Corpus callosum abnormalities in 64 Egyptian patients: Neuropsychological and genetic studies

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Introduction
Corpus callosum (CC) connects the left and right cerebral hemispheres. It is the largest white matter structure in the brain connecting mainly homotopic, as well as heterotopic, brain areas of both hemispheres. It has a major role in everyday behavior. Agenesis of CC can occur as isolated finding on MRI, or more commonly, it is associated with large number of brain anomalies.

Patients and methods
Neuropsychological and genetic assessment was done for 64 cases with corpus callosum abnormalities, whose age ranged from 6 months to 11 years and 9 months, with a mean age of 3 years and 6 months. This study was done from January 2012 till December 2014.

Results
Overall, 12.5% of the cases had chromosomal aberrations, 14% of the cases had identified genetic syndrome, and 73% of the cases were nonsyndromic/unclassified. Variable degrees of mental subnormality were encountered among 58 (92.2%) of 64 studied patients.

Conclusion
Abnormalities of the CC are often associated with cognitive deficits, autism, and epilepsy.

Keywords:
abnormalities, agenesis, chromosomal, corpus callosum, magnetic resonance imaging, neuropsychological evaluation

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Introduction

Corpus callosum (CC) is a brain structure that connects the left and right cerebral hemispheres and is found only in placental mammals. It is the largest white matter structure in the brain and contains several intrahemispheric and interhemispheric myelinated axonal projections (van der Knaap and van der Ham, 2011). It consists of ~250 million fibers. It connects mainly homotopic, as well as heterotopic, brain areas of both hemispheres (Jarbo *et al.*, 2012). It has a major role in everyday behavior, and owing to its variable structure and function among individuals, it has become an important part of the brain for analysis (Junle *et al.*, 2008).

Agenesis of corpus callosum (ACC) can occur as an isolated finding on MRI, or more commonly, it is associated with large number of brain anomalies. It can result from disruption of numerous developmental steps from early midline telencephalic patterning to neuronal specification and guidance of commissural axons; therefore, it is a heterogeneous condition (Schell-Apacik *et al.*, 2008).

The nature and function of the CC not only involves connecting the two hemispheres, but changes in this structure are frequently noted in developmental and psychiatric disorders. In patients diagnosed with schizophrenia, autism (Egaas *et al.*, 1995), mental retardation (MR) (Schaefer and Bodensteiner, 1999), Down syndrome (Wang *et al.*, 1992), attention-deficit hyperactivity disorder (Lyoo *et al.*, 1996), developmental dyslexia (Hynd *et al.*, 1995), and developmental language disorders (Preis *et al.*, 2000; Bloom and Hynd, 2005), malformations in the size and shape of the CC have been found. By providing axonal connectivity across the midline between cortical areas that are needed for different kind of sensory, motor, and emotional processing, it coordinates interhemispheric functions critical for cognition (Paul *et al.*, 2007).

Bimanual coordination skills are needed for numerous everyday activities, such as typing, preparing food, and driving. Sectioning (parts of) of the CC affected interactions between both hands directly; this was proven by research on callosotomy patients who showed the principal evidence for this (bimanual coordination skills) brain–behavior relationship in humans. Subsequently,

the new imaging techniques, such as diffusion tensor imaging, which is a noninvasive in-vivo technique, have boosted the study of the link between microstructural properties of the CC and bimanual performance in normal volunteers (Gooijers and Swinnen, 2014). In the present study, we recruited 64 patients with corpus callosum abnormalities. We aimed at identifying and classifying them according to the closest matching genetic etiology and assessment of their neuropsychological development in correlation to etiology.

Patients and methods

All patients and their parents were included in the study after having a signed informed consent according to the guidelines of the Medical Research Ethics Committee at the NRC. The patients of the current study were recruited from among the 2915 patients referred to the Clinical Genetics Department, National Research Centre, over a period of 2 years (2012–2014). They presented with delayed developmental milestones. They were selected according to their neuroimaging changes showing corpus callosum abnormalities. We recruited 64 patients, with 35 males and 29 females. The age of the studied cases ranged from 6 months to 11 years and 9 months, with mean age of 3 years and 6 months.

