thickness with no gap, [512x512]) using a 1.5 Tesla Philips Gyroscan ACS-NT (Philips Medical System, Best, The Netherlands). The hippocampus lies in a plane which is seen on a midline sagittal section as the line joining the splenium of the corpus callosum to the postero-inferior frontal lobe. Oblique coronal T2-weighted images of the hippocampus were therefore also performed for all patients. Mesial temporal sclerosis was identified by one of two major MRI findings—hippocampal atrophy and increased signal intensity of the hippocampus on T2-weighted images. The most recent MRI studies for scrutinising these features using visual inspection have achieved sensitivities of 87% to 100%.[14,15] Other secondary MR features include temporal horn dilatation, loss of hippocampal internal architecture, decreased hippocampal signal on T1-weighted images, poor parahippocampal grey-white matter definition, and loss of hippocampal interdigitations.

All patients had scalp EEGs, obtained using Nicolet BMSI (Nicolet Biomedical Inc, Madison, US) or Telefactor digital video-EEG (Telefactor, West Cohshohocken, US), and read by one of the authors. All patients with focal lesions at MRI went on to have video-EEG. Interictal or ictal epileptic discharges arising from the region with a lesion identified by MRI were regarded as concordant MRI and EEG evidence.

Patients who were considered suitable candidates went on to have functional brain assessment with the amylobarbitone (Wada) test before surgery. This involves injection of sodium amylobarbitone into the internal carotid artery, which inactivates the regions supplied by this vessel. Language representation and memory performance of the unaffected side of the brain can then be tested. The results were used to further establish lateralised temporal lobe dysfunction and to predict the likelihood of postoperative language or memory decline.

Magnetic resonance imaging lesions were divided into the following three categories:
(1) normal MRI;
(2) evidence of medial temporal lobe lesions; and
(3) evidence of extrahippocampal lesions.

Patients with extratemporal and lateral temporal neocortical MR abnormalities were included in the last group.[2] The presence of MRI lesions were used to investigate the relationship between MRI abnormalities and eligibility for surgery. P values of less than 0.05 were considered statistically significant.

Results

One hundred consecutive adult patients (45 men, 55 women) underwent presurgical evaluation. The age range was 15 to 50 years (mean, 33 years). The diagnostic yield from MRI was 72%; scans were normal for 28 patients. Evidence of mesial temporal sclerosis was found in 30 patients (bilateral in three patients). Other abnormalities included neocortical sclerosis, low grade tumours, neuronal migration disorders, and vascular malformations (Figs 1 to 5). The MR findings are summarised in Fig 6.

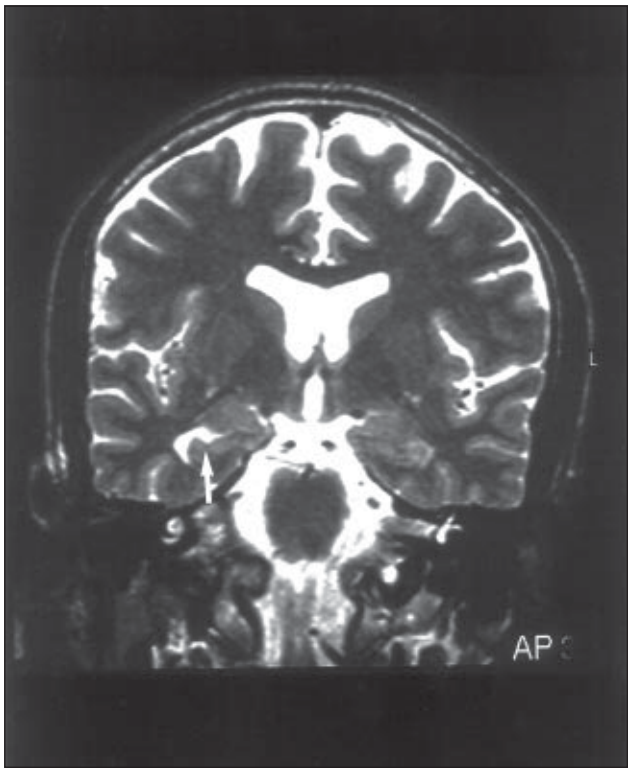

Fig 1. Oblique coronal T2-weighted cranial magnetic resonance imaging showing right hippocampal atrophy with temporal horn dilatation in a patient with refractory temporal lobe epilepsy

Electroencephalograms with surface electrodes were non-localising or non-lateralising for 50% of patients, concordant for 28%, multifocal for 16%, and disconcordant for 4%.

