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Etiology of Acute Ataxia in Children: A Single Center Experience

Çocuklarda Akut Ataksi Etiyolojisi: Tek Merkez Deneyimi

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Abstract

Introduction: Acute ataxia often develops due to mild and self-limiting disorders, but can also result from serious life-threatening disorders. However, limited data are available on its etiology, especially in developing countries. In this study, it was aimed to determine the etiology in children presenting with acute ataxia.

Methods: The charts of patients who presented with acute ataxia between September 2012 and September 2017 were retrospectively analyzed. The final diagnosis, demographic, clinical, laboratory and imaging results of the patients were recorded.

Results: A total of 97 patients were included in the study. Of the patients 56.7% (n=55) were male. The average age was 6.7 (± 4.2) years. By etiology, 58 (59.8%) of 97 patients were diagnosed with acute postinfectious cerebellar ataxia and 14 (14.4%) acute disseminated encephalomyelitis (ADEM). Encephalitis, migraine, Miller Fisher syndrome, epilepsy, and trauma were found to be less common etiological causes, while psychogenic ataxia was found in six patients (6.2%). When compared to other patients, the age was younger, the history of pre-ataxia infection and drug use was higher, and the magnetic resonance imaging abnormality was less in patients with acute postinfectious cerebellar ataxia.

Conclusion: The most common cause of acute ataxia in children is acute postinfectious cerebellar ataxia. Ataxia may also be the first sign of disorders with high mortality and morbidity such as encephalitis, ADEM, MS, Miller Fisher syndrome, trauma.

Keywords: Acute ataxia, child, postinfectious cerebellar ataxia

Öz

Giriş: Akut ataksi daha çok hafif seyirli ve kendiliğinden düzelen bozukluklara bağlı olmakla birlikte hayatı tehdit eden ciddi nedenlere bağlı da olabilir. Bununla birlikte özellikle gelişmekte olan ülkelerde ataksi etiyolojisine yönelik çalışmalar sınırlıdır. Bu çalışmada akut ataksi nedeniyle başvuran çocuklarda etiyolojinin belirlenmesi amaçlandı.

Yöntemler: Eylül 2012-Eylül 2017 tarihleri arasında akut ataksi ön tanısı ile başvuran hastaların dosyaları geriye dönük olarak incelendi. Hastaların son tanıları ile demografik, klinik, laboratuvar ve görüntüleme sonuçları kaydedildi.

Bulgular: Çalışmaya toplam 97 hasta dahil edildi. Hastaların %56,7'si (n=55) erkekti. Başvuru yaşı ortalama 6,7 (± 4,2) yıl idi. Ataksi etiyolojisi açısından incelendiklerinde 97 hastanın 58'i (%59,8) akut postenfeksiyöz serebellar ataksi, 14'ü (%14,4) akut dissemine ensefalomiyelit (ADEM) tanısı aldı. Ensefalit, migren, Miller Fisher sendromu, epilepsi, travma daha az görülen etiyolojik neden olarak saptanırken altı hastada (%6,2) psikojenik ataksi saptandı. Akut postenfeksiyöz ataksi hastalarında yaşın daha küçük, ataksi öncesi enfeksiyon ve ilaç kullanım öyküsünün daha fazla, manyetik rezonans görüntüleme anormalliğinin ise daha az olduğu görüldü.

Sonuç: Çocuklarda akut ataksinin en sık görülen nedeni akut postenfeksiyöz serebellar ataksidir. Bunun yanında ADEM, MS, Miller Fisher sendromu, ensefalit, travma gibi mortalite ve morbiditesi yüksek hastalıkların da ilk belirtisi ataksi olabilir.