All patients were subjected to the following.

Clinical study

Detailed history including personal, pregnancy, delivery, neonatal, postnatal, and onset, and course of the disorder was recorded.

Pedigree construction was designed up to three generation, with particular emphasis on consanguinity, similarly affected family members, other genetic family disorders.

The assessment of growth parameters (weight, height, and head circumference) was done using anthropometric measurements.

Comprehensive clinical examination and investigations included EEG, echocardiography, pelviabdominal ultrasonography, complete eye examination, audiometry, skeletal survey, etc.

Neuroimaging studies

MRI was performed for all patients, as it was our clue for patient selection. All studies included sagittal T1 images, axial T1-weighted images, axial T2-weighted images, and coronal T1-weighted or T2-weighted images.

All neuroradiologic examinations were reviewed with particular attention to the degree of corpus callosum abnormality, presence of the interhemispheric cyst, probst bundle, other commissural fibers, ventriculomegaly as well as the presence and type of associated malformations.

Abnormalities of the CC were categorized according to Hanna *et al.* (2011) into total agenesis, hypoplasia, dysplasia, and dysplasia with hypoplasia. The association with central nervous system malformations was recorded.

Psychological assessment

The assessment of the intellectual function and social adaptation was done using Wechsler Preschool Intelligence Scales (Wechsler, 1997). Vineland Social Maturity Scale was applied for patients who showed no response with the provided scale regardless of their age (Elwan, 2000).

The assessment of behavioral and emotional disorders among the studied patients was done using Revised Problem Checklist (Quay and Peterson 1993). The six subscales measure the following: conduct disorder, socialized aggression, attention problems–immaturity, anxiety–withdrawal, psychotic behavior, and motor tension–excess.

Cytogenetic studies

Conventional cytogenetic analysis, giemsa banding (GTC banding) procedure banding technique, was performed for all patients and parents if indicated according to Verma and Babu (1995). A total of 25 metaphases were analyzed and karyotyped for each case according to ISCN (2013) (Shaffer *et al.*, 2013). Conventional cytogenetic results were further confirmed by fluorescence in-situ hybridization technique. This was also done on peripheral blood lymphocytes according to Pinkel *et al.* (1986).

Results

Our 64 patients included 29 (45.3%) female and 35 (54.7%) male cases. The age of the studied patients ranged from 6 months to 11 years and 9 months, with mean age of 3 years and 6 months (3.5 ± 2.26). A positive family history of a similarly affected sibling/siblings was seen in 14 (21.9%) patients.

The studied cases were classified into three categories: first, with chromosomal abnormalities, representing 8 (12.5%) of 64 patients; second, with syndromic CC abnormalities, representing 14% of the studied patients, and the last

group had nonsyndromic/unclassified CC abnormalities, representing most cases, with 47 (73%) patients.

Consanguinity of parents was present in 34 (53.1%) patients, and they were distributed as follows: 1/8 (8.7%) patients among those with chromosomal aberrations, in 8/9 (88.9%) patients in syndromic cases, whereas 25/47 (53%) patients in nonsyndromic/unclassified cases.

Microcephaly was present in 40/64 patients, representing 62.5% of the studied cases. Autistic behavior (in the form of stereotyped repetitive movements, lack of eye contact, and lack of speech) in association with MR was noted in 39/64 (60.9%) patients. Abnormal EEG changes were found in 22/64 (34.3%) cases; of them, epilepsy was manifested in 18 (81.8%) of 22 patients, whereas four patients had abnormal EEG finding without manifesting seizures, representing 18.2% of the cases.