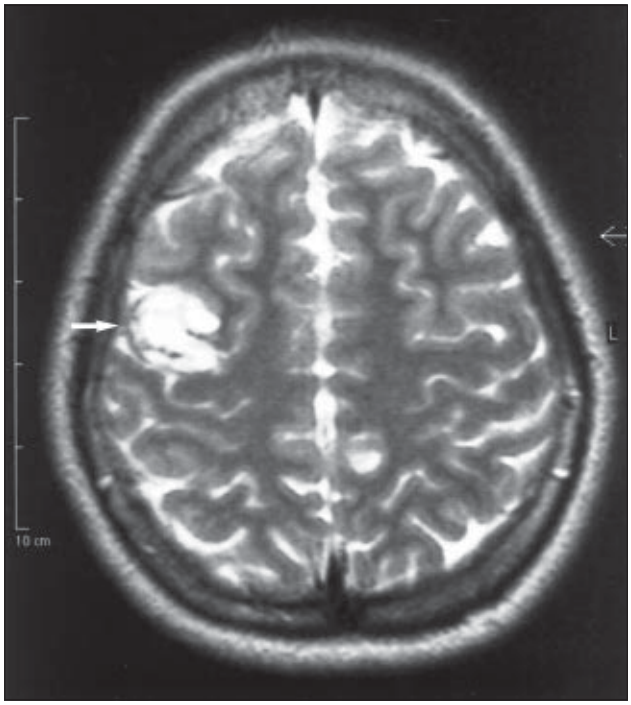

Fig 3. Well-circumscribed right frontal lobe tumour with no surrounding oedema on axial T2-weighted magnetic resonance imaging—postsurgical histology revealed dysembryoplastic neuroepithelial tumour

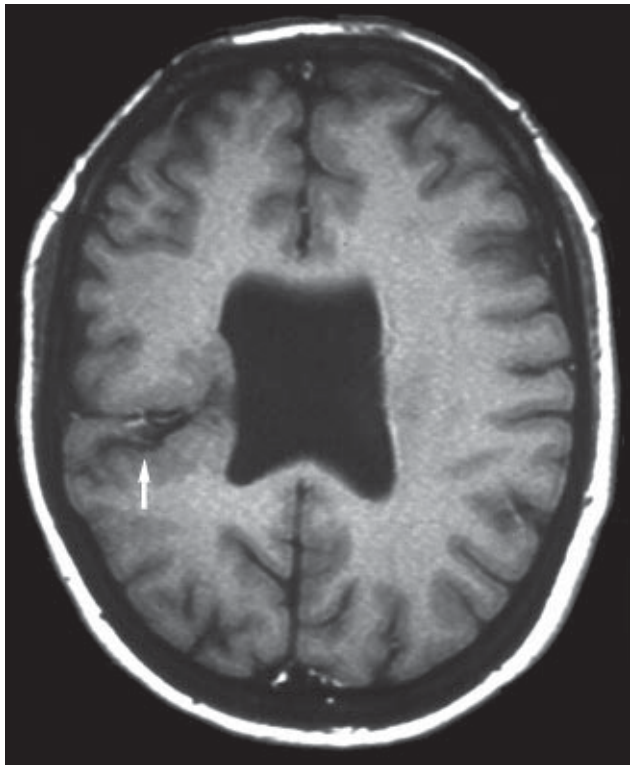

Fig 2. Neuronal migration disorder. Axial T1-weighted magnetic resonance imaging in a patient with schizencephaly exhibiting grey matter lined cleft extending from the ventricular surface to the pial surface of the brain

Twenty-two patients with concordant clinical, EEG, and MRI data were considered suitable for surgery; of these, 20 have been operated on and two have refused surgery. Using EEG information from scalp video-telemetry, 14/30 (47%) patients with MR evidence of medial temporal lobe lesions were regarded as candidates for surgery, whereas the figure was only 8/42 (19%) for those with extrahippocampal lesions (odds ratio=3.7; 95% confidence interval, 1.3-10.6; P<0.012). None of the patients (n=28) with normal MR scans were operated on.

