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Neurofibromatosis and Agenesis of the Corpus Callosum in Identical Twins: MR Diagnosis

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Agenesis of the corpus callosum (ACC) is a complex malformation of the brain that is usually sporadic in occurrence. Documented familial cases are rare in the literature [1–4]. ACC is associated with a long list of clinical [5–9], radiographic [10–18], and pathologic [15, 19–21] anomalies and has been observed as a part of other syndromes [8, 22, 23]. The wide spectrum of neuroanatomic malformations intrinsic to ACC, as well as the frequently accompanying limbic system anomalies, were recently described on MR imaging [24]. This report describes the complex of brain malformations comprising ACC in identical twins and documents, for the first time, the association of ACC with neurofibromatosis, as illustrated by MR.

Subjects and Methods

Two male identical twins, 21 years old, were studied on a GE 1.5-T Signa MR system. Axial, coronal, and sagittal images were obtained through the brain and spinal cord. T1-weighted images used 600/20–25 (TR/TE), and T2-weighted images used 2000–2500/20, 80.

Both twins had clinically diagnosed neurofibromatosis at 7 months of age on the basis of multiple cafe au lait spots and multiple cutaneous neurofibromas [25, 26]. No family history of neurofibromatosis or ACC could be elicited. Two older female siblings had no clinical manifestations of neurofibromatosis; the parents denied cafe au lait spots or cutaneous neurofibromas, but refused to be examined. It was assumed, therefore, that the neurofibromatosis gene in the twins was the result of a new mutation. Both twins were evaluated because of slowly progressive weakness and spasticity involving all extremities.

Results

MR depicted strikingly similar anomalies in the brains of the two patients. Mid-sagittal sections (Fig. 1) demonstrated total absence of the corpus callosum with accompanying gyral malformations. Remarkably identical enlargement of the paraterminal gyrus, in which the septal nuclei are found, was present in both twins. An abnormally shaped lamina terminalis and hypoplastic anterior commissure were identically structured in the midline sections.

Coronal sections of the brain also illustrated virtually identical malformations in the twins. The sine qua non of ACC, Probst's longitudinal callosal bundles [15, 20, 21], were clearly illustrated on these sections (Fig. 2). The classically described four-structure complex of ACC [16, 21, 24], starting from the midline interhemispheric fissure, could be delineated in both patients: (1) enlarged, laterally rotated cingulate gyrus, (2) CSF-filled lateral callosal cistern, (3) bundle of Probst, and (4) medially concave frontal horn. Callosal absence with continuity of the interhemispheric fissure with an elevated third ventricle were present (Figs. 2 and 3), Hippocampi were somewhat hypoplastic (Fig. 3), with secondary keyhole dilatation of the temporal horns of the lateral ventricles [24]. Colpocephaly with white matter deficiency, especially involving the forceps major, was striking (Fig. 4).

MR of the spine revealed extensive neurofibromatosis in both patients, with marked similarity in location and distribution of the neurofibromas. Remarkable was the presence of virtually mirror-image kissing neurofibromas wrapping around the upper cervical cord anteriorly, near the craniovertebral junction, in both patients (Figs. 1 and 4). Identically situated multiple paraspinal neurofibromas were identified bilaterally in both patients (Fig. 5).

Multiple subcutaneous neurofibromas were also identified (Fig. 6).

Discussion

Most cases of ACC are sporadic and have no identifiable cause, but rare reports of families showing autosomal dominant, autosomal recessive, and sex-linked patterns of transmission are found in the literature [1–4, 8]. ACC may be seen in association with chromosomal abnormalities (i.e., trisomy 8, 13, and 18) [8] as well, suggesting a genetic origin. ACC has also been observed as a part of other syndromes, such as the median facial cleft syndrome, Aicardi syndrome, Rub-

