ARAŞTIRMA RESEARCH ARTICLE

NEUROLOGICAL DISORDERS COMBINED WITH AUTISM IN CHILDREN

Sema Saltık MD,[1] Şaziye Senem Başgül MD[2]

[1] Istanbul Medeniyet University Göztepe Research and Training Hospital, Dept. of Child Neurology, İstanbul

[2] Istanbul Medeniyet University Göztepe Research and Training Hospital, Dept. of Child and Adolescent Psychiatry, İstanbul

ABSTRACT

Objective: *A total of 121 autistic children (male/female: 3.1/1) aged between 3-18 years were included in the study to investigate the characteristics of neurological disorders and some of their risk factors in autistic children.*

Material and Method: *Data on the sociodemographic features, developmental characteristics, and physical and neurological findings were noted for all patients diagnosed as autism according to Diagnostic and Statistical Manuel of Mental Disorders, 4th edition, text revision criteria. Results of cranial magnetic resonance imaging and sleep EEG records were re-evaluated. Groups then were organized according to the presence or absence of neurological disorder, of epilepsy and of cerebral palsy associating autism. Chi-square test was used for statistical comparisons among sub-groups.*

Results: *A total of 49 patients (40.4%) had a neurological involvement associating autism. Epilepsy was the most common condition with a 33% rate. Presence of consanguineous parents (32.5%; 16%) and delayed walking (32.5%; 12.3) was significantly higher in patients with seizures as compared to patients without seizures. A history of preterm delivery (46.2%), low birth weight (38.5%), natal and prenatal problems (53.8%), delayed walking (84,6%) and presence of gait problems (100%) were more common in autistics with cerebral palsy than those (7.5%; 7.4%; 18.5%; 11.1%; 12% respectively) in autistics without cerebral palsy. These findings were significant statistically. Epilepsy was significantly more common in cerebral palsy patients (53.8%) than those without cerebral palsy (23.1%) (p=0.01).*

Conclusion: *Neurological disorders are not unusual in autistic children. In case of autistic conditions with a history of low birth weight, prematurity, delayed walking and/or presence of gait difficulties a thorough neurological evaluation may give way for better measures of management and improve the quality of life.*

Key Words: *Autism, neurological disorders, childhood, epilepsy, EEG* ***Nobel Med 2012; 8(3): 113-120***

ÇOCUKLARDA OTİZME EŞLİK EDEN NÖROLOJİK SORUNLAR

ÖZET

Amaç: Çocuklarda otizmle birlikte görülebilen nörolojik sorunların özelliklerini ve risk faktörlerini araştırmak amacı ile 3-18 yaş arasındaki toplam 121 otistik çocuk çalışmaya alındı.

Materyal ve Metod: Mental Bozuklukların Tanısal ve İstatistiksel El Kitabı (gözden geçirilmiş) ölçütlerine göre otizm tanısı konan tüm hastalara ait sosyodemografik özellikler, yürüme yaşı, yürüme bozukluğu varlığı, varsa özellikleri, sözel iletişim şekli, fiziksel ve nörolojik muayene bulguları not edildi. Kraniyal manyetik rezonans ve EEG sonuçları değerlendirildi. Klinik ve laboratuvar sonuçları göz önüne alınarak, hastalar aşağıdaki nörolojik tanıların var olup olmamasına göre 2 gruba ayrıldı (bir nörolojik tanı, epileptik nöbet, serebral palsi). Hasta grupları bazı risk faktörleri açısından ki-kare testi kullanılarak, istatiksel olarak karşılaştırıldı.

Bulgular: Çocukların 49'unda (%40,4) otizme eşlik eden bir nörolojik hastalık saptandı. Nöbet geçirme en sık (%33) nörolojik sorun olarak belirlendi. Nöbet geçirme hikayesi olan hastalar ile olmayan hastalar karşılaştırıldığında, akraba evliliği (%32,5; %16), yürümenin 18 aydan sonra başlaması (%32,5; %12,3), nöbet geçirme hikayesi olan olgularda istatiksel olarak anlamlı yüksek bulundu. Serebral palsisi olan otistik çocuklarda preterm (%46,2) ve düşük ağırlıklı doğum (%38,5), natal ve prenatal problem (%53,8), yürümenin 18 aydan sonra başlama (%84,6) hikayesi ve yürüme bozukluğu varlığı (%100) serebral palsisi olmayan çocuklara göre (sırayla %7,5; %7,4; %18,5; %11,1; %12) daha sık gözlendi. Bu durum istatiksel olarak anlamlı bulundu. Epilepsinin serebral palsili çocuklarda (%53,8) diğer çocuklara (%23,1) göre daha sık görüldüğü tespit edildi (p=0,01).