Discussion

This series shows that mesial temporal lobe epilepsy (MTLE) is the most common form of epilepsy syndrome causing intractable seizures. The second most common finding was neocortical sclerosis and regions of encephalomalacia, which follows a number of insults to the central nervous system, including infarction, encephalitis, trauma, and inflammation. Low-grade tumours were found in six patients. Similar to results from other epilepsy centres, these consisted of low-grade lesions such as oligodendroglioma and dysembryoplastic neuroepithelial tumours. Tumours from oncological centres show a larger range of histological types with more aggressive grading.

Magnetic resonance imaging can identify structural anomalies that are associated with epilepsy. A radiological abnormality alone, however, may not represent the epileptogenic zone as it may be incidental and seizure onset

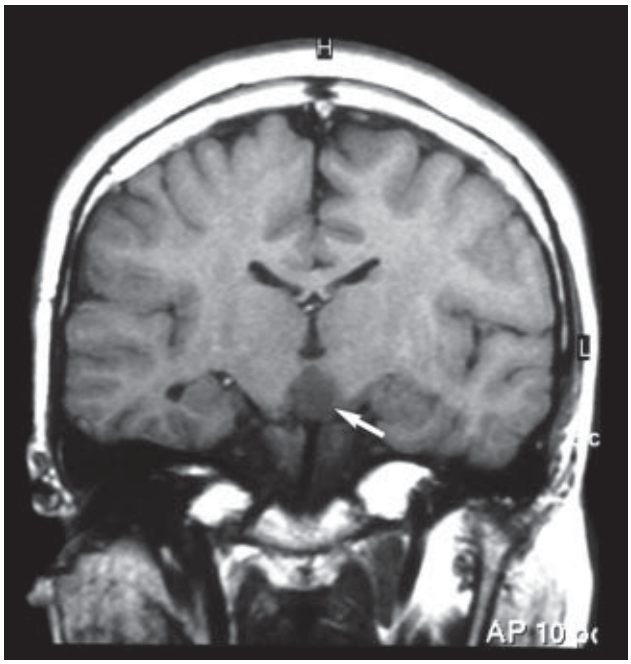

Fig 4. Hypothalamic hamartoma on coronal T1-weighted magnetic resonance imaging in a patient with gelastic seizures (outbursts of laughter), which is associated with this lesion

