MR of Brain Involvement in Progressive Facial Hemiatrophy (Romberg Disease): Reconsideration of a Syndrome

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PURPOSE: To gain further insight into the pathogenesis of progressive facial hemiatrophy, a sporadic disease of unclear etiology characterized by shrinking and deformation of one side of the face. **METHODS:** We investigated possible brain involvement. MR of the head and face was performed in three female patients with progressive facial hemiatrophy. The central-nervous-system findings were correlated to a clinical protocol and a review of the literature. **RESULTS:** One patient with epilepsy had abnormal brain findings confined to the cerebral hemisphere homolateral to the facial hemiatrophy. These consisted of monoventricular enlargement, meningocortical dysmorphia, and white-matter changes. **CONCLUSIONS:** These MR findings, and corresponding neuroradiologic data disclosed by the review, indicate that homolateral hemiatrophy occasionally occurs in a subgroup of patients with progressive facial hemiatrophy. The MR features do not seem consistent with an underlying simple or nutritive atrophic process. We propose chronic localized meningoencephalitis with vascular involvement as a possible underlying cause of the occasional brain involvement in progressive facial hemiatrophy.

Index terms: Face, abnormalities and anomalies; Face, magnetic resonance; Brain, magnetic resonance; Head, magnetic resonance

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Progressive facial hemiatrophy (PFH, also known as Romberg disease and Parry-Romberg syndrome), is a sporadic, but not extremely rare, and puzzling disease. It is characterized by progressive and self-limited shrinking and deformation of one side of the face, which involves different tissues and which may result in crippling final states (1–3). The onset of PFH usually occurs during the first 2 decades but has been reported to occur in patients in their 60s (4). Hair discoloration or circumscribed alopecia often precede the always-occurring progressive lowering of the skin level in unilateral areas of variable distribution. These areas do not cross the midline and may resemble innervation fields of cranial nerves, a resemblance that thus gave rise to Romberg's concept of a neural origin of the atrophy ("trophoneurosis") (1). The subcutaneous fat seems to be responsible for most of the substantial loss (2, 3). Scar-like cutaneous changes, circumscribed osteoporosis, bone deformation, and peripheral cranial nerve dysfunctions also may be present. Epilepsy has been repeatedly reported in patients with PFH (2, 5–8), but this finding was discussed extremely controversially. Although such central nervous system (CNS) symptomatology was regarded as unrelated and purely coincidental by some authors (3), suspected CNS lesions were regarded as a potential cause of the facial changes even in patients without CNS symptoms by others (2, 9). In some series high incidences of abnormal neuroradiologic brain findings have been reported with regard to small samples of PFH patients (9, 10), but no correspondence between abnormalities and physical findings could be established (10). Magnetic Resonance (MR) examination of patients with PFH seemed a suitable modality for further characterization of

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possible CNS pathology in these patients. A correlation of our patient with abnormal CNS findings in MR, together with a review of the literature, supports a potential common etiologic correlation between the CNS and facial hemiatrophy.

Patients and Methods

We examined three women aged 27, 29, and 61 years (M.L., H.S., and H.U.) with a diagnosis (see Discussion) of PFH. All had left-sided, acquired, and progressive facial atrophy. Although the onset of the facial symptoms was either in the second or third (M.L.) decade, the duration of PFH differed (4, 13, and 47 years for M.L., H.S., and H.U., respectively). One patient (H.U.; Fig 1A) had neurologic symptoms of CNS involvement, including complicated left-sided migraine with right-sided hemiparesis, hemianopia, and aphasia since the age of 15 years (1 year after onset of symptoms). A clearly progressive course of medically partially refractory seizures (right-sided focal motor, complex partial, and rare secondary generalized seizures) was experienced after the age of 50. On neurologic examination she had mild aphasia, mild right hemiparesis, and mild cognitive deficits. Another patient (H.S.) reported rare episodes of paresthesia in the region of the facial alterations, which occasionally spread to the homolateral limbs. These paresthesias were judged to be not clearly indicative of CNS involvement.