Sonuç: Otistik çocuklarda nörolojik sorunların görülmesi nadir değildir. Bu nedenle, düşük doğum ağırlığı ve premature doğum, epileptik nöbet hikayesi olan, geç yürüyen ve yürüme sorunları gözlenen otistik çocuklarda daha ayrıntılı nörolojik değerlendirme, bu çocuklarda uygun tedavi desteğini sağlayacağından yaşam kalitesini yükseltebilecektir.

Anahtar Kelimeler: Otizm, nörolojik bozukluklar, çocukluk çağı, epilepsi, EEG **Nobel Med 2012; 8(3): 113-120**

INTRODUCTION

Autism is a neurological and developmental disorder characterized by impairment of social relatedness, communication skills, restriction of interests and stereotyped behaviours. It is defined in the DSM-IV -TR (Diagnostic and Statistical manual of Mental Disorders of the American Psychiatric Association, 4th edition, text revision) as exhibiting at least six symptoms in total, including at least two symptoms of qualitative impairment in social interaction, at least one symptom of qualitative impairment in communication, and at least one symptom of restricted and repetitive behaviour.[1] Autism is believed to be related with central nervous system dysfunction. Autistic children can also have a variety of genetic syndromes as well as neurological problems in addition to their core symptoms, and these are relevant for the treatment and the course of the main disorder.[2] Autism is associated with some neurological problems more frequently than would be expected by coincidence. Neurological comorbidities in autism are not only common, they are also clinically more severe.[2,3] Motor impairment and epilepsy have been reported to be autism's most prevalent neurological comorbidities.[3] Epilepsy is reported to occur in 10-30% of individuals with autism.[3-6] The high concurrence rates of these disorders indicate potentially shared underlying mechanisms.[7] New studies have focused on identifying the genetic causes of this association.[3] Their identification is of high clinical relevance as epilepsy can be treated and may contribute significantly to behavioural and cognitive abnormalities in autistic spectrum disorders. Early assessment of neurological motor impairment to plan the rehabilitation is also important.

MATERIAL and METHOD

The medical records of 156 autistic children that were examined at the departments of child psychiatry, child neurology or the Child Psychiatry and Child Neurology Joint Medical Commission of Istanbul Medeniyet University Göztepe Education and Training Hospital between January 2010 and January 2011 were analyzed. Following a detailed review of the medical records missing data were completed by re-interviewing the parents either by phone, re-examining the patients in the clinic or performing necessary diagnostic tests. A total of 121 patients fulfilling the criteria were included in the study.

Patient inclusion criteria: 1. Aged between 3-18 years. 2. Autism diagnosed according to DSM-IV-TR criteria by the same child psychiatrist in the last one year. 3. Neurological evaluation by the same child neurologist in the last 1 year. →

Patient exclusion criteria: 1. Diagnosis as pervasive developmental disorder-not otherwise specified (PDD-nos), Rett syndrome, disintegrative disorder and Asperger syndrome, or one of the other autistic spectrum disorders. 2. Patients with uncompleted records or who could not be reached by phone or refused to participate in the study.

All parents filled in forms including data the date of birth; gender; family history of consanguinity; presence and characteristics of prenatal and natal problems; time of delivery; weight at birth; presence of seizures during the newborn period; age at the onset of walking; presence and features of gait disorders; characteristics of verbal communication (none-with words-with sentences); presence and characteristics of skin findings and dysmorphic features; presence and characteristics of ophthalmologic and hearing problems (as a result of examination by the ophthalmology and ear-nose and throat specialists); neurological examination findings; presence of febrile seizures and epilepsy; genetic consultation report as indicated (e.g. presence of dysmorphic features); results of blood, urine, and metabolic screening tests; and cranial magnetic resonance imaging (cMRI) scans and sleep electroencephalograms (EEGs) if they were performed. If metabolic tests, cMRIs and EEGs were not performed, the indications of these investigations were re-evaluated.