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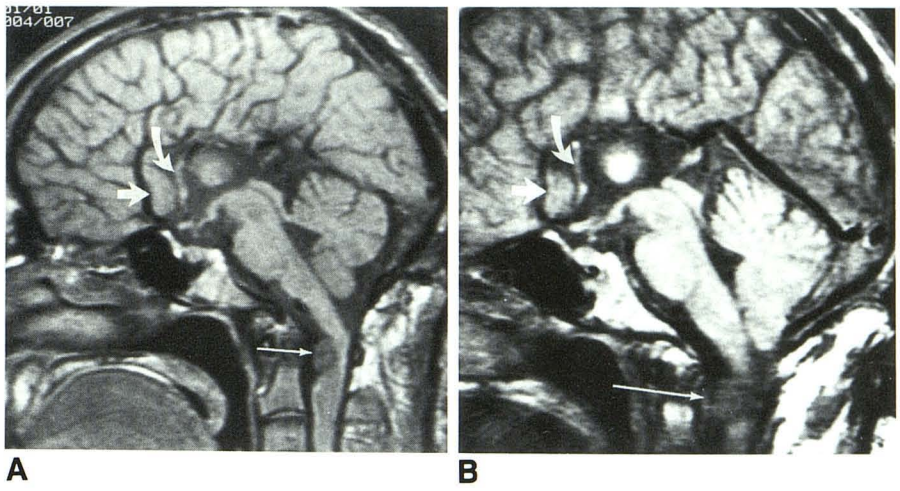

Fig. 1.—*A* and *B*, Mid-sagittal T1-weighted MR images of twin 1 (*A*) and twin 2 (*B*). Note absence of corpus callosum, cingulate gyrus, and sulcus. There are radiating mesial sulci to roof of third ventricle, identically enlarged paraterminal gyri (*thick arrow*), and aberrant lamina terminalis (*curved arrow*). Identical neurofibromas impinge upon cord at level of C1 (*thin arrow*).

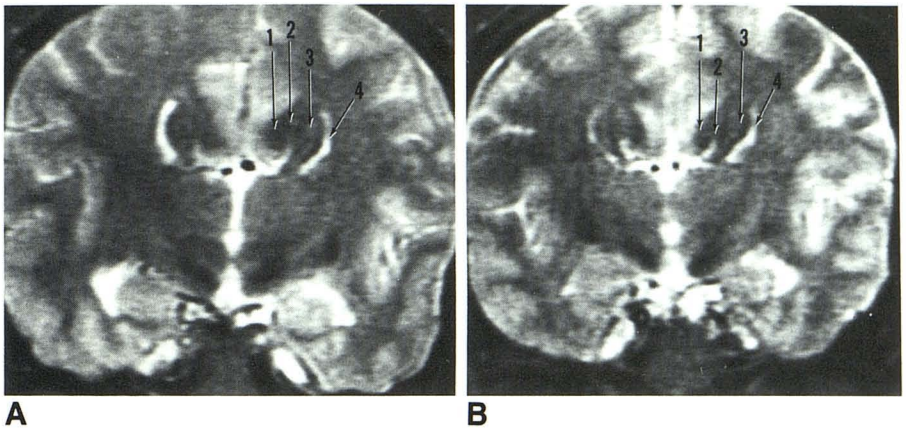

Fig. 2.—*A* and *B*, Coronal T2-weighted MR images of twin 1 (*A*) and twin 2 (*B*). 1 = enlarged, rotated cingulate gyrus; 2 = CSF-filled lateral callosal cistern; 3 = Probst callosal bundle; 4 = concave frontal horn.