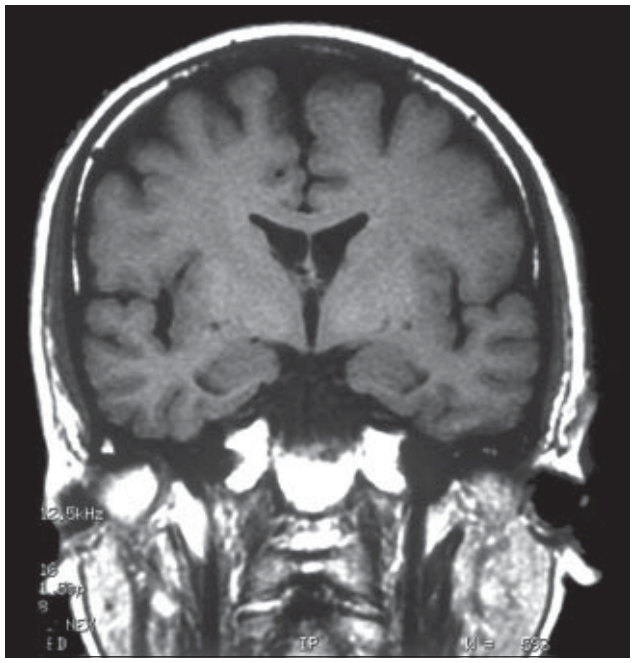

Fig 5. Normal coronal T1 cranial magnetic resonance imaging for comparison

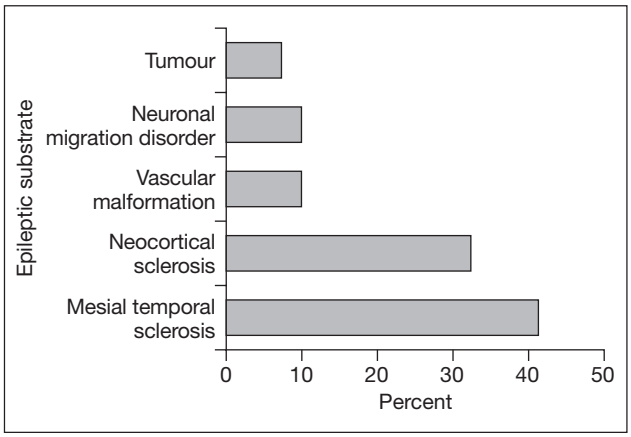

Fig 6. Magnetic resonance imaging abnormalities in patients undergoing preoperative assessment

may arise from other areas. The EEG therefore remains essential for demonstrating electrically excitable tissue.[16,17] For patients with evidence of a lesion outside the temporal lobe or with diffuse pathology such as post-meningitic encephalomalacia, ictal scalp EEG recordings are often poorly localising. Candidates would require invasive EEG using subdural grids and/or depth electrodes. The more uncertain the source of epileptic activity, the more extensive coverage is required, which would lead to higher risk of complications (implantation of intracranial electrodes has a complication rate of 4%).[18-20] In many Asian countries, the facilities and personnel required are not available for prolonged invasive EEG monitoring or functional imaging. Even with these additional investigations, the outcome after surgery is generally poorer compared with those patients with MTLE.[21]

None of the patients with normal MRI were operated on. While this is, in part, a reflection of our hospital practice, it is commonly accepted that absence of a focal lesion renders the work-up more difficult and the prognosis for a good outcome is poorer. This does not imply that patients with a normal MRI should be automatically excluded from surgery, as alternative MRI techniques such as T2-reflexometry, MR volumetric studies and proton spectroscopy may uncover corroborating evidence. The optimum protocol includes an oblique coronal high resolution T2-weighted sequence, using 3-mm thin sections. To date, the imaging sequence should include oblique coronal high resolution T1-weighted volume data (spoiled gradient recalled echo acquisition with 1.5 mm partition size) through the whole brain, which allows reformatting in any plane, measurement of hippocampal volumes, and co-registration with functional data. A coronal fluid attenuated inversion recovery (FLAIR) sequence is also used to increase conspicuity of high T2 signal cortical lesions adjacent to the cerebrospinal fluid space. Quantitative assessment of the hippocampal volume have slightly increased sensitivity but the commonly used quantitative method is demanding and time-consuming,[22,23] and is impractical for routine usage. Measurement of T2-relaxation time may also be quantified and this improves the sensitivity for hippocampal abnormalities.[24] With functional imaging techniques, interictal positron emission tomography may reveal potential epileptogenic areas but is not readily accessible; single photon emission CT is more widely available but requires ictal images. In many established centres, further presurgical assessment may be terminated for patients with normal high resolution MRI and non-localising electroclinical syndrome.

Since the presence of focal and, in particular, medial temporal lobe pathology increases the chances of progression to successful surgical treatment, high resolution

MRI should be performed early in the presurgical evaluation. This would reduce additional stress and inconvenience to patients and optimise the use of resources. Epilepsy centres, however, should not rely on the results of a single test as this would restrict access to surgery. The introduction of semi-invasive/intracranial EEG and more advanced imaging sequences would allow more patients with intractable seizures to benefit from surgery.

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