The abnormal EEG changes were found to be focal epileptogenic discharges in 17 (77.3%) of 22 cases in the form of focal frontotemporal, occipitoparietal, centroparietal, and centrotemporal epileptogenic activity, whereas 4 (18.2%) cases had generalized epileptogenic activity, and hypsarrhythmia was seen in a single (4.5%) case.

Epilepsy was manifested in 18 (28.12%) of 64 studied patients. They were subclassified as follows: focal seizures in 8 (44.4%) of 18 cases, generalized in 4 (22.2%) of 18 cases, myoclonic in two (11.1%) cases, and mixed seizures type in four (22.2%) cases.

Dysmorphic facies was noted in 28 (43.8%) of 64 cases and eye abnormalities were documented in 15 (23%) patients. These were in the form of anophthalmia, iris coloboma microcornea and microphthalmia, congenital glaucoma, and cataract. Skeletal deformities were present in 6/64 cases and were assigned as postaxial polydactyly, clinodactyly, hip dislocation, and mild scoliotic deformity. Other notable systemic involvement was in the form of congenital heart disease and was seen in four (6%) of 64 patients.

Assessment of intellectual function

Among our 64 studied patients, profound retardation was seen in nine (14.1%) patients, severe retardation was in 19 (29.7%) patients, moderate in 17 (26.6%) patients, mild in 13 (20.3%) patients, and borderline in six (9.4%) patients. The assessment of behavior disorder using Child Behavior Checklist (CBCL) was applied for nine (14.1%) patients, as the rest of the cases were mentally affected or they were too young to undergo assessment with the checklist. The CBCL did not show any abnormality in child behavior for the assessed cases.

Radiological findings

The radiological findings of the studied cases with corpus callosum abnormalities showed that total ACC was present 24 (37.5%) of 64 cases, hypoplasia of CC was present in 25 (39%) cases, dysplasia of CC was present in three (4.75%) cases, and hypoplasia with dysplasia was present in 12 (18.75%) cases. On assigning the abnormalities related to CC development, the anterior commissure was present in 63 (98.4%) cases and was only missing in one case. Colpocephaly (dilatation of the posterior horn of the lateral ventricle) was present in 18 (28.1%) of 64 cases, probst bundle was present in 18 (28.1%) cases, and abnormal septum pellucidum was present in one case only (1.6%; Table 1). These data are confirmed by the MRI findings.

Patients with chromosomal aberrations

The number of patients with chromosomal abnormalities in our study was eight (12.5%) cases, with five males and three females. Consanguinity was noted in one (12.5%) family. The MRI findings revealed that five (62%) patients had hypoplasia of CC, one (12.5%) patient with hypoplastic with dysplasia of CC, one (12.5%) patient with ACC, and one (12.5%) patient had dysplastic CC. The psychological evaluation showed that four (50%) cases had severe MR, two (25%) cases had moderate MR, and two (25%) cases had mild MR (Tables 2 and 3).

Patients with syndromic corpus callosum abnormalities

The number of patients with syndromic CC abnormalities in our study was nine cases, with five males and four females. Consanguinity of the parents was present in eight (88.9%) cases. ACC was present in three (33.3%) cases, hypoplastic CC was in five (55.5%) cases, and hypoplasia with dysplasia was present in one (11.1%) case. There were different syndromes diagnosed with CC abnormalities in this study including one case with Vici syndrome, one case with Sotos syndrome (overgrowth syndrome), two cases

Table 1 Percentage of the different recorded abnormalities of the corpus callosum

Abnormalities of corpus callosum	*n* (%)
Hypoplasia	25 (39)
Dysplasia	3 (4.7)
Hypoplasia with dysplasia	12 (18.75)
Complete agenesis	24 (37.5)
Presence of anterior commissure	63 (98.4)
Colpocephaly	18 (28.1)
Probst bundle	18 (28.1)
Absent septum pellucidum	1 (1.6)

Table 2 Studied patients with abnormal corpus callosum and chromosomal aberrations

