Corpus callosum agenesis

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ABSTRACT

Objectives: The objectives are to analyse corpus callosum agenesis in children with various neurological problems in a hospital set-up, and to study the neurological and systemic abnormalities associated with this condition.

Methods: The children with various neurological problems who underwent computerized tomography brain from January 1993 to December 1997, and were found to have corpus callosum agenesis, formed the subjects of this study. These children were examined for any syndromic association, congenital infections or metabolic defects.

Results: Out of 2164 children who underwent computerized tomography brain, 22 had corpus callosum agenesis (1%). Most cases were not syndromic and 64% were males. Epileptic disorders were noted in about one third of cases.

Conclusion: Corpus callosum agenesis an important anomaly in children with neurodevelopment handicaps, usually detected by neuroradiology.

Keywords: Corpus callosum, agenesis, non syndromic, syndromic, neurological abnormalities.

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The corpus callosum is the major commissure between the two cerebral hemispheres helping in the cross information synthesis, command transfer and integrated function of the brain. It's absence may result in severe mental dysfunction, although normal intelligence has been reported in some.[1] Corpus callosum agenesis (CCA) may be partial or complete. It may be an isolated anomaly or an associated anomaly as part of various syndromes. Associated abnormalities of other parts of the brain have also been reported. The mode of inheritance in CCA could be autosomal dominant, autosomal recessive or X-linked. We report 22 cases of CCA seen at Sultan Qaboos University Hospital over a period of five years from 1993.

Methods. Children with various neurological problems, who underwent Computerized Tomography (CT) scan of brain, from January 1993 to December 1997, and were found to have CCA, formed the subjects of the study. These children were subsequently examined for any syndromic association or metabolic defects. Other relevant investigations like blood counts, liver function tests, renal chemistry, karyotyping, electro encephalography (EEG), electrocardiography (ECG), serological tests for toxoplasmosis, rubella, cytomegalovirus and herpes simplex (Torch) profile and thyroid function tests were carried out when indicated. Electromyography (EMG) and muscle biopsy were also carried out in some cases. Magnetic Resonance Imaging (MRI) of brain was not carried out routinely. Elaborate objective tests to detect higher function impairments were not performed.

Results. A total of 2164 children had CT scan of brain for various reasons from January 1993 to December 1997 and 22 were found to have CCA (1.02%). There were 14 male and 8 female children with CCA. The mean age at presentation was 2 years 8 months with a range of 2 days to 10 years. Seizures (36%) and developmental delay (23%) were

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common presentations. The detailed neurological and systemic findings are included in Table 1. Other associated brain anomalies were also seen on the CT scan, cortical atrophy being the commonest. Chromosome analysis done in 8 patients were all normal.[5]

Discussion. The corpus callosum, a forebrain commissure originates from the primitive lamina terminalis. The first callosal fibres form by day 74 of gestation and formation of corpus callosum is complete by 115 days; however the process of myelination continues after birth. The extent of malformation varies from partial to complete agenesis. In partial agenesis, the posterior part is not developed because the corpus callosum develops in an antero posterior direction. However cases of anterior agenesis have also been reported.[1] In CCA, the lateral ventricles are shifted laterally and the 3rd ventricle is enlarged and displaced superiorly with it's roof extending dorsally. (Figures 1 and 2). CCA could be an isolated anomaly or associated with abnormalities in other parts of the brain like heterotopias, microgyria, abnormal cerebral fissures, porencephalic cysts and hydrocephalus.

Callosal agenesis has been reported by several authors. Grogono[2] reported 0.7 per cent of CCA in a large series while Jeret et al[3] came across 33 cases of CCA in a series of 1447 CT scans of brain. Analysis of our data revealed that 22, out of 2164 children who underwent CT scan of brain had CCA (1.02%). Epidemiological surveys[4] have approximately estimated the prevalence of CCA as 1 in 20,000 individuals.[6]

The aetiology is multifactorial[5] but in most of the cases, the cause is unknown. Genetic factors,[1] toxic effects of alcohol on the fetus,[6] endogenous toxins leading to lactic acidosis,[7] vascular and metabolic defects[8] and various congenital infections[1] have been found to be closely associated with the aetiology of CCA.

