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NEUROLOGICAL AND PSYCHIATRIC ASPECTS OF CORPUS CALLOSUM GENESIS

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SUMMARY

This article reports the case of a patient with partial agenesis of the corpus callosum manifested with corpus callosum syndrome together with signs of brain hemispheres dysfunction: mental impairment, epilepsy and pyramidal signs. The patient's malformation is combined with left-handedness while signs of callosal disconnection are not present. Mild cognitive impairment and late epilepsy onset require a multidisciplinary approach since the patient also displays elements of central nervous system malformations.

Key words: *epilepsy - corpus callosum*

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INTRODUCTION

Corpus Callosum Syndrome (CCS), as described by classics of neurology, i.e. - a combination of mental deficiency and motor deficit- does not exclusively refer to corpus callosum damage alone, but includes both lesions of corpus callosum and those of neighbouring nerve structures (Geschwind 1965). However, in clinical practice such syndrome continues to raise marked interest. Therefore, the case of a patient with partial Corpus Callosum Agenesis (CCA) which manifests with mental impairment, late epilepsy onset and other clinical features is described herein.

CASE REPORT

A 35-year old worker, with secondary school education, left-handed, unmarried, experienced first generalised epileptic seizure at age 31. The seizure occurred after a sleepless night combined with alcohol consumption, preceded by gastric aura. Such etiology of epileptic seizures is quite frequent in medical practice. Several months later, another seizure of the same type occurred while the patient was awake and without previous provocations. Postical confusional state which lasted for about 10 minutes was the main reason for seeing a neurologist who proceeded with a workup.

The patient is an only child and lives with his parents who are unrelated. He completed a three-year vocational school but does not have a permanent employment and works occasionally. As a child he was extremely unsociable and shy, and had difficulties in establishing social interactions. He felt isolated and did not practice sports because he "was clumsy due to his feet problems". In his twenties he started going out more often and "had fun and consumed alcohol" and has never had a longer emotional relationship. He has been on medications for several years and denies alcohol abuse ever since. Family anamnesis for epilepsy and mental illness was negative.

The patient's father is left-handed. The patient presented with short central apnea at birth. He has had "feet problems" since his childhood: his left leg is 1 cm shorter and he has therefore used orthopaedic insoles since he started walking. Both triceps surae tendons are shorter. His right hand "has always been clumsy" and his left hand fingers are visibly shorter. The patient did not experience any cardio-respiratory problems.

Neurological findings revealed a cooperative patient without speech impairment. His walk was paraparetic, and tiptoe walk was impossible; leg muscles were hypertonic (spastic type). Myotatic reflex of all extremities was pronounced, legs reflex almost lively; plantar reflex was silent. His feet were contracted and finger posture was atypical. Tactile anomaly was absent, but impaired gesture activity of the left side of the body was revealed. The remaining neurological findings were negative.

The assessment of psychological status showed a well kempt patient, without orientation and consciousness disturbances and absence of difficulties in social contact. Psychomotor agitation was not revealed, he was slightly intrapsychically tense. His complexion was pale, while his general mood was low. He presented lack of disorganised thinking and manic thoughts but was preoccupied with his physical condition. His attention was hypovigil and he presented hypertenacity of attention without sensory delusions and had low vital dynamisms, but no suicidal ideation. Mnestic functions and intelligence seemed both unimpaired.

Diagnostic workup was performed and the results were as follows:

Routine blood and urine analyses as well as amino acid levels were all within the reference ranges.

Standard electroencephalogram (EEG) with hyperventilation provocation and IFS was diffusely dysrhythmic, while asymmetries and paroxysmal discharges were not recorded. Oftamologist finding showed no irregularities.

Conventional brain magnetic resonance (MR-Tesla 1.5) recorded partial agenesis of corpus callosum – genu corporis callosi being the only developed part - as well as mild hydrocephalus. Deformations of the brain ventricular system, such as "bat-wing" configuration, were not revealed.