EEGs had been recorded while awake and sleep (one hour) or only while asleep at various centres using 18-channel instruments with electrodes placed according to the international 10-20 system. EEGs were classified as: 1) without epileptiform activity [normal or abnormal but not epileptiform (e.g., background slowing)], 2) with epileptiform activity (abnormal epileptiform with focal onset, or abnormal epileptiform with generalized onset). EEG activities were re-reviewed and epilepsy was diagnosed by a pediatric neurologist in children with more than one unprovoked seizure and/or an epileptiform EEG. Febrile seizure (FS) was defined in this study as a seizure occurring in childhood between 6 months and 6 years of age associated with a febrile illness not caused by an infection of the central nervous system (CNS), without previous neonatal seizures or a previous unprovoked seizure, not meeting the criteria for other acute symptomatic seizures and without any epileptiform activity in the sleep EEG.

The patients were divided into groups as: Patients with and without a neurological diagnosis associating autism; patients with and without epilepsy, patients with and without epilepsy and/or febrile seizures (E+FSs) and patients with or without cerebral palsy (CP). All groups were also compared for various risk factors for neurological disorders: Those were the presence of a parental consanguinity and prenatal or natal problems, time of delivery, weight at birth, age at the onset of walking, presence of gait problems, and type of verbal communication (patients older than 5 years old included).

Statistical calculations were performed with the NCSS 2007 program for Windows. Besides standard →

Table 1: Features of autistic patients

Features	N	%
Presence of FH of consanguinity	26	21.4
Presence of prenatal, natal problems	27	22.3
Born Preterm	14	11.5
Weight at birth; 2500-3500 gr	70	57.8
< 2500 gr	13	10.7
> 3500 gr	38	31.4
Onset of walking after 18 months of age	23	19
Presence of gait disorders	26	21.4
Cerebral palsy (spasticity 12; ataxia 1)	13	50
Toe walking	13	50
Verbal communication (n:102); None or with words	65	63.7
With sentences	37	36.2

FH: Family history

Table 2: Sleep EEG findings of autistic patients

Pts with sleep EEG	N of Pts (n: 89)	% of Pts (73.5%)
Pts with epileptiform EEG activity	33	37
Pts with epilepsy	27	30.3
Pts without epilepsy	6	6.7
Pts without epileptiform EEG activity	56	62.9

Pts: Patients, EEG: electroencephalogram

Table 3: cMRI findings of autistic patients

Pts that are performed cMRI	N of Pts (n: 76)	% of Pts (62.8 %)
Pts with abnormal cMRI findings	14	18.4
Sequel findings	6	7.8
Hypoxic-ischemic injury	4	5.2
Periventricular leukomalacia	1	1.3
Encephalomalacia	1	1.3
Congenital malformations	4	5.2
Tuberous sclerosis	2	2.6
Neuronal migration disorder	1	1.3
Other (corpus callosum)	1	1.3
Hydrocephaly	1	1.3
Enlargement of lateral ventricles	1	1.3
Retardation of myelination	1	1.3
Nonspecific gliotic lesion	1	1.3
Pts with normal cMRI findings	62	81.5

cMRI: cranial magnetic resonance imaging; Pts: patients

Table 4: Distribution of patients according to the neurological disorder combined with autism

Neurological diagnosis/disorder	N	%
Neurological diagnosis (+)	49	40.4
Epilepsy	24	19.8
Febrile seizures	8	6.6
Epilepsy and cerebral palsy	7	5.7
Cerebral palsy	6	4.9
Tuberous sclerosis and epilepsy	2	1.6
Becker Muscular Dystrophy	1	0.8
Movement disorder	1	0.8
Neurological diagnosis (-)	72	59.5
Genetic (Fragile X)	1	0.8
Abnormal EEG findings	6	4.9

Table 5: Comparison of patients with or without neurological conditions associated autism according to the some risk factors for neurological disorders

