Correlation of MRI and histopathology in epileptogenic parietal and occipital lobe lesions

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Summary

Introduction: To analyze the diagnostic accuracy of MRI in patients undergoing parietal and occipital lobe epilepsy surgery.
Methods: In a retrospective study, we analyzed MRI scans and neuropathology reports of 42 patients who had undergone resective epilepsy surgery in the parietal and occipital lobe between 1998 and 2003. We evaluated, whether lesions were precisely characterized by MRI and whether lesion characterization allowed to estimate postsurgical seizure outcome.
Results: Within the categories epilepsy associated tumors, focal cortical dysplasias, vascular malformations, scarring, and others, MRI was concordant with histopathology in 36 of 42 (86%) lesions. Among the discordant lesions, one lesion was re-classified following MRI—histopathology synopsis, another two lesions represented new tumor entities (angiocentric neuroepithelial tumor, isomorphic astrocytoma) which have been described recently. Seizure freedom (Engel class I) one year following surgery was achieved in 25 patients (60%). Seizure outcome was different for lesion categories (Engel class I: epilepsy associated tumors, 62%; focal cortical dysplasias, 71%; vascular malformations, 75%; scarring, 40%), and was unchanged if no lesion was found on preoperative MRI.
Conclusion: If MRI and histopathology are discordant, not only the MRI findings may be debatable. MRI lesion detection is important, since chance of seizure freedom is low if no lesion is detected.
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Introduction

Parietal and occipital lobe seizures are relatively rare accounting for less than 10% of all partial seizures reported from comprehensive surgical series. In parietal lobe seizures, the most common subjective sensations or auras are paresthesias, dysesthesias or pain; additional parietal lobe symptoms include sexual sensations, apraxias, and disturbances of body image. Conversely, much of the parietal lobe is clinically silent in terms of seizure manifestation. Objective parietal lobe seizure manifestations (e.g. dominant parietal lobe: disturbances of language functions) are rare and most objective manifestations reflect seizure spread outside the parietal lobe. The majority of patients with occipital lobe seizures describe visual phenomena (elementary hallucinations, illusions including metomorphopsia and dyschromatopsia, viual loss) as the initial ictal manifestation.[1] However, these phenomena may also be elicited in temporo-occipital and anterior temporo-mesial structures.[2] Moreover, ictal discharges originating in the occipital lobe seizures usually rapidly spread into anterior areas.[3]

Localizing of the seizure onset was difficult and frequently erroneous in the pre-MRA area,[4] and magnetic resonance imaging (MRI) has become an important tool for localization of the seizure onset zone. Congruity of a MRI lesion, ictal surface EEG focus, and seizure semiology may allow epilepsy surgery without further invasive diagnostic procedures. In patients, in whom seizure semiology and scalp EEG recordings are inconclusive, a MRI lesion may generate a hypothesis for intracranial electrode implantation. Whether a lesion is detected by MRI, depends on the quality of the MRI scan and the expertise of the MRI reader.[5] When a lesion is detected, the risk of invasive presurgical work-up and potential epilepsy surgery must be weighted against the estimated chance of seizure freedom following surgery. In this context, two questions are of interest: (1) Are the lesions correctly characterized by MRI? (2) Does the seizure outcome following surgery depend on the type of the MRI lesion?

In the present study, we retrospectively analyzed the MRI and neuropathology reports of patients with parietal and occipital lobe epilepsies who had undergone resective epilepsy surgery between 1998 and 2003.

Methods

Study group

The study group comprised all patients with drug-resistant parietal and occipital lobe epilepsies who had a high resolution MRI and were operated following presurgical work-up at the University of Bonn Medical Center between 1998 and December 2003.

MRI

MRI was performed using 1.5 or 3 Tesla systems (Gyroscan ACS-NT, Gyroscan NT-Intera, Gyroscan Intera, Gyroscan 3 T Intera, Gyroscan 3T Achieva, Philips Medical Systems, Best, The Netherlands) according to a standardized protocol that has been described previously.[6,7] In brief, we first acquired a sagittally oriented 3D-T1-weighted gradient echo sequence with 1 mm^3 isotropic voxels. Displaying the sagittal 3D-T1-weighted gradient echo sequence, the next two sequences, an axial FLAIR fast spin echo and an axial T2-weighted fast spin echo sequence with a slice thickness of 5 mm and an interslice gap of 1 mm were angulated either along the length axis of the hippocampus or the anterior comissure—posterior comissure-line (a.c.—p.c.-line). How the slices were angulated, depended on seizure semiology and EEG findings, and was decided after patient's history was reported from the transferring epileptologist.

