Hallermann-Streiff Syndrome Associated With Complete Agenesis of the Corpus Callosum

ABSTRACT

Hallermann-Streiff syndrome is a rare clinical entity with unknown etiology characterized by a birdlike face, microphthalmia, a beaked nose, hypotrichosis, and proportional small stature. We present a 4-year-old boy in whom magnetic resonance imaging showed complete agenesis of the corpus callosum, which has not been presented in the literature. (*J Child Neurol* 2005;20:691–693).

Hallermann-Streiff syndrome or oculomandibulodyscephaly is a rare congenital anomaly of unknown etiology described by Hallermann[1] and Streiff.[2] Steele and Bass summarized the clinical features of 50 cases reported in the literature.[3] The most common features of this syndrome are dyscephaly, frontal or parietal bossing, hypotrichosis, cutaneous atrophy, dental anomalies, mandibular hypoplasia, high arched palate, congenital cataracts, microphthalmia, micrognathia, and dwarfism.[3–5]

We report a 4-year-old boy with Hallermann-Streiff syndrome in whom magnetic resonance imaging (MRI) showed complete agenesis of the corpus callosum, which has not been reported in the literature to our knowledge.

Case Report

The patient was a 4-year-old boy. He was referred to the Department of Pediatrics owing to difficulties in feeding and breathing, vomiting, diarrhea, and spasticity in his arms and legs. This was the first child of second-degree consanguineous parents, and he was born by spontaneous vaginal delivery following 9 months of uneventful pregnancy. His birthweight was 2.6 kg. He had a history of pneumonia, sepsis, and meningitis followed by a ventriculoperitoneal shunt operation owing to hydrocephalus 3 years previously. The physical examination revealed a small child with a height of 71 cm, weight of 10 kg, head circumference of 45 cm, and a birdlike face. The skull was brachycephalic. He had hypotrichosis of the scalp, microphthalmia, blue sclera, nystagmus, a thin and beaklike nose, low-set ears, microstomia, a hypoplastic mandible, and a high arched palate (Figure 1). He also had mental and motor retardation. Evaluation of the eye showed optic atrophy. Examination of the respiratory and cardiovascular systems revealed bilateral coarse rhonchi. Examination of the genitourinary tract showed a bilateral inguinal hernia with cryptorchidism and a small penis. In the musculoskeletal examination, spasticity in the upper and lower extremities was prominent. These clinical features were compatible with the diagnosis of Hallermann-Streiff syndrome. MRI of the sagittal plane (Figure 2A) revealed complete absence of the corpus callosum with radial arrangement of the sulci of the medial hemisphere terminating at the roof of the third ventricle, a brachycephalic head shape, especially with parietal bossing, and a small fourth ventricle. On the axial (Figure 2B) and coronal (Figure 2C) images, the anterior interhemispheric fissure was communicating with an elevated third ventricle. Dilatation of the third and lateral ventricles, bat-wing configuration of the lateral ventricle, and well-delineated encephalomalacic areas in the right frontoparietal region were detected.

Discussion

Hallermann-Streiff syndrome is principally characterized by dyscephaly (usually brachycephaly), a parrot nose, mandibular hypoplasia, proportionate dwarfism, hypotrichosis, bilateral congenital cataracts, and microph-

