Psychosis in Apert's Syndrome with Partial Agenesis of the Corpus Callosum

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A 19-year-old male with Apert's syndrome developed psychotic symptoms that responded to haloperidol. He was also found to have partial agenesis of the corpus callosum and enlarged lateral ventricles on a head CT scan. The implications of these findings in the context of psychotic symptoms are discussed. There are no previous reports of psychosis in patients with Apert's syndrome.

Key Words: psychosis, Apert's syndrome, agenesis of the corpus callosum

INTRODUCTION

Apert's syndrome (Type 1, Acrocephalosyndactyly) is recognized as the prototype of the acrocephalosyndactylies (Pfeiffer 1982). Craniosynostosis, syndactyly involving the hands and feet, and central nervous system (CNS) abnormalities are commonly present. Central nervous system defects include ventriculomegaly, hydrocephalous, megalocephaly, agenesis of the corpus callosum, and associated abnormalities of limbic structures (Cohen 1990; Cohen and Kreiborg 1990). Mental retardation is also commonly present. This paper describes a case of psychosis associated with Apert's syndrome, the first to the knowledge of the authors.

Case report

Mr. S, a 19-year-old male with Apert's syndrome, was admitted to the psychiatric hospital with hallucinations directing him to commit suicide by putting his head in fire. Referential ideas from the radio occurred, especially when songs by Guns and Roses were played. He felt that these songs had a special meaning and were played particularly for him. He reported that people did not like him and talked behind his back. These symptoms had worsened over a two-month period. Low mood was reported to be present for the past 5 years.

He had one previous hospitalization 4 months earlier because of suicidal ideation, and was diagnosed as having an adjustment disorder with depressed mood. No psychotic symptoms were present at that time and no medications were prescribed. He had completed high school, although he had been in special education. The medical record indicated that his intelligence was below average. Neuropsychological testing was not done. Premorbidly the patient was a loner, had not dated, and indicated being teased about his appearance at home and at school. Past medical history revealed craniectomy in infancy and enucleation of the left eye. There was no history of head trauma or seizures.

On examination of his mental status, it was found that he was alert, attentive, oriented in all spheres, and displayed good eye contact. His speech was dysarthric. Vegetative symptoms of depression were absent. His mood was dysphoric with a restricted affect. Thought processes were goal-oriented without loose associations. Psychosis was noted in the form of ideas of reference, suspiciousness, and

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auditory hallucinations ordering him to commit suicide. There were no overt delusions. He scored 29 out of 30 on the Mini Mental Status Examination. Judgment and insight were limited.

Physical examination revealed cranio-facial malformations, syndactyly of his hands, and malformations of his feet. Cranial nerve examination revealed poor peripheral vision of his right eye; the pupil was oblong, but reactive to light. He had a left eye prosthesis. Motor examination revealed a 5 out of 5 strength throughout. Sensations to touch, pinprick, and vibration were intact. Reflex examination revealed 3+ quadriceps reflexes while all other reflexes were 2+. Plantars were up-going on the right side. Gait was normal, tandem walk was poor, and Rombergs was negative. Finger-to-nose, heel-knee-shin, and rapid alternating movements were intact. The rest of his physical exam was unimpressive.

Laboratory tests were within normal limits. However, a head CT scan revealed enlarged lateral ventricles with partial agenesis of the corpus callosum. A working diagnosis of psychotic disorder not otherwise specified was made, and treatment was started with thioridazine (100 mg per day) and lorazepam (½ mg at bedtime). The antipsychotic was switched to haloperidol in the morning (2 mg) and at bedtime (½ mg) because of intolerable anticholinergic side effects. Psychotic symptoms remitted in 4 weeks, no depressive symptoms were observed. The patient was discharged from the hospital after the suicidal ideation had remitted.