Risk factors	Add. neurological diagnosis (-) N of pts: 72 (%)	Add. neurological diagnosis (+) N of pts: 49 (%)	*p
Gender Male Female	59 (81.9) 13 (18.1)	33 (67.3) 16 (33.7)	0,065
Presence of FH of consanguinity	10 (13.9)	16 (32.7)	0,014
Presence of prenatal, natal problems	14 (19.4)	13 (26.5)	0.358
Preterm delivery	7 (10)	7 (14.3)	0.387
Weight at birth; 2500-3500 gr < 2500 gr > 3500 gr	40 (55.6) 6 (8.3) 26 (36.1)	30 (61.2) 7 (14.3) 12 (24.5)	0.305
Weight at birth; <2500 gr or >3500 gr	32 (44.4)	19 (38.8)	0.535
Onset of walking after 18 month of age	6 (8.3)	17 (34.7)	0.0001
Presence of gait disorders	9 (12.5)	17 (34.7)	0.004
Verbal communication; None With words With sentences	14 (24.1) 20 (34.5) 24 (41.4)	17 (38.6) 14 (31.8) 13 (29.5)	0.253
Sleep EEG with epileptiform activity	6 (14.3)	27 (57,4)	0.0001
Abnormal cMRI findings	1 (3.70)	13 (26.5)	0.014

Pts: patients; add: additional; FH: family history, cMRI: cranial magnetic resonance imaging, *: χ^2 test

descriptive statistical calculations (mean and standard deviation), the unpaired t-test was used to compare the groups, and the Chi square test to evaluate qualitative data. The statistical significance level was established at $p<0.05$.

RESULTS

Patient information: There were 92 (76%) males and 29 (24%) females (ratio 3.1:1) in our study group. The mean age was 9.30±4.2 (range 3-18) years. The clinical features of all autistic patients are listed in Table 1. The mean weight at birth was 3200 ±776 grams. The mean age at the onset of independent walking was 16.7±7.6 months. Among the patients with CP, signs of spasticity were prominent in 12 and ataxia in 1. Predominating picture was choreoathetosis in another patient. No neurological deficit was found in 13 patients with toe walking or with a history of toe walking.

Skin changes were present in two patients who were diagnosed as tuberous sclerosis. No patient had hearing problems. Dysmorphic features were present in 3 patients, chromosomal analysis supported Fragile X syndrome in one of them.

Sleep EEGs were recorded in 89 patients; and 37% of them had epileptiform activity (Table 2).

The cranial MRG findings of the patients are summarized in Table 3. Sequale lesions were the most common (7.8%) cMRI finding in autistic children.

A neurological diagnosis combined with autism was present in 49 patients (40.4%). Table 4 shows the distribution of the patients according to the neurological disorder. Seizures (febrile or afebrile) were seen in 41 patients (83.6%) and were the most common symptom in our study group.

Comparison of patient groups

Patients with a neurological diagnosis other than autism had a significantly lower rate of family history of consanguinity compared to patients without a neurological diagnosis other than autism. The percentage of patients who could walk independently only after 18 months of age and who had surviving gait difficulties was significantly higher in patients with a neurologic diagnosis than those without that trait (Table 5).

Patients with epilepsy had a higher rate of delay in onset of independent walking (later than age 18 months) as compared to ones without (Table 6).

Females were more common among patients with E+FSs. Parental consanguinity and delay in walking was significantly more common in patients with E+FSs (Table 7).

A history of preterm delivery, low birth weight, natal and prenatal problems, delayed walking and the presence of a gait difficulties were seen more commonly in patients with CP. Epilepsy was significantly more common in CP patients than those without (Table 8).

DISCUSSION

We analyzed the characteristics of neurological disorders combined with autism in a group of autistic children →

in this study. The neurological status of the patients was basically determined by the evaluation of the psychosocial-motor-speech development history, seizure history, detailed neurological examination, and sleep EEG and cMRI. Specific dysfunctions frequently encountered in autism were dysfunctional posture and muscle tone, and disturbed fine manipulation.[8] Sleep disorders and especially insomnia have been reported in up to 83% of children with autistic spectrum disorders.[3] We did not look for any fine motor abnormalities or sleep problems in our group, instead, tried to uncover clear neurological abnormalities. A neurological disorder combined with autism was found in 40% of our patients. However, this rate may be over-expressed since our cases consisted of patients who were brought not only to psychiatry but also to the child neurology clinics. Only, it can still be stated that such a high incidence of accompanying neurological disorders in autistic individuals does not seem solely as an epi-phenomenon, rather a meaningful relationship may exist between those two conditions.