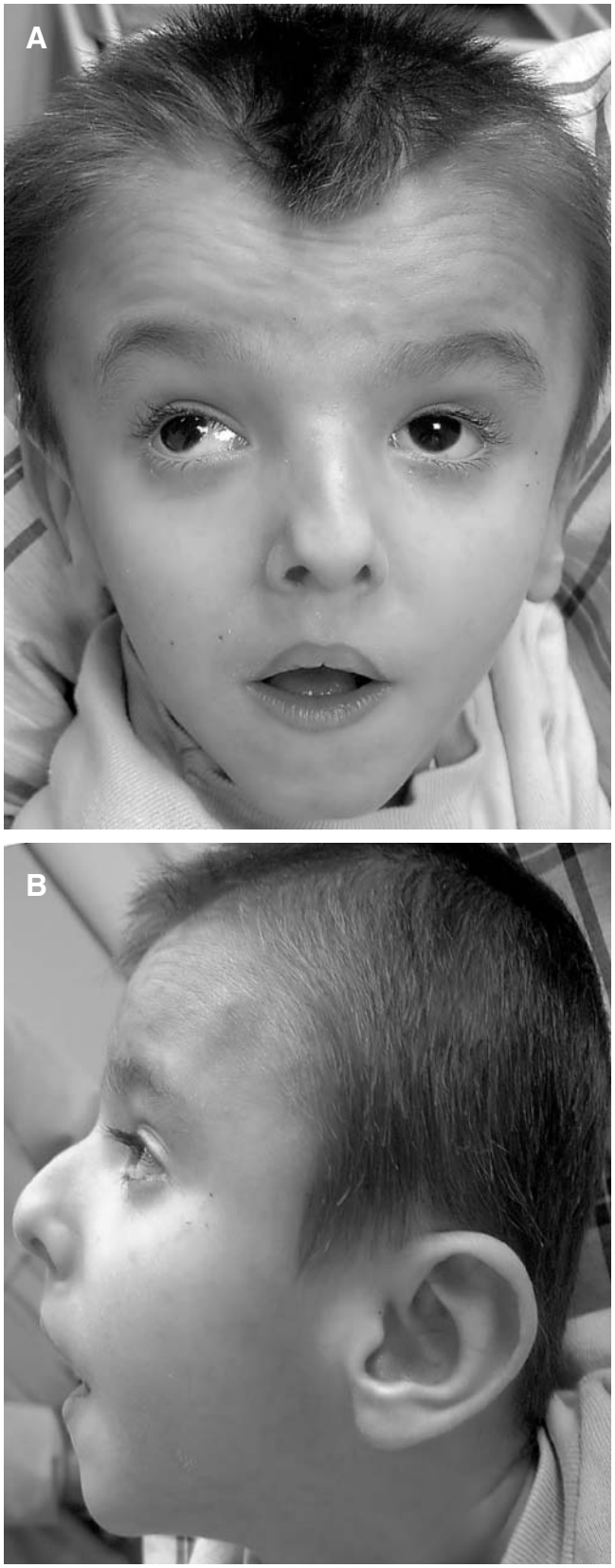

Figure 1. *A,* Face and *B,* profile of a 4-year-old boy with Hallermann-Streiff syndrome.