DISCUSSION

This case is interesting because psychosis lasting 2 months occurred in a patient with Apert's syndrome having partial agenesis of the corpus callosum. No other similar reports have been found. A literature search revealed the presence of paranoid ideation in a patient with Asperger's syndrome and a lipoma in the splenium of the corpus callosum (David et al 1993). In a review of developmental syndromes associated with callosal abnormalities (Aicardi et al 1987), psychosis has not been reported as an associated manifestation. The occurrence of psychosis in a neurologically-impaired patient points to a potential relationship between psychosis and structural brain abnormalities. Severe psychiatric disturbance has been reported to be associated with abnormalities of corpus callosum (Swayze et al 1990; David et al 1993). Swayze et al (1990) reported an increased prevalence of agenesis of the callosum (a neurodevelopmental anomaly) in patients with schizophrenia, and discussed the possible underlying neuromechanisms. They also indicated that corpus callosum abnormalities, along with those associated with limbic structures, may result in the occurrence of psychosis. Limbic structure abnormalities have also been reported in Apert's syndrome (De Leon et al 1987), which might predispose these patients to the development of psychosis. It can be speculated that disruption of genetic control of callosal development may result in psychosis. Another purported model suggests that the corpus callosum may be important in regulating activity within the cerebral hemispheres and that its agenesis may result in psychosis (David et al 1993).

Other abnormalities like cavum septum pellucidum and cavum vergae have been reported in Apert's syndrome (Miller et al 1986) and also in patients with schizophrenia (Degreef et al 1992). David et al (1993) speculated on disordered interhemispheric integration as a plausible model for psychiatric phenomenon, especially psychosis. The patient studied here had partial agenesis of the callosum, which raises these very issues. Neurological disorders, toxic disorders, and metabolic disorders have been known to cause secondary psychoses (Cummings 1985). The characteristic symptoms include delusions of a persecutory nature involving threats of harm, theft or conjugal infidelity. Thought disorder accompanied by Schneiderian first-rank symptoms along with hallucinations are also observed. Auditory hallucinations are observed commonly amongst nondemented psychotic patients while visual hallucinations are more frequent among patients with toxic-metabolic brain disorders.

Temporal lobe epilepsy, extrapyramidal syndromes, demyelinating diseases, brain infections, stroke-related syndromes, and Alzheimer's disease are among structural brain diseases associated with psychosis (Cummings 1988). In an extensive review of organic psychosis, Cummings (1988) describes the occurrence of psychosis with left-sided temporal lobe seizure foci approximately 14 years after the first seizure. Cerebral trauma resulting in psychosis has usually involved the temporal lobe. Among extrapyramidal syndromes, psychosis has been reported in 50% to 80% of patients with Huntington's disease (Rosenbaum 1941). Other extrapyramidal syndromes associated with psychosis include idiopathic basal ganglia calcification (Fahr's disease), Wilson's disease, and post-encephalitic Parkinson's disease (Cummings 1988). Disorders involving the brain stem and cerebellum such as posterior fossa cysts, neoplasms, and Friedreich's ataxia have also been associated with psychosis (Heath et al 1983; Trimble and Cummings 1981). Psychosis has been reported in 50% of the patients with Alzheimer's disease characterized commonly by persecutory delusions (Leuchter and Spar 1985). The HIV syndrome has also been reported to produce psychosis (Halevie-Goldman et al 1987). There is no definite explanation for the mechanism of psychosis associated with structural abnormalities.

Cummings (1988) has noted that most brain lesions and diseases associated with psychotic symptomatology involve dopaminergic projections, especially in the limbic system. There are three dopamine mediated projections: 1. the mesolimbic system projects to the septal nucleus, amygdala, and olfactory structures. The limbic system also has projections to the striatum, nucleus accumbens, and substantia nigra; 2. the mesocortical projections reach the frontal cortex, anterior cingulate, and medial temporal cortex; and 3. the mesostriatal system projects to the basal ganglia. Feelings of fear, sadness, and pleasure have been reported during

intraoperative stimulation of the limbic structures suggesting that ongoing dysfunction of these structures may result in abnormal experiences such as delusions or hallucinations. Systematic studies examining the relationship of callosal and other congenital neurodevelopmental abnormalities with psychosis should help our understanding of the cerebral basis of psychotic symptoms.

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