All patients underwent MR examinations of the cranium and face. Two patients were examined on a 0.5-T system (patients H.U. and H.S.) and one patient on a 1.5-T system (patient M.L.). The examinations included axial T2- and axial and coronal T1-weighted images before and after administration of contrast medium (0.1 mmol/kg gadopentetate dimeglumine; Magnevist, Schering, Berlin, Germany). The images were analyzed cooperatively by three of us (K.T., S.F., and H.H.); the present study is confined to the cranial findings.

A systematic review of neuroradiologic findings from patients with progressive courses of facial hemiatrophy was performed. All identified reports of abnormal skull radiography findings, and of normal or abnormal pneumoencephalographic, computed tomographic (CT), and MR findings were reviewed for the consideration of CNS symptoms (epilepsy, hemiparesis, hemianopia, and unilateral cerebellar coordination deficits). Normal, abnormal homolateral, and abnormal contralateral radiologic intracranial findings (reports of cerebral or cerebellar hemiatrophy, parenchymal lesion, and calcification irrespective of modality) were then correlated to the CNS symptoms. Pathologic findings of three autopsies and two brain biopsies of patients with PFH will be summarized shortly.

Results

MR Findings

All three of our patients presented extracranial abnormalities; however, these are not the subject of this paper. The brain scans of two patients without CNS symptoms were normal. The T2-weighted images of the third patient (H.U.) revealed hyperintensity of the white matter in the homolateral cerebral hemisphere that included the vascular territory of the anterior cerebral artery but was not confined to it (Fig 1B and 1C). This area, especially at the left frontal and parietal convexities and interhemisperic surfaces, showed ill-defined sulci without the typical signal of cerebrospinal fluid (Fig 1D–1F). The left lateral ventricle was widened, especially in the anterior horn and body, whereas the roof of the lateral ventricle showed somewhat undulated outlines (Fig 1D–1F). The enlargement of the ventricle and the reduced width of sulci seemed disproportional. These findings suggested meningeal adhesions (Fig 1D–1F). In most of the dismorphic meningocortical zones the meninges could not be differentiated after gadopentetate dimeglumine application. Enhancing vascular structures of equivocal pathologic significance were seen at the frontal interhemispheric surface and left temporal surface, which most likely represent cortical veins (Fig 1E).

Review

Seventeen reports of normal findings of pneumoencephalography, CT, and MR in patients with PFH were identified. In 11 of these patients no CNS symptoms were reported, whereas six others had seizures; this group is not reported in detail here. Twenty-two patients had abnormal neuroradiologic findings. From these, 18 of 22 patients had abnormal neuroradiologic findings on the side of the facial hemiatrophy (5–19); 17 of 18 of those had CNS symptoms, most often focal seizures. The most frequent abnormality was homolateral cerebral hemiatrophy (16 of 18 patients); three of 18 had cortical calcifications, all at the external margins in the hemisphere homolateral to the facial involvement (8, 11). For one of them (who had skull radiography alone) this was the only pathologic finding (11), whereas the two others also had homolateral cerebral hemiatrophy. The CT scans of one patient revealed homolateral diffuse cortical or meningeal contrast enhancement without obvious hemiatrophy (17). Homolateral parenchymal-CT hypodensities, dysproportion of significant ventricular enlargement, and small and dysmorphic sulci that were reminiscent of the MR findings in patient H.U. may be recognized retrospectively on the