In non syndromic forms, the genetic transmission is rare, although few autosomal recessive, autosomal dominant, X-linked recessive and dominant cases are on record.[5] In our series one family had two siblings (male and female) with CCA. The other members of the family including the asymptomatic siblings could not be screened. This was possibly inherited as autosomal recessive. It was not feasible to screen all the family members of the affected children; hence it is possible that autosomal dominant inheritance pattern could have been missed. One case of X-linked recessive inheritance was documented, having features of Aicardi syndrome.

Various chromosomal defects including trisomies 18, 13 and 8 have been reported in medical literature with CCA. Serur et al[9] reviewed 81 cases of CCA from medical literature, of which 21 had trisomy 8, 14 had trisomy 13 and 18 had aberrations of chromosomes 17 and 18. In the syndromic form of CCA, where agenesis is a constant feature, other significant manifestations[5] include infantile spasms, disc coloboma, retinal lacunae and vertebro-costal anomalies (Aicardi syndrome), episodic hypothermia and diaphoresis (Shapiro syndrome) and sensory – motor neuropathy (Andermann syndrome). The Aircardi syndrome, an X-linked dominant disorder, seen only in girls account for about 1-4 per cent of cases of infantile spasms.[5] Other syndromes in which CCA is an inconstant feature are orofacial-digital syndrome,[10] Dandy Walker syndrome,[11] Apert syndrome,[12] Meckel syndrome,[13] DiGeorge syndrome[14] and Goldenhar syndrome.[15] The clinical manifestations of CCA can be described under non syndromic and syndromic forms. The non syndromic forms are more commonly encountered.[5] Most patients have mental retardation, seizures, microcephaly or macrocephaly.[5] In a series of CCA published by Jeret et al,[16] global developmental delay was seen in 82% cases and seizures in 43%. Seizures

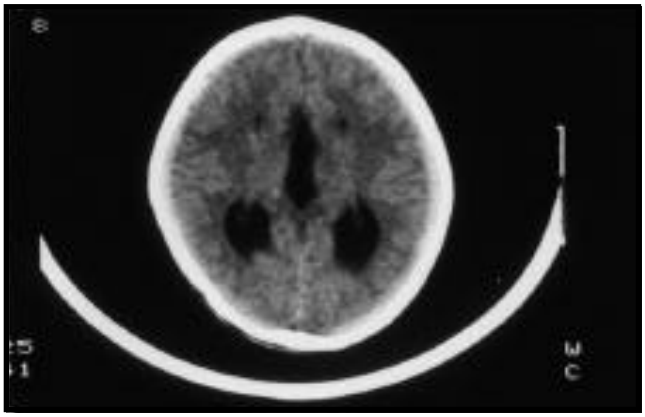

Figure 1 - Cranial CT scan showing elevation of dilated third ventricle.

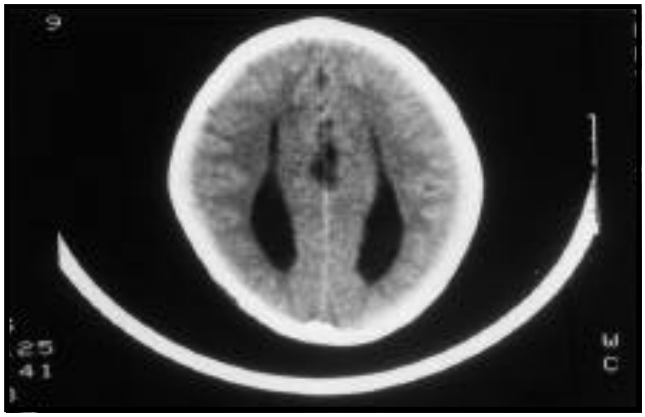

Figure 2 - Cranial CT scan showing lateral displacement of the lateral ventricles.

