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**Hemifacial atrophy:  
a neurocutaneous disorder  
with coup de sabre deformity,  
telangiectatic naevus,  
aneurysmatic malformation  
of the internal carotid artery  
and crossed hemiatrophy**

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Sirs: Hemifacial atrophy occurs as a result of various maldevelopments of innervation or vascular supply (congenital hemifacial microsomia, progressive hemifacial atrophy) and inflammations (localised scleroderma, bulbar poliomyelitis) [3, 9]. It comprises a group of syndromes often occurring in association with intracerebral abnormalities. We recently saw a patient with hemifacial atrophy and multiple neurocutaneous defects: coup de sabre deformity and facial telangiectatic naevus associated with homolateral cerebral hemiatrophy, aneurysm of the internal carotid artery (ICA), hypoplasia of the middle cerebral artery (MCA) and crossed hemiatrophy and hemiparesis of the body. As far as we know, such an association has not previously been reported.

The 35 year-old man was admitted to the Neurological Department following a grand mal seizure. He was born normally at term following a pregnancy characterised by an imminent abortion during the 4th month. There was no family history of epilepsy or neurological disease. The patient was first seen at 3 months of age because of a pronounced asymmetry of the skull and face, including the orbits, the left

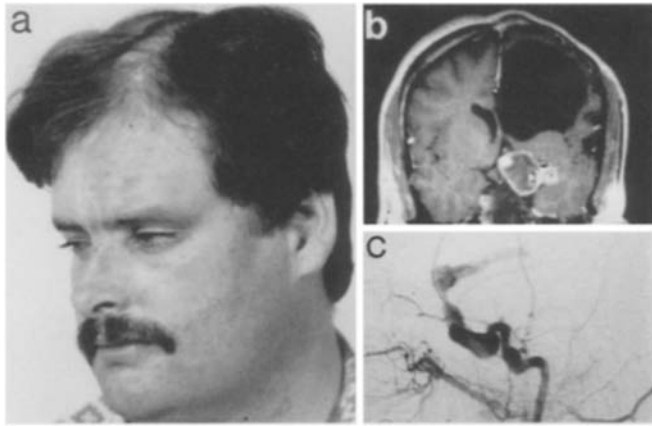
side being diminished in size. It was noted that the child had a facial vascular naevus extending from the hairline to the upper eyelid, just to the left of the midline. The left palpebral fissure was slightly narrowed, and the left corneal diameter was 1–1.5 mm smaller than the right. There was no choroidal angiomas. Photographs taken at the time showed a distinct furrow somewhat left to the midline of the forehead and corresponded with the present findings. The child did not suffer from epileptic seizures and intracranial calcification was not seen on plain radiographs of the skull. The heart, lungs and abdomen and radiographs of the chest and skeleton were normal. At that time the tentative diagnosis was Sturge-Weber syndrome.

At age 7 months it was noted that he showed signs of developmental retardation. Moreover, he had a slight, spastic, right-sided arm-dominant hemiparesis. An EEG showed patterns of left-sided parietal and occipital intermittent rhythmical theta activity on a normal background. The cerebrospinal fluid was normal. At age 22 months the facial naevus was described as being paler. Gait evaluation showed decreased right-sided associated movements, with slight pes equinus on the same side. The patient was admitted to hospital when aged 7 years because of left-sided headache. A left-sided hemifacial hypotrophy, with two parallel, linear, pigmented sites of local atrophy in the midline of the forehead and 2 cm lateral to the left, so-called coup de sabre, was recorded. Investigations included normal examinations of the eyes. Skull radiographs showed calcification of the falx, enlargement of the sella turcica and a slight left-sided parietal protrusion with increased transparency. The diagnosis was altered to Parry-Romberg syndrome.