Next, coronal FLAIR fast spin echo (slice thickness 3 mm), coronal T2-weighted fast spin echo (slice thickness 2 mm), and coronal T1-weighted inversion recovery sequences (slice thickness 5 mm, interslice gap 0.5 mm) were obtained. If axial sequences were angulated along the hippocampal length axis, slice orientation was perpendicular to axial slices. If axial sequences were angulated along the a.c.—p.c.-line, coronal FLAIR sequence was tilted along the brain stem, but the coronal T2-weighted sequence perpendicular on hippocampal length axis. If a lesion suggestive for a tumour was detected, axial and/or coronal T1-weighted spin echo sequences (slice thickness 5 mm, interslice gap 1 mm) before and following Gd-DTPA injection were acquired.

Further pre-surgical work-up

Further pre-surgical work-up included vidoe-EEG-monitoring in all patients, whereas other investigations (ictal and interictal SPECT, Subtraction ictal SPECT co-registered to MRI (SISCOM), PET, depth electrodes, subdural grid or strip electrodes) were performed as deemed necessary in each patient.[8]

Surgery

Surgical approaches targeted to resect the epileptogenic zone while sparing eloquent cortex. The size and location of the epileptogenic zone was usually determined following the implantation of subdural

grid electrodes in 32 patients. Extended lesionectomies were performed in 34 patients.

Histopathology

Surgical specimens submitted for neuropathological evaluation were microscopically analyzed using haematoxylin—eosin (HE), haematoxylin—eosin—luxol-fast-blue (HE—LFB) and Nissl staining. Immunohistochemical studies included reactions with a monoclonal antibody directed against Vimentin (V9, Dako), polyclonal antibodies directed against glial fibrillary acid protein (GFAP), a monoclonal antibody directed against human neurofilament protein (2F11, Dako), a monoclonal antibody directed against neuronal specific enolase (NSE), a monoclonal antibody to synaptophysin (SY 38, Dako), a monoclonal antibody directed against Ki67 (MIB1, Dako), and a monoclonal antibody directed against CD 34 (QBend 10, Immunotech) using standard protocols and the avidin-biotin-peroxidase complex with diaminobenzidine as chromogen.[9]

Postsurgical outcome

Patients were re-examined at routine intervals three months, six months and one year following surgery. Seizure outcome after one year was determined according to Engel's classification.[10]

Results

Study group

The study group included 42 patients (20 males) with a mean age of 27 (7—50) years, who had suffered from drug resistant epilepsies for 2—42 years. Forty patients were studied with 1.5, two patients with 3 Tesla systems.

MRI, histopathology, and postsurgical outcome (Table 1)

With respect to the histopathological diagnoses we divided the lesions into the following categories(Table 1):

1. Epilepsy-associated tumors (n = 13)
   Five gangliogliomas and five dysembryoplastic neuroepithelial tumours (DNTs) were diagnosed correctly. One ganglioglioma was misclassified on MRI as focal cortical dysplasia. One ''MRI ganglioglioma'' each was histopathologically classified as angiocentric neuroepithelial tumour (ANET) (Fig. 1) and isomorphic astrocytoma (IA) (Fig. 2), respectively. Both are new entities, which have been described recently.[11—14] Seizure outcome was excellent (Engel class I) in eight patients (62%).

2. Focal cortical dysplasias (FCDs) (n = 16)
   According to the classification of Palmini and Lüders there were 14 FCDs with balloon cells (FCD IIb), one FCDs without ballon cells (FCD IIa), and one mild malformation of cortical development (mMCD).[15,16] On MRI, we described 11 FCD IIb and 5 FCD without further classification as these lesions lacked the subcortical hyperintensity tapering towards the lateral ventricle suggestive of FCD IIb.[17] One FCD diagnosed by MRI was histopathologically classified as mMCD, which seems debatable since it was a circumscribed cortical signal hyperintensity and not only a blurring of the grey/white matter interface (Fig. 3). One year following surgery, 11 patients (69%) were seizure free (Engel class I).