Case no	Age (years)	Sex	Consanguinity	FH	Mental retardation	Radiological findings	Karyotype
1	3 6/12	Male	Positive	Positive	Moderate MR	Hypoplasia of CC	46, XY, t(7,15)(q21, q21)
26	6	Male	Negative	Negative	Mild MR	Hypoplasia of CC	47, XY+mar (9;22) which proved to be of maternal origin later balanced translocation
30	2 2/12	Female	Negative	Negative	Mild MR	Hypoplasia of CC, CVH, dilated ventricles	5p- 46, XX, del 5 p14.2-pter
41	2 11/12	Female	Negative	Negative	Severe MR	Dysplasia of CC	46 XX, add 5p Maternal karyotype: 46, XX, t(1;5)(q41;p15) balanced translocation
50	1 2/12	Male	Negative	Negative	Severe MR	Hypoplasia with dysplasia of CC	47, XY, +mar
56	2 4/12	Female	Negative	Negative	Severe MR	ACC	46, XX, add (1) (q44)
57	2 6/12	Male	Negative	Negative	Moderate MR	Hypoplasia of CC	46, XY, t,(1q; 13;22)
62	2 6/12	Male	Negative	Negative	Severe MR	Hypoplasia of CC	47, XY, +mar 46, XY (30%) (47, XY, +13 (70%

Aut. features, autistic features; CC, corpus callosum; cons., consanguinity; CVH, cerebellar vermian hypoplasia; FH, family history; MR, mental retardation.

Table 3 Mental retardation with different types of callosum abnormalities in the chromosomal aberration group

Radiological findings	Number of cases	Sex	Mental retardation
Hypoplasia of CC	5	4 males	Mild MR: one case
			Moderate MR: two case
			Severe MR: one case
		1 female	Mild MR
Dysplasia of CC	1	1 female	Severe MR
Hypoplasia with dysplasia of CC	1	1 male	Severe MR
ACC	1	1 female	Severe MR

ACC, agenesis of corpus callosum; CC, corpus callosum; MR, mental retardation.

with Acrocallosal syndrome, one case with Joubert syndrome, two cases with ptosis–blepharophimosis–MR syndrome, and two cases with Micro–Martsolf syndrome (Table 4 and 5).

The psychological evaluation showed that five (55.6%) cases had severe MR, three (33.3%) cases had moderate MR, and one (11.1%) case had profound MR. The intellectual assessment of cases with syndromic CC abnormalities shows moderate to profound affection. This may be attributed to associated brain or other congenital anomalies.

Patients with nonsyndromic/unclassified corpus callosum abnormalities

The major group in our series was the nonsyndromic/unclassified CC abnormalities, which represent 73.4% of cases (47 patients), with 25 males and 22 females. Consanguinity was positive in 25 (53.2%) cases. Family history of similarly affected family member was positive in six (12.8%) cases. CC abnormalities were in the form of hypoplasia in 14 (29.8%) cases, dysplasia with hypoplasia in 11 (23.4%) cases, dysplasia in two (4.2%) cases, and total agenesis in two (4.2%) cases.

Most cases displayed hypoplasia of CC with or without dysplasia or dysplasia only, representing 27/47 (57.44%) cases, and five (10.6%) cases displayed ACC associated with other brain abnormalities, whereas 15 (31.9%) cases displayed ACC without other brain abnormalities (Tables 6 and 7).

From this table, complete ACC shows more affection of the neurodevelopmental outcome as 17 (70%) of 24 cases of the ACC group are severely affected. In the hypoplasia group, the neurodevelopmental outcome is borderline to moderate affection in 17 (68%) of 25. The last two groups (hypoplasia with dysplasia and dysplasia) show that the neurodevelopmental outcome is borderline to mild to moderate affection is 12/15 (80%). The intellectual function is more severely affected in the ACC group in comparison with the other groups.

Discussion

Abnormalities of CC may be either an isolated anomaly or occur in association with other neuroanatomical lesions and/or congenital anomalies, and recorded with different genetic causes. Neuropsychological outcome varies considerably from normal to profound intellectual disability depending on the etiology (Palmer and Mowat, 2014).