When we examined the patient at age 35 years there was a slight left-

sided hemifacial atrophy, predominantly involving the maxillary region as well as the masseter muscle. A circumscribed defect in the cranial bone was present covered by hyperpigmented atrophic skin on the left forehead extending to the frontal processus maxillae and the ala nasi. There was circumscribed alopecia, and a pale telangiectatic naevus on the left cheek reaching the upper cervical region (Fig. 1 a). Neurological examination revealed a right hemiparesis including a slight volitional facial paresis. Other cranial nerve functions and extraocular movements were normal and the pupils were of equal size. Visual acuity and optic fundi were normal. Assessment of visual fields, both by confrontation and Goldmann perimetry, revealed a wedge-shaped defect in the temporal field of the right eye. Graphaesthesia and joint position sense were diminished in the right arm. Other modalities of sensation were unimpaired. Muscle strength of the right extremities was 4/5 on a manual muscle testing scale. There was a dystonic posture of the right hand. Tendon reflexes were more active on the right. There were no pathological reflexes or long tract signs and the plantar responses were flexor. The right extremities were shorter, the right hand and foot being shorter and narrower than their left-sided counterparts.

There was no clinical evidence of dysfunction of the autonomic nervous system. Deficits of verbal performance and verbal memory were noted by neuropsychological testing. The EEG revealed slowing over the left hemisphere with a left temporal slow wave focus and a few sharp- and -slow-wave complexes. Skull radiographs confirmed the previously noted asymmetry with irregular areas of decreased density in the left frontal and parietal bones, sellar erosion and multiple calcifications in the falx. Computed tomography and magnetic resonance imaging (Fig.



**Fig. 1** a Left hemifacial atrophy with coup de sabre deformity on the forehead, circumscribed alopecia and bony malformation of the skull. b T1-weighted, contrast-enhanced MRI (coronal view) showing enlarged left lateral ventricle with lateralization of the falx and dilatation of the widely thrombosed internal carotid artery (ICA) with residual contrast-enhanced vessel lumen. c Left carotid angiogram (lateral projection, early arterial phase) demonstrates diffuse dilatation of the ICA

b) revealed left cerebral hemiatrophy with porencephaly of the superior frontal and parietal left hemisphere widely communicating with the markedly enlarged left ventricle. Left temporal areas showed rarefaction of the sulci at the convexity. The intracranial part of the ICA was enlarged over most of its length. These findings were confirmed by intra-arterial digital subtraction angiography, with an elongated and ectatic ICA in the cavernous and intracerebral parts (Fig. 1c). Slow flow was observed in the hypoplastic MCA in the late arterial phase (not shown). There was no evidence of arteriovenous shunting.

Laboratory examinations produced normal results. In particular, no circulating antibodies could be found directed against nuclear antigens (extractable nuclear antigens, double stranded DNA, histones) or mitochondrial antigens using indirect immunofluorescence, ELISA and Western blot techniques.

The patient had first presented with hemifacial atrophy with ptosis, coup de sabre deformity and telangiectatic naevus at the early age of 3

months. Circumscribed alopecia, progressive contralateral hemiparesis and total hemiatrophy with slight sensory deficits and dystonic posture of the hand appeared at a later stage. The combination of these signs together with documented intracranial major vessel abnormality has not previously been reported.

The early onset of clinical and radiological abnormalities suggests that the cerebral hemiatrophy is best explained by prior intrauterine ischaemia in the ICA territory due to vascular malformation [3, 6]. As a consequence, contralateral limb and trunk atrophy with hemiparesis gradually developed during subsequent growth.

The homolateral trophic and skin abnormalities on the face share many of the external features of both the non-hereditary phenotypes of Sturge-Weber syndrome [11] and progressive hemifacial atrophy [1, 3, 9]. In progressive hemifacial atrophy a coup de sabre deformity and circumscribed alopecia may typically appear in the forehead [1, 3, 14]; facial telangiectatic naevi are the primary clinical features of Sturge-Weber syndrome [11]. Abnormalities and dysfunctions of the central nervous system have been reported in both disorders, e.g. cerebral hemiatrophy, enlargement of the ventricles, mental retardation, epilepsy, hemiparesis and hemianopia [1, 9, 11, 14]. Areas of meningocortical dysmorphia, cerebral microvascular malformations and calcified haemangiomas

are occasionally found in progressive hemifacial atrophy [1].