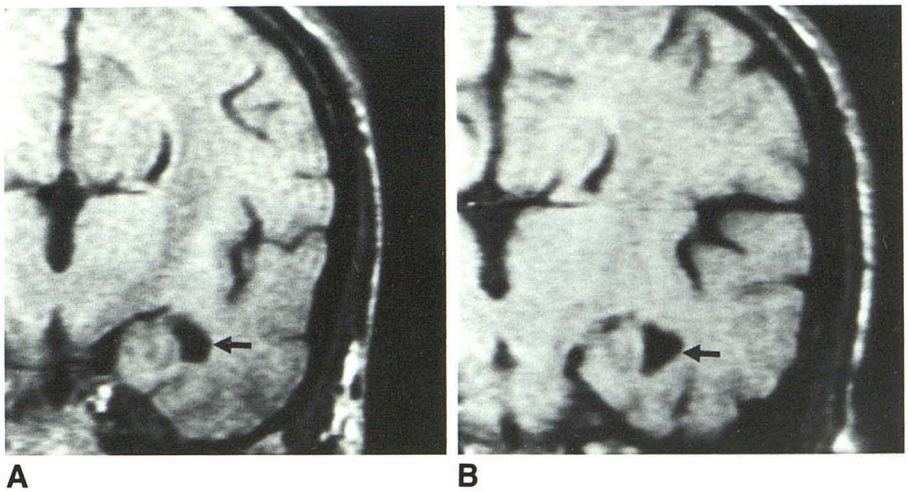

Fig. 3.—*A* and *B*, Coronal T1-weighted MR images of twin 1 (*A*) and twin 2 (*B*). Keyhole dilatation of temporal horn (*arrow*) is caused by hippocampal hypoplasia. Note continuity of interhemispheric fissure with dilated third ventricle.

enstein-Taybi syndrome [8], the basal cell nevus syndrome [22], and tuberous sclerosis [23]. No association with neurofibromatosis can be found in the literature.

ACC can present as an isolated entity, but in at least 80% of cases there are associated anomalies of the CNS [6, 12, 16]. The advent of MR has allowed depiction, for the first time, of malformations of the limbic system that were previously described only in the pathologic literature [15, 21, 24].

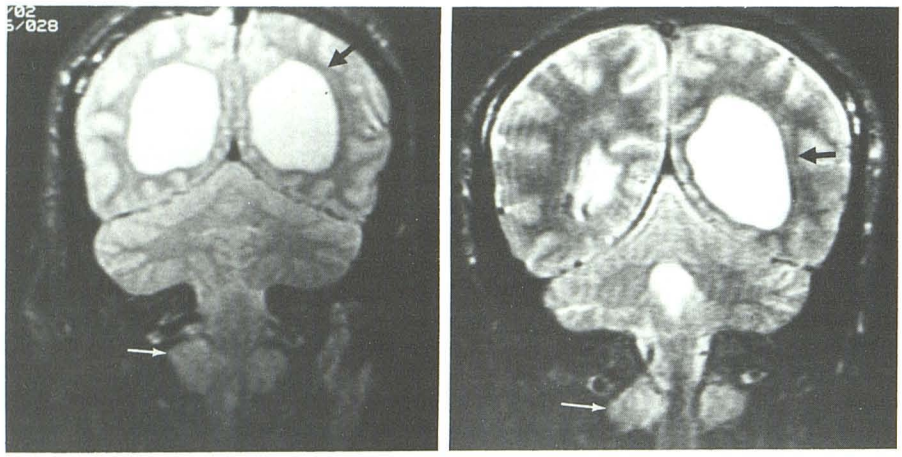

Fig. 4.—*A* and *B*, Coronal T2-weighted MR images of twin 1 (*A*) and twin 2 (*B*). Note poorly formed deep white matter (*black arrow*) around colpocephalic lateral ventricle (twin 2 has had ventriculostomy in right lateral ventricle). Identical kissing neurofibromas wrap around cord just below foramen magnum (*white arrow*).