Anahtar Kelimeler: Akut ataksi, çocuk, postenfeksiyöz serebellar ataksi

Introduction

Acute ataxia is a condition in which walking, speech and/or eye movements cannot be performed correctly, harmoniously and in a balanced manner due to the incoordination of voluntary muscle movements related with various reasons, especially cerebellar pathologies, that started suddenly in a previously healthy child.[1] It is usually seen in children as unsteady gait or walking refusal. It is not a common symptom in childhood, but is seen with a frequency of 1/100,000-500,000, and

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it constitutes 0.02% of pediatric emergency department admissions.[2-4] In the etiology, there are many causes such as cerebellar pathologies, infections, postinfectious inflammatory diseases, toxins and trauma, especially postinfectious and drug-induced cerebellar ataxias.[5,6] Studies on the etiology of ataxia are insufficient and mostly done in developed countries. It is thought that acute ataxia is mostly seen due to infectious and genetically inherited diseases in developing countries, which receive a lot of immigration from abroad and where the frequency of consanguineous marriages is high. However, studies on this are very limited. In this study, it was aimed to determine the causes of acute ataxia in our country and thus to determine which diagnostic tests should be done first.

Materials and Methods

The files of 2,197 patients who were admitted to the outpatient clinic with the prediagnoses of acute ataxia, chronic ataxia, balance disorder, and gait disorder between September 2012 and September 2017 in University of Health Sciences Turkey, Dr. Behçet Uz Children's Education and Research and Surgery MDG or who were hospitalized in any department of our hospital were retrospectively reviewed. After excluding 2001 patients with these signs and symptoms, chronic metabolic disease, cerebral palsy, hydrocephalus, meningitis sequelae, orthopedic diseases and congenital hip dislocation, and a total of 99 patients with missing data and refused medical procedures, a total of 97 patients were included in the study. Approval for this study was obtained from the Local Ethics Committee of University of Health Sciences Turkey, Dr. Behçet Uz Children's Education and Research Hospital, and Surgery Training and Research Hospital (date: 30.03.2017, protocol no: 2016/119).

Age, gender, diagnosis, history of trauma, history of consanguinity, vaccination history, recent infection history of the subjects included in the study were recorded. Complete blood count, serum alanine transferase, aspartate transferase, C-reactive protein, sedimentation, glucose in cerebrospinal fluid (CSF), chlorine, protein, CSF culture, CSF viral polymerase chain reaction (PCR), hepatitis serology, toxoplasma -rubella-cytomegalovirus-herpes virus, Ebstein-Barr virus, human immunodeficiency virus serology, respiratory viral PCR and urine toxic substance results were recorded. Cranial magnetic resonance imaging (MRI), electroencephalography (EEG), electroneuromyography, and visual evoked potential examination reports were evaluated.

Physical examination, laboratory and imaging records in the files were examined to confirm the etiological diagnoses. Bacteriological cultures (blood and CSF culture) and viral serology results were evaluated for the diagnosis of bacterial or viral infection. Imaging methods were used when necessary for the differential diagnosis of acute ataxia. The two most common etiologic causes, postinfectious cerebellar ataxia and acute disseminated encephalomyelitis (ADEM) groups were compared with the other diagnosis group.

Statistical Analysis

The study was planned as a cross-sectional study and statistical analyzes were performed using SPSS V.17.0 software. The conformity of the variables to the normal distribution was examined using analytical methods (Kolmogorov-Smirnov/ Shapiro-Wilk tests). Descriptive statistics were presented by giving the mean ± standard deviation for normally distributed variables, and by giving the median (interquartile range interval) value for non-normally distributed variables. In the comparisons between continuous variables in triple independent groups, Kruskal-Wallis test and post-hoc Dunn's test, in paired groups, variables with normal distribution were analyzed with t-test in independent groups and Mann-Whitney U test in case of non-normal distribution. Chi-square trend and post-hoc Benjamini-Hochberg test were used for comparisons between discrete (categorical) variables in triple-independent groups, and Pearson's chi-square test or Fisher's Exact chi-square test was used in paired groups. Cases with a p-value below 0.05 were considered statistically significant.

Results

A total of 97 patients with ataxia were included in the study between September 2012 and September 2017. The mean age at admission was 6.7 (± 4.2) years. It was determined that 56.7% (n=55) of the patients were male and 43.3% (n=42) were female. When examined in terms of ataxia etiology, 58 (59.8%) of 97 patients were diagnosed with acute post-infectious cerebellar ataxia and 14 (14.4%) were diagnosed with ADEM (Table 1). In terms of infectious agents, it was seen that the most common cause was secondary to upper respiratory tract infections. However, the most common cause of ataxia secondary to infections was found to be postinfectious cerebellar ataxia.