The recurring themes in the literature on the pathogenesis of progressive hemifacial atrophy include linear scleroderma [4], chronic inflammatory processes [8, 14], trauma [5] and defects of vascular supply [7, 12]. Circumscribed scleroderma may not entirely be ruled out in our patient, although circulating antinuclear antibodies could not be detected.

There are occasional reports that suggest that lesions of the homolateral cervical sympathetic innervation, either central or peripheral, may be involved in the pathogenesis of progressive hemifacial atrophy [10]. Interestingly, a telodiencephalic ischaemic syndrome, characterised by homolateral sympathetic deficits, contralateral hemiparesis and occasional hemianopia due to infarction of the ICA has previously been described [13]. In supratentorial strokes, lesions can reach subcortical areas affecting homolateral, uncrossed cortico-hypothalamic and hypothalamo-spinal sympathetic pathways [2]. In this patient, both the transient homolateral ptosis, suggesting a slight sympathetic dysfunction, and the contralateral delayed-onset dystonia of the hand could serve as an indication of ischaemic subcortical involvement including striatal or diencephalic regions.

In conclusion, this case suggests a developmental disorder with vascular dysplasia as the common thread for the overlapping phenotypic features. A neurovascular aetiology has been hypothesised both in progressive hemifacial atrophy [7] and linear scleroderma en coup de sabre [4] as well as in the Sturge-Weber syndrome [11]. The spectrum of neurocutaneous signs possibly represents a phenotypic continuum, which in turn points to a common pathogenetic process of congenital dysplastic abnormalities involving both the skin and the nervous system.

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## **No evidence of Borna disease virus-specific antibodies in multiple sclerosis patients in Germany**

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Sirs: Borna disease virus (BDV) causes chronic inflammatory central nervous system (CNS) diseases in naturally infected animals. BDV infections are endemic among horses and sheep in Central Europe [18]. Furthermore, several animal species can be infected experimentally and develop a spectrum of neuropsychiatric symptoms related to the virus isolate and certain host factors [13]. Borna disease results from the persistent intrathecal viral replication and the immune response against BDV antigens [14]. BDV is highly neurotropic and has recently been shown to be a negative, single-stranded RNA virus with a non-seg-

mented genome of approximately 9 kb in size and with a genomic organization similar to members of the order Mononegavirales [5, 7, 12]. BDV replicates in cell nuclei of neural origin [6], and RNA splicing contributes to the generation of mature BDV-specific mRNAs. These unique features of a highly neurotropic RNA virus distinguish BDV from all other known mammalian RNA viruses.

Inflammatory CNS diseases can be experimentally induced in persistently BDV-infected, but initially symptomless rats by adoptive transfer of virus-specific CD4<sup>+</sup>Th1 lymphocytes, whereas T-cell transfer before infection protects against disease [14]. There are several reasons for investigating a possible involvement of BDV infection in human chronic inflammatory diseases of the CNS: the wide host range and various neuropsychiatric disease patterns observed in naturally and experimentally infected animals; the detection of BDV-specific antibodies in sera [1, 2, 15, 16, 17] and of BDV antigens as well as BDV-specific RNA in peripheral blood monocytes [4] from psychiatric patients; and the immunopathological mechanisms of CNS inflammation in BDV-infected animals [14]. A recent report of BDV seroprevalence in patients with multiple sclerosis (MS) and other chronic CNS diseases [3] has drawn our attention to a possible BDV infection in MS. This possible association is intriguing because two frequently discussed pathomechanisms in MS are intrathecally persisting viral infection and immunopathologically induced inflammation and demyelination.

We analysed paired cerebrospinal fluid (CSF) and serum in 19 German MS patients and serum in an additional 31 MS patients. All patients had been diagnosed as having definite MS according to widely accepted criteria [10]. The samples had been taken as part of routine clinical investigations. CSF and serum analysis was performed to support the clinical