The most common neurological disorder accompanying autism is epilepsy. Many reports have linked autism and epilepsy since autism was first described in 1943 by Dr. Leo Kanner. In a prospective community-based study of newly-diagnosed childhood epilepsy, 2.2% of the participants with overall normal cognitive abilities had an autistic spectrum disorder, which is higher than the estimates for the general population (0.5%-0.9%).[9] On the other hand, epilepsy has been reported to occur at rates typically around 25% (5% to 40%) in individuals with childhood autism.[3-6,10-13] These differences are most probably due to the heterogeneity of the samples with respect to age, gender, and intellectual level, and the co-morbidity of the cases with "syndromic" autism, for example tuberous sclerosis. It may also vary depending on the criteria used to diagnose epilepsy.

There was a history of seizures in 40 of our 121 (33%) autistic cases. The diagnosis was febrile seizure in 8 and epilepsy in 32 of these 40 patients. An underlying etiological cause, consisting of CP in 21% and tuberous sclerosis in 6% for a total of 27%, was present in the patients diagnosed with epilepsy. Seizures are reported to occur in patients diagnosed with the more symptomatic subset of individuals with autism.[14-16] The risk of epilepsy in autism appears to be associated with the degree of intellectual disability, mental retardation and language regression.[10,12,17]

In other words, epilepsy becomes more prevalent the lower the IQ. Epilepsy may also be seen more frequently in individuals with autism who have lower receptive language abilities.[18] The only significant criterion increasing the rate of epilepsy among autistic children was the delayed walking in our study. Taking into account that CP was present in 21% of our autistic epilepsy patients, this could be due to the additional underlying neurological problem and the symptomatic etiology. Epilepsy is reported in 35% of CP patients in general.[19] Our rates were comparably much higher as 53% and 61% for epilepsy and for E+FS, respectively, in the autistic patients. CP patients combined with autism had a statistically significantly higher rate of epilepsy and febrile seizures in our study (Table 8). It may be argued that concurrent CP in autistic children can further increase the seizure risk. →

Table 6: Comparison of patients with or without epilepsy according to the some risk factors for neurologic disorders

Risk factors	Pts without epilepsy n: 89 (%)	Pts with epilepsy n: 32 (%)	*p
Gender Male Female	71 (79.8) 18 (20.2)	21 (65.6) 11 (34.4)	0.108
Presence of FH of consanguinity	18 (20.20)	8 (25.00)	0.573
Presence of prenatal, natal problems	18 (20.2)	9 (28.1)	0.357
Preterm delivery	11 (12.64)	3 (9.40)	0.614
Weight at birth; 2500-3500 gr < 2500 gr > 3500 gr	51 (57.3) 10 (11.2) 28 (31.5)	19 (59.4) 3 (9.4) 10 (31.3)	0.954
Weight at birth; <2500 gr or >3500 gr	38 (42.7)	13 (40.6)	0.839
Onset of walking after 18 month of age	12 (13.5)	11 (34.4)	0.01
Presence of gait disorders	17 (19.1)	9 (28.1)	0.286
Verbal communication; None With words With sentences	20 (28.2) 23 (32.4) 28 (39.4)	11 (35.5) 11 (35.5) 9 (29)	0.581
Abnormal cMRI finding	5 (11.4)	9 (28.1)	0.063

Pts:patients; FH:family history; *: χ^2 test

Table 7: Comparison of patients with or without E+FSs according to the some risk factors for neurologic disorders

Risk factors	Pts without E+FSs n: 81 (%)	Pts with E+FSs n: 40 (%)	*p
Gender Male Female	66 (81.5) 15 (18.5)	26 (65.0) 14 (35.0)	0.046
Presence of FH of consanguinity	13 (16)	13 (32.5)	0.038
Presence of prenatal, natal problems	17 (21)	10 (25)	0.618
Preterm Born	10 (12.66)	4 (10)	0.553
Weight at birth; 2500-3500 gr < 2500 gr > 3500 gr	44 (54.3) 9 (11.1) 28 (34.6)	26 (65) 4 (10) 10 (25)	0.512
Weight at birth; <2500 gr or 3500 gr>	37 (45.7)	14 (35)	0.263
Onset of walking after 18 month of age	10 (12.3)	13 (32.5)	0,008
Presence of gait disorders	14 (17.3)	12 (30)	0.109
Verbal communication; None With words With sentences	17 (26.2) 21 (32.3) 27 (41.5)	14 (37.8) 13 (35.1) 10 (27)	0.289
Abnormal cMRI finding	5 (13.9)	9 (22.5)	0.334