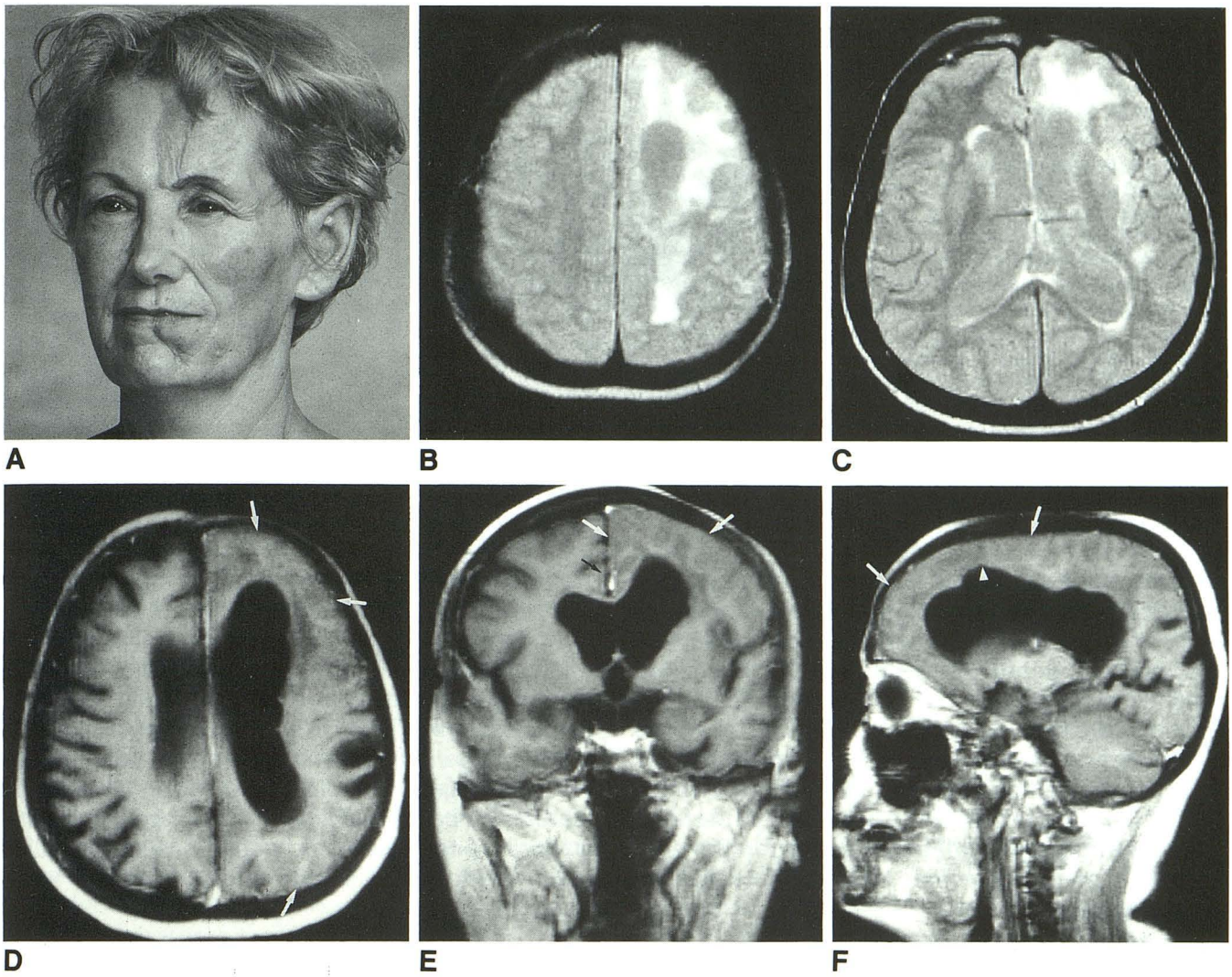

Fig. 1. Patient H.U., 61 years old, 47-year history of progressive facial hemiatrophy of the left face and left-sided migraine accompanied by right-sided deficits. Complex partial seizures, right-sided simple partial seizures, and secondary generalized epilepsy since the age of 28, with progressive course after the age of 50. Slight right hemiparesis and slight aphasia.

A, The areas of maximum atrophy are seen in the left temporal regions and at the lower portion of the chin. Clear border at the frontal midline.

B and *C,* T2-weighted transversal images (1600/70/1 (repetition time/echo time/excitations)) show white-matter hyperintensity in wide area of the left frontal and parietal lobe anterior and superior to the lateral ventricle. The extracranial field of cutaneous and subcutaneous substance loss and the area of brain involvement are adjacent. (Extracranial lowering of skin level is better recognized in T1-weighted images.)