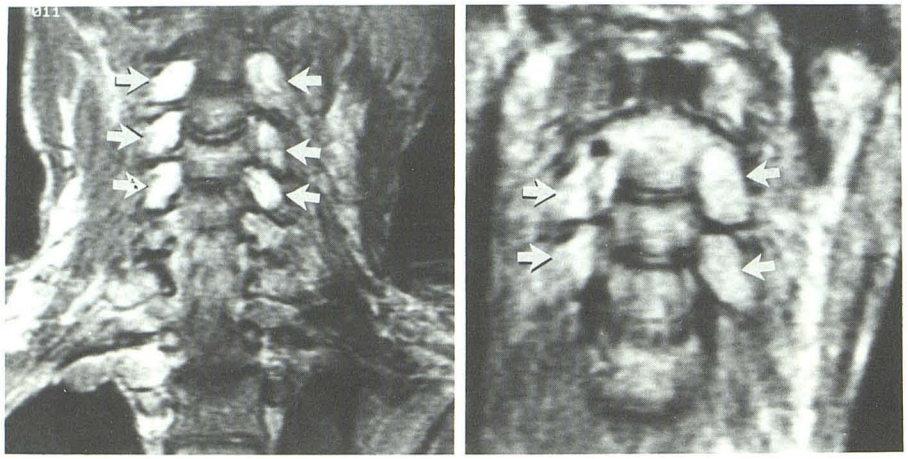

Fig. 5.—*A* and *B*, Coronal T2-weighted MR images of twin 1 (*A*) and twin 2 (*B*). Mirror-image bilateral neurofibromas (*arrows*) are present at multiple levels in cervical spine.

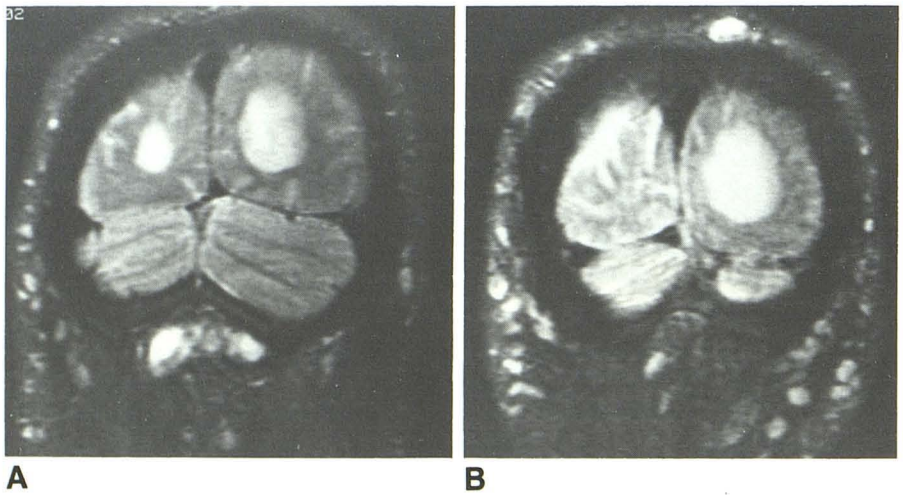

Fig. 6.—*A* and *B*, Coronal T2-weighted MR images of twin 1 (*A*) and twin 2 (*B*). Numerous high signal intensity subcutaneous neurofibromas are present in both patients.

In addition, there is a very high occurrence of non–nervous system malformations in patients with ACC [6], most frequently involving facial structures (especially the eye) and cardiovascular and genitourinary systems.

Neurofibromatosis is a relatively common autosomal dominant trait, which occurs with a frequency of approximately 1:3000 [26]. It is thought to be one of the most common mutations known in humans [27, 28]; at least 50% of cases are the consequence of a new mutation [25, 26]. Lesions of the CNS may be seen in association with this entity; tumors, including gliomas (many of which involve the optic pathways), acoustic neuromas, meningiomas, and neurofibromas [25, 26] occur in 5–10% of cases.

This report illustrates the first known association between neurofibromatosis and ACC, as seen in identical twins. The occurrence of ACC in these twins with neurofibromatosis strongly implies a genetic transmission. MR not only provides an elegant demonstration of both disease entities, but also dramatically illustrates the virtually identical appearance of these patients' malformed brains and extensive neurofibromatosis. The role of MR in syndromes such as ACC and neurofibromatosis is not yet fully established, but it clearly is valuable in the diagnosis and medical management of these entities. In addition, further understanding of possible genetic associations, many of which may be unsuspected clinically, may be achieved with MR. Furthermore, psychological and social management of these patients may be aided by full identification of their neuroanatomic status.

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