3. Vascular malformations (n = 4)
   While two cavernomas were diagnosed correctly, one small lesion was considered to be a cavernoma on MRI but histopathologically classified as arterio-venous malformation (AVM). One occipital atrophic lesion with calcifications and

Table 1 Lesion categories, discordant MRI diagnoses, and seizure outcome one year following surgery

Lesion category	n	Discordant MRI diagnosis	Outcome/Engel I
Epilepsy-associated tumours	13	3[a]	8 (62%)
Focal cortical dysplasias	16	1[b]	11 (69%)
Vascular malformations	4	2[c]	3 (75%)
Scars	6		3 (50%)
Other	1		0
No lesion	2		0

[a] MRI: One ganglioglioma was diagnosed instead of an ANET (see Figure 1), One ganglioglioma instead of an isomorphic astrocytoma (see Figure 2), One FCD instead of a ganglioglioma.
[b] MRI: One FCD was diagnosed instead of a mMCD (see Figure 3).
[c] MRI: One cavernoma was diagnosed instead of an AVM, 1 Sturge-Weber angiomatosis instead of an unknown lesion.
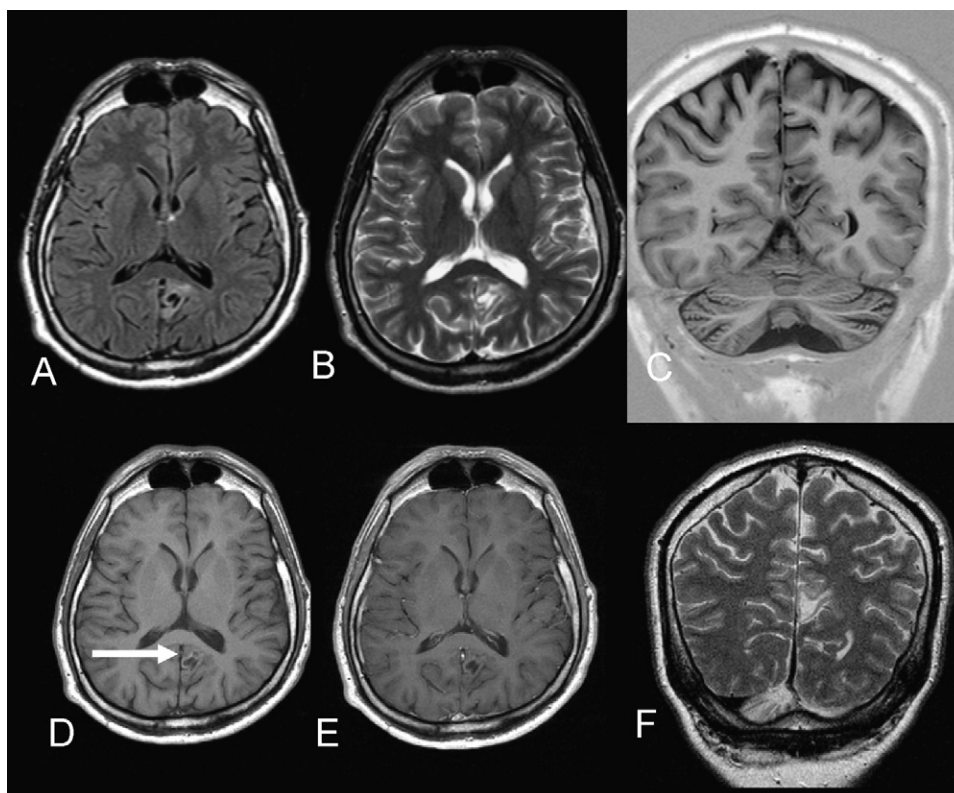
Figure 1 Angiocentric neuroepithelial tumour (ANET). Axial 5 mm thick FLAIR (A), T2-weighted TSE (B), T1-weighted SE (C), contrast enhanced T1-weighted SE (D), coronal 5 mm thick IR (E), and 2 mm thick T2-weighted TSE images. Note a cortical and subcortical lesion within the left cuneus with a cystic component in its centre. The cortex is hyperintense on unenhanced T1-weighted images (arrow in D), the lesion does not enhance GD-DTPA (E).

without a clear MRI diagnosis was considered to represent a circumscribed Sturge Weber angiomatosis although the patient had no (trigeminal) nevus flammeus. This patient and both patients with cavernomas were seizure free one year following surgery (75%).