Pts: patients, FH: family history, E+FSs: Epilepsy or febrile seizures, cMRI: cranial magnetic resonance imaging, *: χ^2 test test

Table 8: Comparison of patients with or without cerebral palsy according to the some risk factors for neurologic disorders

Risk factors	Pts with cerebral palsy n: 108 (%)	Pts without cerebral palsy n: 13 (%)	*p
Presence of FH of consanguinity	21 (19.40)	5 (38.5)	0.115
Presence of prenatal, natal problems	20 (18.50)	7 (53.80)	0.004
Preterm Born	8 (7.55)	6 (46.2)	0.0001
Weight at birth; 2500-3500 gr < 2500 gr > 3500 gr	64 (59.3) 8 (7.4) 36 (33.3)	6 (46.2) 5 (38.5) 2 (15.4)	0.003
Weight at birth;<2500 gr or 3500 gr>	44 (40.70)	7 (53.8)	0.366
Onset of walking after 18 mnth of age	12 (11.1)	11 (84.6)	0.0001
Presence of gait disorders	13 (12.00)	13 (100)	0.0001
Verbal communication; None With words With sentences	27 (29.3) 30 (32.6) 35 (38)	4 (40) 4 (40) 2 (20)	0.524
Presence of epilepsy	25 (23.1)	7 (53.8)	0.018
Presence of E+FSs	32 (29.6)	8 (61.5)	0.021
Abnormal sleep EEG findings	28 (36.4)	5 (41.7)	0.724
Abnormal cMRI finding	6 (9.5)	8 (61.5)	0.0001

Pts: patients, FH: family history, E+FSs: Epilepsy or febrile seizures, cMRI: cranial magnetic resonance imaging, *: χ^2 test

The main limitation of our study is the lack of information with respect to cognitive function. We included children over 5 years of age to be able to clinically observe the development of language, as a cognitive skill. Due to problems of obtaining satisfactory information from many parents, we were unable to differentiate cases in which speech never had started or a regression in speech took place later. Thus, language development was assessed during the examination so that our study results could be more meaningful. The percentage talking in a fully comprehensible manner with sentences was 40% in non-epileptic autistic children and 29% in those with epilepsy. The percentage was even lower, as 27%, when children with febrile seizures were also included in this group. The language development was slower in children with seizures compared to those without but the difference was not statistically significant. Similarly, Tuchman et al. found no difference in the risk of epilepsy when comparing autistic and nonautistic dysphasic children.[20]

Gender also plays a strong role in relative risk with epilepsy found to be much more common in autistic girls.[10,20] The percentage of girls with autism and only epilepsy was higher than those without epilepsy in our study but this difference was not statistically significant. However, we found a higher tendency to seizures in females when autistic patients with epilepsy and febrile seizures were considered together. Nomura et al. considered the epilepsy in autism to be one of the pathognomonic symptoms of autism and not a secondary manifestation.[21] Epilepsy should be suspected in children in the autism spectrum who have paroxysmal events. Taking a detailed history of seizures in every autistic child is therefore very important. It is necessary to investigate seizures in more detail especially when autistic patients have other symptomatic etiological problems such as tuberous sclerosis and CP while routine sleep EEG tests can also be recommended.

Review of home or school videos in addition to routine EEG may help in clarifying the diagnosis of epilepsy. EEG is not recommended within the practice parameters for autism unless there is evidence of clinical seizures or regression or a high index of suspicion for epilepsy.[22] However some authors feel that EEG should be considered routinely in children with autistic spectrum disorders, especially in more impaired individuals.[23] The rate of documented epileptiform EEG abnormalities varies from 10.3% to 72.4% of patients with autistic spectrum disorders.[14-16,24] Determining the true incidence of isolated EEG abnormalities in autistic patients is difficult as routine EEGs were not part of the work-up. Tuchman and Rapin studied 392 autistic children with available sleep EEGs and reported that the EEG was epileptiform in 59% of the 66 epileptic children and 8% of the 335 nonepileptic children.[25] In our group, 89 (73%) patients had a sleep EEG and 33 (36%) of them showed epileptic EEG activity. This activity was observed in 84.3% of the 32 patients with epilepsy, 67.5% of the 40 cases with epilepsy or febrile seizures and 12 of the 49 patients who had no described clinical seizures.