D, Enhanced axial T1-weighted image (315/14) demonstrates wide areas with disappearance of the sulci at the convexity and interhemispheric surface of the left hemisphere, and corticomeningeal dysmorphia (*white arrows*). The lateral ventricle of the same side is enlarged. Enhancing vascular structures most likely representing cortical veins are of uncertain significance.

E, Coronal view (enhanced T1-weighted image (315/14)) showing the disappearance of fluid-filled sulci and dysmorphia at the convexity and interhemispheral surface (*white arrows*). Note slight, patchy enhancement of vascular structure that most likely represents a cortical vein (*arrow*) and lowering of skin level.

F, Sagittal view (enhanced T1-weighted image (315/14)) through the left lateral ventricle showing the loss of subarachnoideal space (dysgyria or corticomeningeal dysmorphia) (*white arrows*). Note the bizarre undulated outline of left lateral ventricle (*white arrowhead*).

CT illustrations of some patients (6, 8, 10) (see Fig 2) but were not explicitly described.

Contralateral abnormal neuroradiologic findings were described in a total of four of 22 patients (9, 10, 20). Only one of those four patients had a report of CNS symptoms (9). Three of four had reports of contralateral ventricular enlargement, but quantification and illustration are available for only one of these patients (9). The CT scan of the fourth (neurologically asymp-

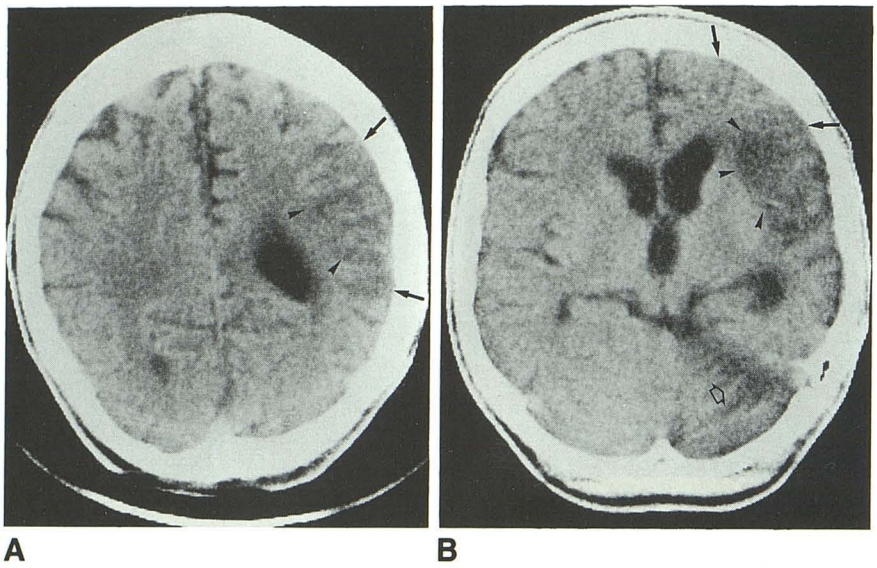

Fig. 2. Patient D.A.M., 24-year-old man. Seven-year history of left-sided PFH, right-sided tonic-clonic convulsions, and secondary generalized seizures. Reprinted with permission from Speciali and Resende (6).

A and *B*, The CT images show moderate ventricular enlargement of the frontal and temporal horns of the left lateral ventricle, homolateral to the facial changes. Hemiatrophy of external accentuation is seen in the left cerebellar hemisphere (*open arrow*). Slight hypodense changes of the parenchyma of the left cerebral hemisphere (*arrowheads*) and loss of sulci and external subarachnoidal fluid and gyral dysmorphia of the left cerebral hemisphere (*arrows*) are detectable, but changes are not as obvious as in MR. The findings of Patients U.H. and D.A.M show a high degree of correspondence.

tomatic) patient showed a hyperdense and nonenhancing lesion of the contralateral postcentral white matter (10). The total ratio of homolateral to contralateral pathologic findings was 18:4; the same relation confined to patients with reported CNS symptoms was 17:1.