4. Gyral scars (n = 6)

Six gyral scars were diagnosed correctly. Three of the six (50%) patients achieved seizure freeness one year following surgery. Initially, one scar was histopathologically considered as FCD IIa. Since MRI signal changes remote from the resected lesion itself indicated a more widespread and rather destructive process (Fig. 4), extended immunohistochemical investigations with antibodies against NeuN, synaptophysin, glial fibrillary acidic protein and CD68 were performed in additional tissue specimens of the lesion, which was re-classified as gyral scar.

5. Other

One HIV-negative African woman with a history of seizures for three years had a contrast-enhancing cortical lesion along the left intraparietal sulcus surrounded by a large oedema which was suspicious on an infection and correctly classified

as tuberculosis. She did not become seizure free following operation and drug therapy.

6. No lesion

Two patients without lesions on MRI were operated on electrophysiological basis, only. Both specimens were histopathologically unrevealing, and none of the patients became seizure free.

Discussion

This series of patients with drug-resistant parietal and occipital lobe epilepsies shows a high concordance (86%) between MRI and histopathological diagnoses: Within the category epilepsy-associated tumors all five DNTs were diagnosed correctly. One lesion was considered a FCD on MRI but histopathologically represented a ganglioglioma. If MRI lesions do not have intracortical cysts and do not enhance Gd-DTPA it is difficult to distinguish both entities. Histopathologically, a ganglioglioma is sometimes surrounded by dysplastic cortex. Moreover, both entities have common moleculargenetic alterations (increased incidence of polymorphisms in TSC2 gene)
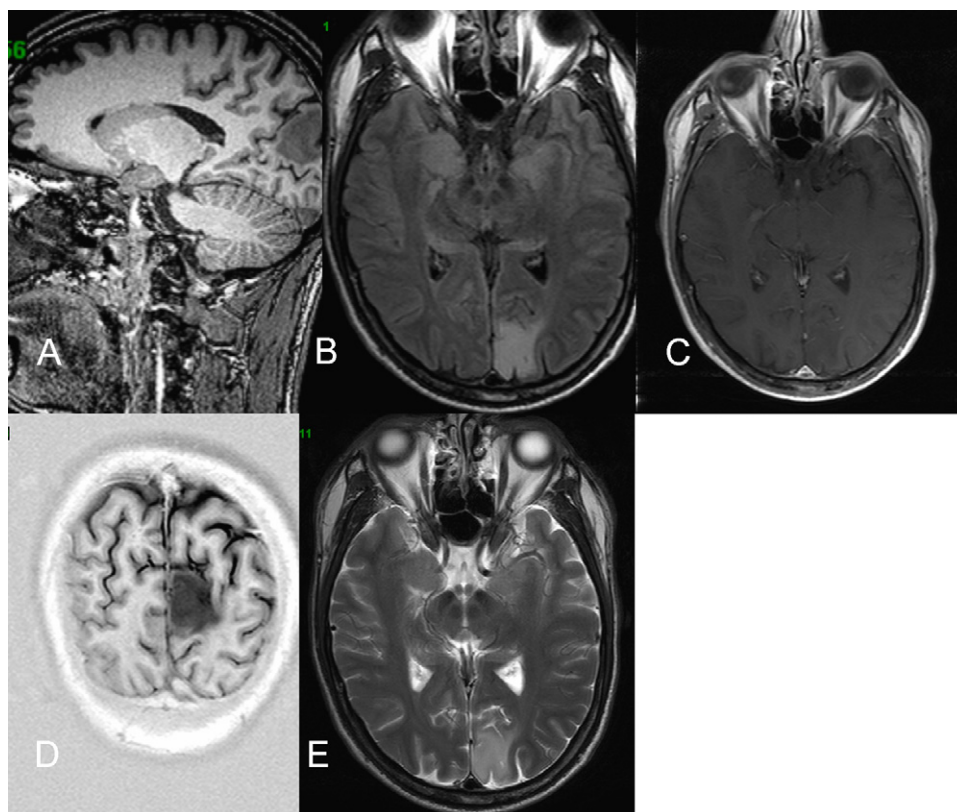
Figure 2 Isomorphic astrocytoma. Sagittal 1 mm thick 3D-T1-weighted MDEFT (A), axial 5 mm thick contrast enhanced T1-weighted SE (C), and T2-weighted TSE (E) images, coronal 5 mm thick IR images (D). Note a homogenous lesion in the left cuneus which is predominantly located in the subcortical white matter. The lesion is relatively hypointense on T1-weighted and hyperintense on FLAIR and T2-weighted images. It does not enhance GD-DTPA (C).