CP was present in 10.7% of our autistic cases. Fombonne et al. report CP in 2.9% of their 174 autistic cases.[26] A prevalence of 2.9-3.8 per thousand is reported for the population while an autism rate of 8% was found among CP cases.[19] It is therefore necessary to discuss the CP-autism relationship as well. Birth weight and gestational age have been reported to be the leading prenatal and perinatal risk factors for CP.[27] The presence of prenatal and natal findings, low birth weight, preterm delivery and late onset of walking were similarly seen to be risk factors for CP among our autistic patients as well. Careful neurological evaluation is therefore necessary regarding early rehabilitation for autistic cases that have a history of such factors. Motor impairment in autism actually manifests as both delays and deficits, with delays found in gross and fine motor domains and deficits found in praxis, coordination and gait.[3] An estimated 60%-80% of autistic people have motor signs that include poor muscle tone, poor motor planning, and toe walking. The mean age of onset of independent walking was 16.7±7.6 years in our group. →

A history of late onset of walking (after 18 months of age) was found in 23% of all patients. It was significantly more common in patients with an additional neurological diagnosis such as CP and epileptic or febrile seizures compared to patients without an additional neurological diagnosis of CP, and epileptic or febrile seizures respectively.

Gait problems were seen in 26 (21.4%) patients. The neurological examination was abnormal in 13 of these patients, linked to spasticity in 12 patients and ataxia in 1 patient. Another 13 patients had normal neurological examination, except, and suffered from toe walking. This sign was seen more frequently in patients with CP; and, toe walking was the most frequent sign of a gait disorder. A careful examination is apparently necessary to differentiate some signs of CP versus autism.

A cMRI was present for 76 (63%) of our cases but only 14 (18%) showed abnormal findings. The most common abnormality pertained to sequel lesions. The presence of abnormal MRI findings was a risk factor for the presence of neurological disorders and especially CP as was expected. However, they were not related to epilepsy or febrile seizures.

Various characteristics in the history may serve for probable risk factors for concurrent neurological disorders in autistic individuals. A family history of consanguinity was present in nearly a fifth of the study group. This number is similar to previously reported rate of parental consanguinity for the Turkish population in general.[28] However, in the autistic group with neurological disorders that rate was significantly higher than in the general population. Patients with seizures, on the other hand, had the highest rate (especially those with febrile seizures where the rate was 50%).

Recent studies have shown an association between low birth weight and autism.[29,30] The evidence linking prematurity and autistic spectrum disorders is controversial.[31] In a large population-based study to estimate the birth weight- and gestational age-specific risks for autism, both factors were found to be associated with an approximately two-fold increased risk.[32] Preterm delivery was present in 14 (11.5%) of our autistic cases. Preterm delivery and low birth weight were seen as risk factors for CP in our autistic group. A surprising finding was a high percentage (31.4%) of children with a birth weight above 3500 grams among autistic patients. This percentage was even higher in patients without a neurological diagnosis associating autism (36.1%). Although this finding, independent from co-existing pathological conditions, seems to be a feature mainly associating autism, further studies on greater patient populations seem necessary for more conclusive results.

When the 102 autistic patients older than 5 years of age were evaluated for verbal communication, 65 patients (63.7%) were proved to be either speechless or had some telegraphic speech with a limited number of words. A group of 37 patients (36.2%) could build-up sentences. No differences were found between patients with and without a neurological disorder according to type of verbal communication (Table 5-8). We therefore interpreted the language problems as a specific feature of "non-symptomatic" autism in our study.

In conclusion, a multidisciplinary approach is very important for the diagnosis and follow-up of autism as we currently have inadequate information on the underlying etiologies. Autism combined with neurological disorders is generally known to have a worse prognosis than autism alone. A detailed neurological evaluation is therefore recommended for autistic children with low birth-weight, premature birth, delayed onset of walking and gait disorders, as well as epilepsy. Identification of such conditions may provide important tools both for the etiological approach to autism and also for its prognosis.

C **CORRESPONDING AUTHOR:** Sema Saltık MD Acıbadem cad. Park sitesi No: 146 , H Blok D: 9 , Üsküdar, İstanbul semasaltik@superonline.com

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