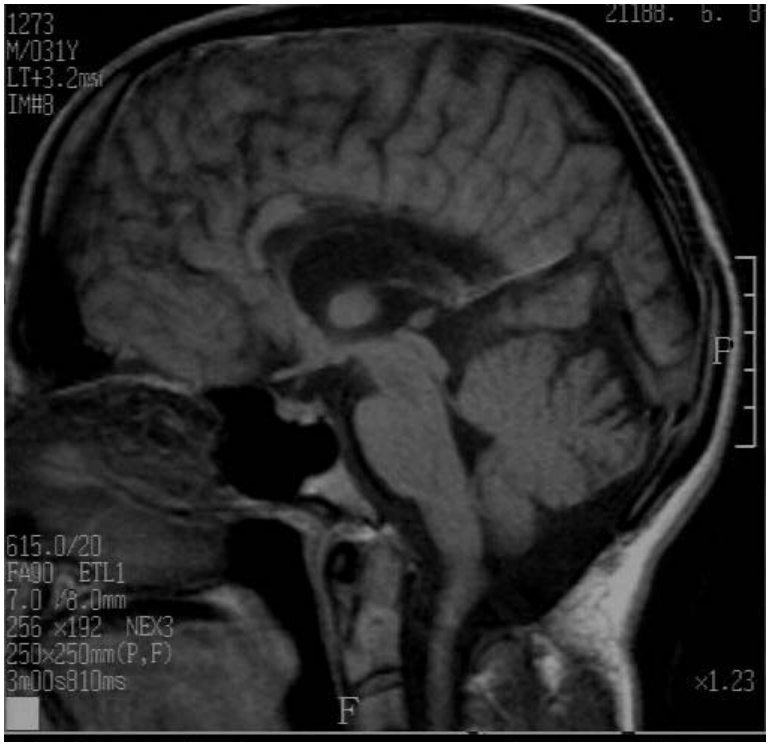

Figure 1. Partial agenesis of corpus callosum

Psychodiagnostic assessment revealed the patient's intellectual mnestic functions to be below average, especially the nonverbal intelligence and his learning abilities to be average. Moreover, he displayed rigid thinking and impaired critical thinking. The patient's sensory-motor function presented considerable impairments which indicated organic cerebral dysfunction. His personality revealed sensitivity to paranoid content and a limited adaptive capacity. As to interpersonal relations, the patient denied psychopathological behaviours.

The patient refused further genetic analysis as well as extended psychological testing.

The choice of a specific antipsychotic-lamotrigine (100 mg/day) proved to be effective since it ensured a good seizure control. The patient has been on lamotrigine monotherapy for three years and has not experienced any epileptic seizures. He claims to feel well. Control EEG- NAD.

DISCUSSION

Corpus callosum is a complex commissural system which interconnects cerebral hemispheres. Ontogenetically, the aforesaid system, the largest neopallium connection, is the most recent brain section.

Congenital brain malformations, pathologies pertaining to paediatric competence, are rarely diagnosed in adults. (Tomasović & Marušić 2007). Corpus Callosum Agenesis (CCA), total or partial, occurs in approximately 14% of central nervous system anomalies (Nieto-Barrera et al. 1994). The prevalence of this developmental brain anomaly is difficult to establish. In a series of 445 consecutive MRI analyses its incidence is 1.6% a year (Bodensteiner 1994). This malformation, a consequence of either dominant or recessive autosomatic heredity, is an expression of mutation of a development regulating gene. It is mostly diagnosed prenatally or in early childhood, mainly by means of neuroradiological testing (Nieto-Barrera et al. 1999, Moutard et al. 2003, Bedeschi et al. 2006).

Clinical symptoms of CCA are quite different, the most common being macrocephaly, facial dysmorphy, in combination with different levels of mental retardation, epileptic seizures, vision and other nerve impairments (Tissot et al. 1964). CCA is associated with the following syndromes: Dandy-Walker, Aicardi, Toriello-Carey and Andermann (Barišić et al. 2003 & Aicardi 1998).