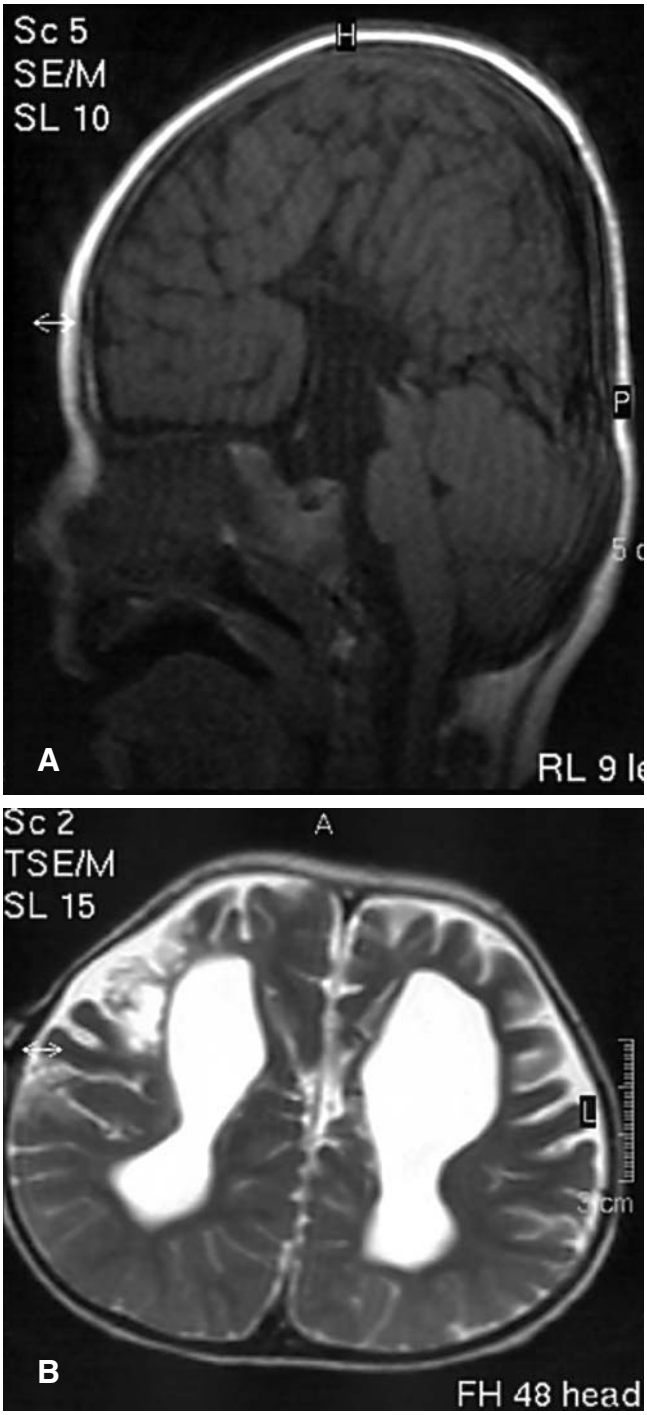

Figure 2. Magnetic resonance images (MRIs) of the head of a 4-year-old boy with complete callosal agenesis with Hallermann-Streiff syndrome. *A,* Sagittal T_1-weighted MRI shows brachycephaly with parietal bossing and complete agenesis of the corpus callosum with radial or spoke-wheel arrangement of the gyri along the interhemispheric fissure and a high-riding third ventricle. *B,* Axial T_2-weighted MRI demonstrates dilated, widely spaced, parallel lateral ventricles with encephalomalacic change near the right lateral ventricle. Note the pump of the ventriculoperitoneal shunt in the subcutaneous tissue on the right side. *C,* Coronal T_2-weighted MRI reveals dilatation in the third and lateral ventricles. A hyperintense encephalomalacic area appears near the right ventricle. Note the high-riding third ventricle in continuity with the interhemispheric fissure.

thalmia.[3–5] Our case revealed the clinical findings of Hallermann-Streiff syndrome, except cataract (see Figure 1). The etiology remains obscure. Most cases with Hallermann-Streiff syndrome have been sporadic, although cases with chromosomal abnormalities, such as elongation of one of the arms of the tenth chromosome[6] and the possibility of an autosomal recessive inheritance or a dominant mutation with parental mosaicism, have been described.[7] We did not perform chromosomal analysis in our case.

Brachycephaly, scaphocephaly, platybasia, shallow sella turcica, absence of the mandibular condyles, hypoplasia of mandibular rami, increased number of wormian bones, and mental retardation were reported as the clinical and radiologic findings of cranial involvement.[4] Hou previously reported a case with choanal atresia, a small cerebellum, generalized organic aciduria, hypothyroidism, and DNA repair defect.[8] In our patient, brachycephaly with parietal bossing (see Figure 2A), mental and motor retardation, hypoplasia of the teeth and mandible, dilatation of the ventricles, except the fourth ventricle, and typical MRI findings of complete agenesis of the corpus callosum were all present.

The formation of the corpus callosum and its precursors occurs between about the eighth and twentieth weeks of gestation.[9] Most parts of the cerebrum and cerebellum form at the same time. Therefore, anomalies of the corpus callosum are often associated with other brain anomalies and syndromes, such as Dandy-Walker malformation, anomalies of neuronal migration, encephalocele, cortical atrophy, encephalomalacia and midline facial anomalies, Aicardi's syndrome, Apert's syndrome, Chiari II malformation, Cogan's syndrome, oral-facial-digital syndrome, Rubinstein-Taybi syndrome, and Shapiro syndrome.[9,10] In our case, encephalomalacic areas (see Figure 2, B and C), in addition to the callosal agenesis, were imaged together with hydrocephalus, which was probably due to the meningitis infection 3 years previously.

To our knowledge, complete callosal agenesis has not been reported in children with Hallermann-Streiff syndrome in the literature. This association might be regarded as a casual finding or the possibility arises that a single sporadic mutant gene (a pleiotropic gene) is responsible for a number of distinct and seemingly unrelated phenotypic effects. The corpus callosum develops between the eighth and twentieth weeks of gestation, whereas Hallermann-Streiff syndrome probably results from a developmental disorder, which arises in the course of the fifth to sixth gestational weeks.[8] Therefore, genetic or environmental factors can cause embryologic abnormalities affecting cranial structures during this developmental period.

In conclusion, the existence of complete agenesis of the corpus callosum appears to represent a casual abnormality or pleiotropy in this patient with Hallermann-Streiff syndrome and has not been encountered and reported previously.