and a FCD is sometimes considered as precursor lesion of a ganglioglioma.[18] Accordingly, Barkovich et al. consider DNTs and gangliogliomas as neoplastic lesions within the category "malformations due to abnormal neuronal and glial proliferations".[19] Two lesions were considered as gangliogliomas while the neuropathologist classified them as angiocentric neuroepithelial tumour (ANET) and isomorphic astrocytoma, respectively. The ANET is a recently described epilepsy associated tumor (together 18 cases) with histopathological features of infiltrating astrocytoma and ependymoma. It has a specific MR imaging appearance consisting of a cortical/subcortical location, a handle-like extention towards the lateral ventricle and a ribbon-like cortical hyperintensity on T1-weighted images. The tumor is hyperintense on T2-weighted images, has no calcifications, and does not enhance Gd-DTPA.[11,12] The isomorphic astrocytoma (around 20 cases known so far) is an infiltrating tumour with a low cellularity and "no" mitoses. Accordingly, it is relatively hypointense on T1-weighted and hyperintense on T2-weighted images. The cortical/subcortical tumor has no calcifications and does not enhance Gd-DTPA.[13,14] Within the category focal cortical dysplasias, 11 FCD IIb

exhibited a typical MR imaging appearance consisting of a mild cortical hyperintensity and a distinct funnel-shaped subcortical hyperintensity tapering towards the lateral ventricle.[17] In three FCD IIb a mild subcortical hyperintensity was less apparent. One lesion was histopathologically classified as FCD IIa, one as mMCD. On MRI, both lesions showed a circumscribed cortical hyperintensity on FLAIR sequences indicating that the correlation between histopathology and MRI is not close.

Among the vascular malformations two cavernomas with signal characteristics indicating loculated areas of hemorrhage and thrombosis of varying age surrounded by areas of hemosiderin-stained brain were easily appreciated on T2-weighted images. Another lesion with a diameter of 1 cm had the same signal characteristics, no tubular flow void structures were seen in the vicinity. Whether the occipital atrophic and calcified lesion truly represents a Sturge-Weber angiomatosis remains unclear: The association of occipital calcifications and epilepsy has been described by numerous authors, and up to 77% of patients with this picture have celiac disease.[20—23] However, in contrast to our case, calcifications are usually bilateral, and there is no
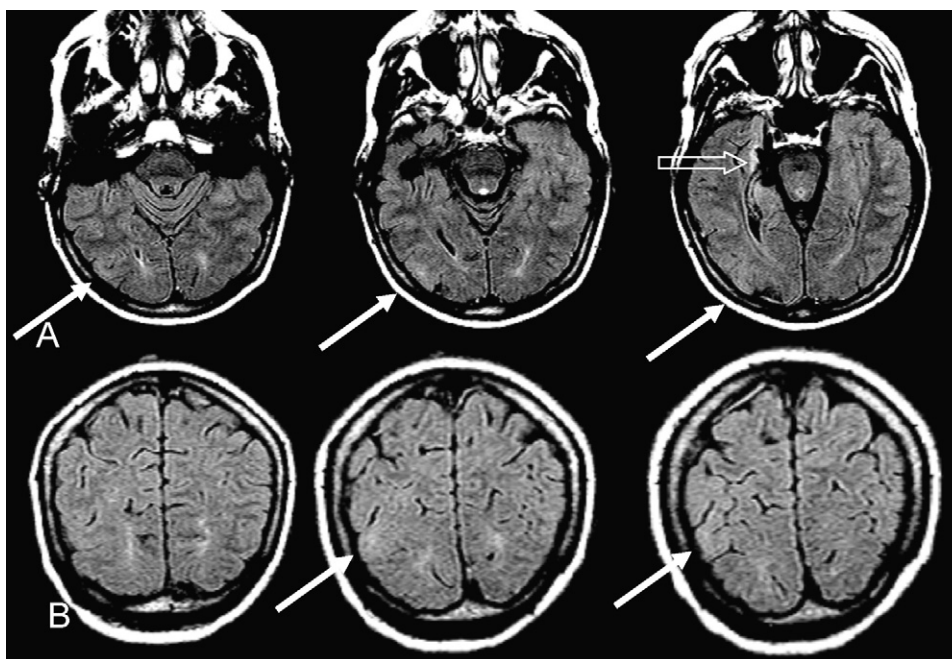
Figure 3 Axial 5 mm thick (A) and coronal 3 mm thick (B) FLAIR TSE images show a circumscribed cortical hyperintensity without subcortical signal alterations (arrow). These MRI findings are compatible with a FCD IIa but untypical for an mMCD in which blurring of the grey/white matter interface is a usual finding. Note also that this lesion was overlooked nine years ago when the patient underwent right-sided selective amygdalohippocampectomy due to a presumed seizure onset zone in the right hippocampus (hollow arrow in A).