CCA has also been reported in several cases of nonketotic hyperglycinemia (Lynn et al., 1980). If isolated, the prognosis of CCA syndrome is mostly favourable (Bodensteiner 1994). Asymptomatic patients have also been reported (Gunav et al. 1998).

Mental disorders are similar to those of prefrontal syndrome i.e.: mood oscillations, irritability, apathy regarding one's own condition, poor concentration and, above all, memory deficits, also dominant in the patient presented (Tissot et al. 1964). CCA is associated with all types of epilepsy. Numerous authors described the relation between epileptogenesis and corpus callosum (Grewal et al. 1997, Khanna et al. 1994, Luef et al. 1992, Gastaut et al. 1993). Epilepsy occurs in up to 35% of the patients affected with CCA, usually before the age of 8. Partial seizures are more frequent (Grewal et al. 1997, Gastaut et al. 1993). Taylor M. and David A.S. found that 32 out of 55 examined patients suffered from epilepsy, 28 displayed different types of mental retardation, while only 9 patients did not manifest any neurological disturbances (Taylor et al. 1998). Gunay and colleagues described three patients affected by total ACC who had the onset after 10 years of age (Gunay et al., 2008). Asynchrony of electrical activity is often recorded by EEG. Khanna S. and colleagues used positron emission tomography to localise tiny areas of abnormal brain metabolism responsible for epileptogenicity (Khanna et al. 1994).

Late age of onset of epilepsy, i.e. in the fourth decade of life, as in the patient described herein, is rare in patients affected by this malformation. A sleepless night together with alcohol consumption might have been provoking factors at that specific age. The second seizure which occurred without provocation at that age was a good reason to conduct neurological workup which revealed a malformation of the great cerebral commissure. Epileptic digestive neurovegetative manifestation, gastric aura, indicates that epileptic activity might be localised in the insular region, although EEG does not reveal any focal activity (Van Buren et al. 1963).

There are usually no abnormalities detected by neurologic findings in such patients who are often asymptomatic (Nieto-Barrera et al. 1999, Ramelli et al. 2006). However, the patient described displays certain singularities which expand the phenotype spectrum and indicate the participation of neighbouring cerebral areas. Bilateral pyramidal syndrome limited to muscular hyperflexion, contracted feet and hypotrophic legs (one is shorter) may indicate the patient being affected by a subtype of Andermann syndrome. On the other hand, the absence of sensory-motor neuropathy, severe mental dysfunction and psychotic manifestations, as well as the presence of mild bilateral pyramidal signs exclude such possibility (Dupré et al. 2003). Corpus callosum is larger in left-handers (Denny 2008). The described patient continues the series of Croatian articles on CCA inaugurated by a magisterial article by Dogan K. and colleagues and continued by contributions by Barišić I. and colleagues. (Barišić et al. 2003 & Dogan 1968). Manifestation of left-handedness (right hemisphere domination) in the patient's family is probably the cause of apractic manifestations in his right, and not in his left hand. Such manifestation is usually the rule in dissociation CCS, in the strict sense. The onset of epileptic seizures in adulthood is always associated with organic brain damage, provoking factors such as toxic substances, somatic diseases or external factors such as stress. The patient was mentally unobtrusive, although psychological testing (first such testing experienced by the patient) confirmed mild cerebral dysfunction as well as latent sensitivity to paranoid content. The introduction of lamotrigine in the patient's therapy has assured a good control of epileptic seizures and normalisation of the brain bioelectric activity. Moreover, according to anamnestic and heteroanamnestic data, the patient's psychological functioning as well as psychosocial communication have also been improved.

CONCLUSION

It should be emphasized that the onset of epileptic seizures in adulthood requires urgent EEG and brain MRI. Psychological testing and a detailed psychic status assessment are particularly important since early diagnosis and treatment of "hidden" deficits and personality changes, together with medicament treatment and adequate support can significantly improve patient's quality of life.

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