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Nonconvulsive Status Epilepticus Precipitated by Carbamazepine Presenting as Dissociative and Affective Disorders in Adolescents

ABSTRACT

Nonconvulsive status epilepticus can be confused with psychiatric disorders. Inappropriate drug treatment can represent a precipitating factor. We describe two patients with idiopathic generalized epilepsy in whom nonconvulsive status epilepticus, aggravated by carbamazepine, was misdiagnosed as psychiatric disorder. A 14-year-old girl experienced a tonic-clonic seizure at age 12 years preceded by monthly episodes of confusion with awkward behavior since age 9 years. She was treated with carbamazepine, and the episodes of confusion became more frequent, leading to a diagnosis of dissociative disorder. An electroencephalogram during one of these episodes revealed nonconvulsive status epilepticus. Substitution of carbamazepine with valproic acid controlled the episodes of status epilepticus. A 23-year-old woman presented at age 16 years with a tonic-clonic seizure. Since early adolescence, she had had episodes of depressive mood, worsening of school performances, and facial tics. Carbamazepine treatment caused worsening of the depressive episodes and facial tics. An electroencephalogram during a typical episode revealed nonconvulsive status epilepticus. Carbamazepine substitution with valproate led to seizure freedom and behavioral improvement. Nonconvulsive status epilepticus should be suspected and searched for in patients with epileptic seizures and ictal or fluctuating behavioral disorders. (*J Child Neurol* 2005;20:693–696).

Nonconvulsive status epilepticus is characterized by changes in behavior, memory, affect, or level of consciousness, often with alteration in muscular tone and fine facial or limb jerks for at least 30 minutes accompanied by electroencephalographic (EEG) evidence of seizures.[1,2] The identification of nonconvulsive status epilepticus was made possible just over 50 years ago with the advent of EEG. Tomson et al reported an annual incidence of nonconvulsive status epilepticus of 1.5 in 100,000 inhabitants.[3]

Nonconvulsive status epilepticus probably represents one of the greatly underrecognized or misdiagnosed epileptic conditions.[4–6] This disorder can be divided into two major forms: generalized with bilateral diffuse synchronous seizures (absence) or partial with lateralized seizures (complex partial).[7] Typical absence status epilepticus is recognized at onset in only 19% of patients and is often misdiagnosed as depression, postictal confusion, post-traumatic amnesia, toxic states, hysterical behavior, or schizophrenia or is ignored.[3,8] Seventy-five percent of cases occur before the age of 20 years. The cardinal behavioral features of typical absence status vary from mild to marked obtundation, withdrawal, delayed reactions, and confusion.[9] They are often accompanied by eyelid myoclonus and/or perioral myoclonus.[5]

Misdiagnosis with psychiatric disorders is particularly frequent because mental retardation has a comorbidity with nonconvulsive status epilepticus.[4] Common symptoms contributing to a psychiatric misdiagnosis are severe alterations of consciousness, including ictal confusion, lethargy, unresponsiveness, catalepsy, and mutism. Milder manifestations are a "dreamy state," slowness of response, slow ideation, withdrawal, and minor perceptive and expressive impairment.[10] Impairment of verbal functioning can range from confused speech to mild slowness and poverty of speech, up to monosyllabic speech. A variable degree of amnesia can be associated.

Some "positive" symptoms can be present, such as bizarre behavior, hallucinations, laughing or crying or singing, agitation or aggression, and anorexia with weight loss. Milder "positive" manifestations and experiential phenomena can be a rush of thoughts, a fear of losing control of the mind, the feeling that the heart beats faster, feeling hotter, a strange feeling of not being oneself, and feeling worried or uncomfortable. Nonconvulsive status epilepticus could therefore be misdiagnosed as a dissociative disorder, a panic disorder, a depressive disorder, a brief psychotic disorder, or other mental disorders.

The precipitating factors of nonconvulsive status epilepticus include antiepileptic drug withdrawal, discontinuation of medication, sleep deprivation, excess alcohol intake, fatigue, menstruation, psychotropic medications (phenothiazines, butyrophenones, lithium), and emotional stress.[1,5]

In recent years, there has also been a growing awareness of the potential aggravation of seizure disorders by antiepileptic drugs.[11–22] Antiepileptic drugs can aggravate preexisting seizures and trigger new seizure types.