Histologic examinations of facial specimens in PFH revealed proliferative interstitial neurovasculitis (21, 22). Electron microscopy demonstrated lymphocytic infiltrates and alterations of basement membranes and endothelia in smaller facial vessels (22). Mendel's patient, who had no CNS symptoms, had normal histologic brain findings (21). Fromhold-Treu reported the autopsy findings of a patient with a severe course of PFH and CNS symptoms (23). The autopsy findings were homolateral meningeal coatings with thick brownish pigment, new vascularization, and ecchymosis. The arachnoidea was opaque, fibrotic, and thickened, and appeared adherent to the surface of the left hemisphere. The dismorphic and flat homolateral cortical sulci were filled by thickened pial layers, and the cortical gyri of the homolateral hemisphere were atrophic. A patient examined by Stief exhibited gross hemispheral asymmetry that was histologically characterized by severe disseminated microvascular changes with vascular stasis in the hemisphere homolateral to the facial changes (4). Meningeal adhesions and thickened, opaque leptomeninges were noted, but no lateralization of this feature was mentioned. Fünfgeld, Jakob, and Wartenberg analyzed a brain biopsy of a patient who had PFH and partial epilepsy (24). Histology revealed homolateral subacute meningoencephalitis. The investigators found severe fibrous pial proliferation with massive perivascular lymphocytic infiltrations in gray and white matter and glial proliferation. Wolf and Verity performed cerebral and cerebellar biopsies in a patient with PFH and CNS symptoms (5). The cerebellar findings included gliosis, degenerative and vacuolar changes, and leptomeningeal fibrosis. Atypical small tortous leptomeningeal vessels with hyalinazation of the walls were interpreted as possible microvascular malformation; no inflammatory changes were noted.

Discussion

The different pathogenetic models that have been presented to explain PFH can be roughly divided into two groups. The first group was introduced by Romberg (1) and suggests a "trophoneurosis," that is, that dysfunction of trophic fibers of peripheral nerves leads to the facial atrophy; this model has prevailed to date. Acquired lesions of the CNS and a heredodegenerative etiology involving hypothalamic centers were also discussed as origins of such trophic dysfunction (2), because these were thought to provide a potential common explanation for the obvious cerebral involvement in patients with PFH presenting with epilepsy (2). The autopsy findings of facial proliferative neurovasculitis (21) were generally explained as results of the trophic nervous dysfunction. Surprisingly this interpretahion provoked only little opposition (22). The second group of pathogenetic models was first introduced by Lande (25) and was based on the

assumption of a primary localized disease of different facial tissues. Mechanical disturbances of the nerves within such areas were believed to explain the irregularly occurring cranial nerve syndromes as secondary changes. This model, and Möbius's concept of an unknown infectious agent (26) as cause of the tissue alterations, gained little acceptance. Recently Abele et al, on the basis of a single observation, proposed that bacteria of the borrelia species may play a role in the etiology of at least a part of PFH (27).

Circumscribed or linear scleroderma (morphea) *en coup de sabre (saber* thrust) of the face, is a dermatologic syndrome that closely resembles PFH (2). Among others Möbius (26), Wartenberg (2), and Rees (28) have stated their views that the clinical differentiation of both syndromes is impossible. A commonly accepted differentiaton by means of laboratory and histomorphologic examinations (22, 28) apparently has never been established. With regard to this difficulty, and in accordance with these authors, we made no efforts to distinguish between PFH or localized scleroderma *en coup de sabre*. All of our patients had clinically evident and MR-proved involvement of different facial tissues; PFH seemed an appropriate diagnosis, because multitissue involvement seems better described in PFH. In addition, no patient had the thickening, rigidity, or reddish aspect of the skin that justify the unequivocal diagnosis of localized scleroderma.