CC abnormalities and full characterization of the anomalies in its different parts have been increased in frequencies since the widespread clinical use of MRI. Variable degrees of intellectual disability are present nearly in 25% of patients with isolated ACC who are diagnosed antenatally (Palmer and Mowat,

Table 4 Descriptive data of patients with syndromic corpus callosum abnormalities

Case no	Age (years)	sex	Consanguinity	FH	Autistic features	Epilepsy	Psychological evaluation	Radiological findings	Syndrome
21	7/12	Male	Positive	Negative	Positive	Negative	Severe MR	Hypoplasia (anterior remnant)	Vici syndrome
42	2 4/12	Male	Negative	Negative	Negative	Negative	Moderate MR	Hypoplasia with dysplasia CC	Overgrowth syndrome (Sotos)
49	1 6/12	Male	Positive	Positive	Positive	Negative	Moderate MR	ACC	Acrocallosal syndrome
58	2 6/12	Male	Positive	Negative	Positive	Negative	Severe MR	ACC	Acrocallosal syndrome
59	1	Male	Positive	Negative	Positive	Negative	Severe MR	ACC, MTI	Joubert syndrome
60	4	Female	Positive	Positive	Positive	Negative	Severe MR	Hypoplasia of CC	Ptosis-Blepharophimosis-Mental retardation
61	1 9/12	Female	Positive	Positive	Positive	Negative	Severe MR	Hypoplasia CC	Ptosis-Blepharophimosis-Mental retardation
63	7/12	Female	Positive	Positive	Positive	Negative	Moderate MR	Hypoplasia of CC, CBA	Micro Syndrome
64	2 8/12	Female	Positive	Positive	Negative	Negative	Profound MR	Hypoplasia of CC, CBH	Martsolf syndrome

ACC, agenesis of corpus callosum; CBA, cerebellar atrophy; CBH, cerebellar hypoplasia; CC, corpus callosum; FH, family history; MR, mental retardation.

Table 5 Degree of mental retardation in different types of callosum abnormalities in the syndromic group

Radiological findings	Number of cases	Sex	Mental retardation
Hypoplasia of CC	6	4 females	Moderate MR: two case
			Severe MR: three cases
		2 males	Profound MR
ACC	3	3 males	Moderate MR: two case
			Severe MR: three cases

ACC, agenesis of corpus callosum; CC, corpus callosum; MR, mental retardation

Table 6 Relation between mental retardation and corpus callosum abnormality in the nonsyndromic/unclassified corpus callosum abnormalities group

	ACC	Hypoplasia	Hypoplasia with dyplasia	Dyplasia
Borderline MR	0	4	1	1
Mild MR	3	2	5	1
Moderate MR	3	6	3	0
Severe MR	6	3	1	0
Profound MR	8	0	0	0

ACC, agenesis of corpus callosum; MR, mental retardation.

2014). Among those with normal intelligence, in longitudinal neurocognitive follow-up studies, subtle neurological, social, and learning deficits may be evident. So, the detection of ACC should be carefully clinically assessed to determine and manage the underlying condition. It is clearly recognized that genetic factors contribute to anomalies of CC in most cases. Less commonly, they can result from antenatal infections and vascular or toxic insults. Nowadays, it is increasingly recognizable that ACC, particularly the isolated form, may result from an interaction of a number of 'modifier' genetic and environmental factors (Dobyns, 1996; Edwards *et al*., 2014). Furthermore, abnormalities in CC were recorded in a large number of genetic conditions as a consistent feature (Palmer and Mowat, 2014). Owing to unavoidable limitations of MRI quality in most of patients, the anterior commissure appearance was not reliable to be taken in consideration and classification.