Table 1 - Corpus callosum agensis

No	Age at presentation	Sex	Mode of presentation	Neurological abnormalities	Other systemic abnormalities	Other abnormalities on CT brain	Chromosomal study	Any other investigation
Non syndromic								
1	1Y 7 M	M	Seizures, developmental delay	Microcephaly, spasticity	Left optic nerve dysplasia	Poor grey & white matter differentiation	-	Torch-ve
2	3Y 6M	M	History of infantile spasm (sibling of No. 3)	Mental retardation	-	Calcification left parietal region	-	-
3	7Y	M	Talipes equino varus bilateral (sibling of No. 2)	Mental retardation, CSF rhinorrhoea	-	-	-	-
4	8Y	M	Developmental delay	Mental retardation, Microcephaly	Myopia, retinitis	-	-	Torch-ve
5	5Y	F	Developmental delay, speech delay	Microcephaly, spasticity	Hypothyroid, anaemia	-	-	-
6	3D	M	Multiple congenital anomalies	Macrocephaly, hypotonia	Facial dysmorphism neck webbing cryptorchidism	Cortical atrophy	N	-
7	7M	F	Chorea, poor vision	Hypotonia, cortical blindness	Deafness, syndactyly	Cortical atrophy	N	Echo cardiography N
8	7M	M	Developmental delay	Microcephaly, spasticity, cortical blindness	Deafness	Cortical atrophy	-	Torch-ve
9	5Y	M	Developmental delay	Microcephaly	-	-	-	-
10	6Y	M	Dysphagia	Spasticity, cerebellar signs	-	Enlarged cisterna (MRI) underdeveloped parietal cortex & operculum	N	-
11	3Y	F	Delayed development	Microcephaly, spasticity	Diabetes insipidus	-	N	-
12	4M	F	Seizures	Spasticity	Multiple congenital anomalies, cleft palate	Holoprosencephaly	-	Echo cardiography N
13	7M	M	Seizures, developmental delay	Mental retardation		Cortical atrophy	-	-
14	6Y	M	Speech, developmental delay	Microcephaly		-	-	-
15	7M	F	Developmental delay, seizures	Microcephaly, hypotonia	Retinitis pigmentosa, sensorineuronal deafness	Agenesis of cerebellar vermis	N	Torch CMV+ve
16	2D	M	Jitteriness	Hypotonia	Respiratory diffuculty, lung haemorrhages	-	-	-
17	7M	F	Macrocephaly	Hypotonia, macrocephaly	-	Hydrocephalus	-	EMG N muscle biop. N
18	2Y	F	Developmental delay, seizures	Hypotonia, spasticity, deafness, blindness	-	-	N	-
19	1.5M	M	Congenital anomalies	Spasticity	ASD, VSD, cleft palate hepatosplenomegaly	-	-	Torch-ve
20	3M	F	Developmental delay	Microcephaly, spasticity	Cortical atrophy	-	-	-
Syndromic								
21	10Y	F	Seizures (Orofacialdigital syndrome)	Mental retardation	Abnormal buccal frenula, polydactyly, syndactly	Arachnoid cyst, left frontal region	N	-
22	7D	M	Seizure (DiGeorge syndrome)	Hypotonia	Facial dysmorphism	-	N	Hypocalcaemia

ASD=Atrial septal defect, VSD=Ventricular septal defect, CMV=Cyto Megalo virus, Y=years, M=months, D=days, Biop-biopsy, No=Number

in these children may be of any type and could manifest even in early neonatal period. A diagnosis of cerebral palsy was made in 31% of the cases, reported by Jeret et al.[16] Although a large head is common, indications for shunting should be extremely conservative as many of these cases of "hydrocephalus" spontaneously stabilize without raising any problems.[17] An unknown, albeit small proportion of cases of CCA remain asymptomatic.[17] The diagnosis of CCA rests on neuro imaging; cranial ultrasonography in infancy and CT scan or MRI of the brain in later years. The latter technique is far superior for the diagnosis of partial agenesis, while cranial ultrasonography serves as an easy alternative for the diagnosis of complete agenesis.[18] In our experience, the radiological diagnosis of CCA has been mostly coincidental, hence neuroradiological imaging remains an absolutely essential investigation of developmental delay.

Antenatal diagnosis is possible from 20 weeks of gestation. A decision to terminate is difficult to take without reservation until more is known about the incidence of asymptomatic cases. Blum et al[19] reported that six of twelve infants with antenatally diagnosed callosal agenesis had a normal development at 2-8 years of age. Infants with associated manifestations or chromosomal anomalies had a poor outcome. Fetal karyotyping, looking for associated anomalies and thorough antenatal sonographic examination of the foetus may be of immense help in deciding to terminate pregnancy.

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