atrophy and no contrast enhancement.[23] Our patient had no apparent celiac disease but whether patients with occipital calcification and without apparent celiac disease are carriers of a latent form of the disease is also a matter of debate.[23]

Gyral scars are typically recognized due to a focally widened subarachnoid space and a hyperintense and atrophic cortex on long TR/long TE sequences. Due to nulling of the CSF signal, this pattern is best appreciated on FLAIR MRI perpendicular to the brain surface. In this series, one lesion with this pattern was initially considered as FCD IIa.

However, since MRI showed atrophic and on FLAIR sequences hyperintense cortex remote from the resected tissue itself, further immunohistochemical investigations were performed in extended portions of the lesion, which was re-classified as gyral scar.

There are several papers about parietal and occipital lobe epilepsies in the literature, that mainly focus on seizure semiology, the localizing value of different imaging modalities, and seizure outcome.[1,3,4,24—31] The proportion of developmental lesions (malformations of cortical development, cortical dysplasias), epilepsy-associated tumors,
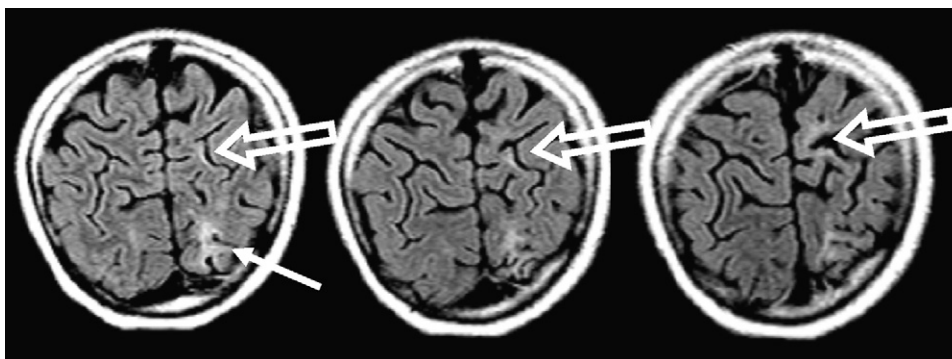

Figure 4 Coronal 3 mm thick FLAIR TSE images show an occipital lesion which was initially histopathologically classified as FCD IIa (arrow). The atrophic and hyperintense cortex also above the parieto-occipital fissure is suggestive of a more widespread process with gyral scarring (hollow arrow). Extended immunohistochemical investigations led to the diagnosis gyral scar.

vascular lesions, and "defects" (scarring, trauma) is similar to our series,[28,29] the proportion of seizure free patients higher for patients with epilepsy associated tumours than developmental abnormalities.[26,30,31] However, new (neuropathological) classification schemes and tumor entities as well as advances in MRI make a direct comparison between these series of the late 1990s and ours difficult.

If we consider these advances during the past years (e.g. 3 Tesla scanners) and the debatable cases in this series (see Figs. 3 and 4), we believe that characterization of epileptogenic lesions has to rely on both, MRI and histopathology.

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