In the present study, we studied 64 cases with CC abnormalities. The diagnosis was based on their neuroimaging findings. There were 35 (54.7%) males and 29 (45.3) females, with a mild male sex predominance. The presence of CC abnormalities may be owing to high consanguinity rate in the studied population. This is quite in accordance with several studies (Jeret *et al*., 1987; Shevell, 2002; Bedeschi *et al*., 2006).

The consanguinity rate in this series was 34 (53.1%) patients, however, it seems variably dependent on the etiology. In patients with chromosomal aberrations, consanguinity was present in 1/8 (8.7%) case only, documenting the lack of the role of consanguinity in chromosomal aberration. On the contrary, in the syndromic group, consanguinity was present in 8/9 (88.9%) cases, which is highly suggestive of the predominance of the autosomal recessive pattern of inheritance among them. The single case in the syndromic group with negative consanguinity was with overgrowth syndrome (Sotos syndrome), which is inherited in an autosomal dominant pattern or de novo mutation. In the unclassified group, consanguinity was found in 25/47 (53%) cases, which points to the possibility of an undiagnosed recessive form that needs to be tested regarding the known genes of isolated/nonsyndromic CC abnormalities, i.e., *C12orf57,* which is the causative gene of Temtamy syndrome (Hanna *et al*., 2011; Akizu

Table 7 Mental retardation in corpus callosum abnormalities in all studied patients

Mental retardation	Corpus callosum abnormalities			
	ACC	Hypoplasia	Hypoplasia with dyplasia	Dyplasia
Borderline MR	0	4	1	1
Mild MR	3	4	5	1
Moderate MR	4	9	4	0
Severe MR	10	6	2	1
Profound MR	7	2	0	0
Total	24	25	12	3

ACC, agenesis of corpus callosum; MR, mental retardation.

et al., 2013), or *CDK5RAP2,* which is identified as a novel causative gene for isolated ACC. *CDK5RAP2* is also found to be incriminated in autosomal recessive primary microcephaly, also known as MCPH 3 (Jouan *et al.*, 2015), and subsequently, whole exome needs to be sequenced to identify new genes.

The most frequent clinical findings among the reported patients in the literature are MR (60%), visual problems (33%), speech delay (29%), seizures (25%), and feeding problems (20%). Furthermore, even in cases with no developmental delay and normal intelligence, mild behavioral or social problems as well as the attention-deficit hyperactivity disorder have been described (Schell-Apacik *et al.*, 2008). In the present study, variable degrees of MR were seen among 58 (90.6%) of 64 patients, learning disability in 4% of cases, and manifest epilepsy in 28.1% of cases, whereas abnormal EEG finding was present in 34.4% of cases, visual and eye problem in 23.5%, microcephaly in 62.5%, and autistic behavior in 60.9% of cases.

Schell-Apacik *et al.* (2008) studied 41 patients with ACC and found that 12% had a genetic syndrome. It is similar to our study, as we assigned 9/64 cases as recognizable syndromes (14% of cases), in which CC abnormalities are one of its features, such as, Vici, Acrocallosal, Joubert, Sotos, Mico–Martsolf, and Blepharophimosis–Ptosis intellectual disability syndromes. Other syndromes in which ACC is a cardinal feature are Mowat Wilson, Andermann, Temtamy, Aicardi, Chudley–McCullough, Donnai–Barrow, FG, Genitopatellar, and Toriello–Carey syndromes.

Furthermore, we assigned 17 (26.5%) of 64 cases with known syndromic and chromosomal cause. Such results are nearly similar to Bedeschi *et al.* (2006), who studied 21 (33%) of 62 cases with identified a syndromic and chromosomal cause, whereas Schell-Apacik *et al.* (2008) assigned 11 (39%) of 28 studied cases with detectable syndromic or chromosomal causes. We postulated that the lack of new technology as comparative genomic hybridization and molecular tests in our study hindered identification of more chromosomal and specific genetic syndrome.