CNS symptoms, most frequently epilepsy, were reported in 15% of patients. These symptoms are difficult to explain by models of trophoneurosis, because the vascularization and nutrition of the brain are commonly believed to be independent of neurotropic influences (which were suspected to be responsible for PFH). Although we found an obvious lack of relatively recent autopsy findings, most likely because of low mortality of PFH, earlier neuroradiologic series have reported a high incidence of abnormal pneumoencephalographic findings in about two out of three patients with PFH (9, 10) and a lack of correspondence between CT and physical findings (10). Our review of the literature contrarily revealed typical patterns of findings in patients with PFH. These were: 1) normal findings were much more frequently reported in patients without CNS symptoms; and 2) pathologic findings of neuroradiologic investigations in CNS-symptomatic patients were reported far more frequently at the side of the facial alterations; the most frequent finding was cerebral hemiatrophy. There are divergent findings of contralateral ventricular enlargement in pneumoencephalography of three patients, but the criteria remain unclear in two reports. We conclude that a typical pattern exists of predominantly cerebral abnormalities homolateral to the facial atrophy, which may be found nearly exclusively in CNS-symptomatic patients. The leading feature is cerebral hemiatrophy; CT hypodensity, cortical calcification, and meningeal enhancement also have been reported. It would seem that the contralateral cerebral involvement plays only a minor role, if any.

Our normal MR findings of the brain in two patients were consistent with the assumptions that CNS involvement is occasional, and pathologic findings have to be expected in CNS-symptomatic patients. The MR abnormalities of patient H.U. described above are consistent with the pattern revealed by the review, in view of CNS symptoms and cerebral hemiatrophy. Correlates of the unusual findings of meningocortical dysmorphia and white-matter changes seen in our patient can be retrospectively recognized in some earlier CT illustrations. We present the findings of patient D.A.M., whose case was reported earlier by one of us (J.G.S.) (6), to demonstrate the similarities of findings (Fig 2). These features are uncommon in other forms of cerebral hemiatrophy, in the Dyke-Davidoff-Masson syndrome (29) or bilateral cerebral atrophies, for example. Therefore, we suspect an atypical, not primarily trophic process leading to secondary brain atrophy in PFH.

The histologic findings of facial changes in PFH are unequivocal and revealed proliferative interstitial neurovasculitis (21, 22). Surprisingly, we found little discussion of the possibility that this inflammatory process, sometimes seen decades after the onset of the disease, would not seem a plausible effect of trophic nerve dysfunction (22). Evidently all abnormal brain autopsies and biopsies describe meningeocortical alterations homolateral to the facial wasting. A final diagnosis, however, was proposed in only one of the four patients claiming subacute meningoencephalitis (24) and has been discussed little since. None of the four pathologic examinations supports the assumption of simple nutritive brain atrophy in the patients with CNS involvement in PFH. Regarding the intervals between the onset of symptoms and the autopsy and biopsy examinations, it must be considered that fibrosis and gliosis (4, 5, 23, 24) and vascular alterations (4, 13, 24) well may be present at different stages of an under-

lying inflammatory process. Therefore, the other biopsy and autopsy findings (4, 5, 23) do not necessarily contradict the proposed diagnosis of meningoencephalitis (24). Although we cannot provide supporting biopsy results, and CSF analysis revealed normal findings in patient H.U. at 60 years of age, we propose that the cerebral MR findings in patient H.U. could be consistent with chronic and focal (hemispheral) meningoencephalitis as first described by Wartenberg, Fünfgeld und Jakob (24). The occasional CNS manifestations and the facial alterations may thus be explained as parts of a common underlying inflammatory process.

Conclusions

Homolateral cerebral hemiatrophy seems to be the typical finding in a subgroup of PFH patients with (occasionally occurring) CNS involvement in Romberg syndrome.

We believe that a chronic inflammatory process leading to atrophy of various tissues of the face and sometimes, by local invasion, of parts of the brain is a highly plausible explanation for PFH. CNS involvement itself and its morphologic features demonstrated by MR are not consistent with models of trophoneurosis, and these should be abandoned.

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