Al-Hashim *et al.* (2016) found that dysmorphic features were present in 61% of the studied patients, whereas in our current study, we found dysmorphic features were seen in 43.8% of the studied patients. Eye abnormalities in our study was present in 23% whereas Al-Hashim *et al.* (2016) found in her study that eye abnormalities were present in 46%. Heart abnormalities were seen in 21% in the aforementioned study, whereas in the current study, it was 6%.

The assessment of mental subnormality revealed that profound MR was seen in 9 (14.1%) patients, severe in 19 (29.7%) patients, moderate in 17 (26.6%) patients, mild in 13 (20.3%) patients, and borderline in six (9.4%) patients. These results are nearly similar to the results of Bedeschi *et al.* (2006), who found that MR of varying severity was evident in 83% of the cases (52/63) and was distributed as follows: profound (16%), severe (42%), moderate (21%), and mild (21%). Two of their patients were borderline MR and nine patients had normal intelligence quotient. They suggested that profound and severe MR was mainly associated with a more complex picture of multiple malformations. Such observation was in accordance to our study. Hinkley *et al.* (2012) stated that impairments in specific cognitive skills, in particular verbal processing speed and executive function, in patients with corpus callosum abnormalities were attributed to defect in functional connections between specific regions within the frontal, parietal, and occipital cortices, and the degree of 'under-connectedness'. This was clarified through application of functional imaging tools, namely, magnetoencephalography and tractography.

In our study, severe and profound MR predominated among patients with complete ACC than patients with other CCA. This is in accordance with the study done by Brown *et al*. in 2001 who stated that the degree or type of dysgenesis does not significantly affect performance on specific tasks; however, overall development of children with ACC is likely improved by the presence of a portion of the CC (i.e., partial ACC). Moreover, the results showed that the psychological evaluation of patients with syndromic corpus callosum abnormalities (CCA) and chromosomal aberrations is more affected than the nonsyndromic/unclassified group. This is in accordance to what has been stated by Kovac (2011) that the results of the case study literature are most dramatically influenced by the inclusion of participants with multiple comorbidities and chromosomal disorders, as children with additional

diagnosis or abnormalities consistently exhibit mild to severe cognitive delay.

The CBCL in our studied cases did not result in any abnormal behavior, and this may be attributed to young age of the studied patients (mean age = 3.5 ± 2.26 years). Older children with CC abnormalities may experience greater behavioral problems as they enter school owing to increased social and academic demands (Badaruddin *et al.*, 2007).

In our study 18/64 (28.1%) cases exhibited epilepsy. Doherty *et al*. (2006) found that 27.3% of the individuals with ACC had seizure disorders, and 41.2% had at least one seizure. They also stated that individuals with ACC were reported to have hypotonia significantly more often than their siblings. In our study, 44/64 (68.75%) patients had hypotonia, normal muscle tone was present in 17.2%, and increased muscle tone was present in 14.1%. However, a recent study by Al-Hashim *et al*. (2016) found that patients with normal tone represented 45%, with hypotonia 36%, and with hypertonia 19%.

Sotiriadis and Makrydimas (2012) reported that the most common brain anomalies associated with CC abnormalities are posterior fossa anomalies, interhemispheric cysts, and neuronal migration disorders. In our series, we had 17/64 cases with associated brain anomalies, representing 26.5% of cases. Similarly to their report, the most encountered brain anomalies were interhemispheric cysts, posterior fossa anomalies (Dandy–Walker variants, cerebellar vermis hypoplasia, and molar tooth image), and migration disorders in the form of heterotopia and polymicrogyria.

Conclusion

In our study, CC abnormalities are more common in males. They are either idiopathic, or associated with chromosomal abnormalities or syndromes. The abnormalities of the CC are associated with various degrees of MR in which syndromic cases exhibit more retardation and show more significant parent consanguinity than nonsyndromic cases.

We concluded that CC abnormalities could be a simple or serious neurological insult that has many intellectual and neurological consequences.

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Conflicts of interest
There are no conflicts of interest.

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