A detailed history was taken and physical examination was performed in all patients in terms of possible trauma. Only one patient had a history of trauma. The MRI of the patient, who had a history of head trauma due to falling from the stairs, was found to be normal. Complete recovery was achieved in the follow-up of the patient, who was followed up with the diagnosis of concussion syndrome.

When the drug use histories were questioned before the ataxia complaint started, it was seen that 21 (21.6%) patients used antibiotics. Ataxic gait was detected in one patient after meningococcal vaccination two days ago. This patient refused imaging and lumbar puncture. Post-vaccination undesirable

effects were reported to the Turkish General Directorate of Primary Health Care Services of the Ministry of Health. It was decided that ataxia was coincidental because a cause-effect relationship could not be established between ataxia and the vaccine due to the inability to obtain the necessary sample for appropriate research and analysis. However, ataxia was thought to be due to the vaccine, since no etiology could be found in the history, examination and other examinations, there was a close temporal relationship between ataxia and vaccination, and spontaneous recovery was observed.

When 97 patients who were investigated for the etiology of ataxia were examined in terms of infections they had before their complaints started, it was found that 30 (30.9%) patients had upper respiratory tract infection (URTI) and 12 (12.4%) patients had chickenpox. Nine of these patients were born before 2011, and three of them were after 2011. It was learned that two of the three patients who were born after 2011 and were not vaccinated against varicella belonged to families who had migrated from Syria, and one of them did not have any vaccine other than BCG vaccine. According to the results of respiratory PCR samples taken from patients with URTI symptoms and then admitted with ataxia, rhinovirus and influenza B virus were detected at most (Table 2).

When acute postinfectious ataxia, central nervous system demyelinating disease and other etiology groups were compared, it was seen that the age of acute postinfectious ataxia group was younger, the history of infection and drug use before ataxia was higher, and MRI abnormality was lower. There was no difference in routine laboratory tests. As expected, MRI abnormalities were more common in the group consisting of ADEM and MS patients (Table 3).

Discussion

Although acute ataxia may occur due to life-threatening diseases such as central nervous system tumors or infections, it is mostly seen as a result of mild and self-resolving disorders.[5,7,8] Etiology can be determined in most of the patients with the history, detailed physical and neurological examination, routine examinations and neuroimaging methods. Studies have reported that the most common causes of acute ataxia are acute postinfectious cerebellar ataxia, drug intoxications, Guillain-Barré syndrome (GBS) and migraine, respectively.[2,7,9] In this study, it was seen that the cause was postinfectious cerebellar ataxia in 60% of children presenting with acute ataxia, followed by causes such as ADEM, psychogenic ataxia, encephalitis, MS, and migraine.

Postinfectious cerebellar ataxia, which is the most common cause of acute ataxia in children and reported in the range of 30-75% in previous studies, was similarly found to be the etiological cause in 60% of the patients in our study.[2,5,7,8,10,11] Similar to another study, the age of children diagnosed with acute postinfectious cerebellar ataxia was found to be lower than that of children due to other causes.[11] The duration of ataxia was short and ataxia resolved spontaneously in most patients. Ataxia may be related to acute cerebellitis, which may rarely cause tonsillar herniation.[12] Although acute cerebellitis was not detected in any patient in our study, acute cerebellitis should be considered in the differential diagnosis of all children presenting with acute ataxia, since it is associated with high mortality if not treated promptly.

While pre-ataxia varicella infection was detected in 50-70% of patients with postinfectious cerebellar ataxia in studies conducted before varicella vaccination, in another study (n=71/120) in which varicella vaccination was routinely performed, none of the patients with postinfectious cerebellar ataxia had a history of varicella infection.[4,5,7,13] The frequency of varicella 12% in patients with acute postinfectious cerebellar ataxia in our study was lower than in prevaccine studies, as expected. However, the reason why it is higher than the rates in patients who receive routine vaccination may be that

Table 1. Distribution of patients presenting with ataxia according to clinical diagnoses

Diagnosis	Number	Percentage (%)
Acute postinfectious cerebellar ataxia	58	59.8
CNS demyelinating diseases	18	18.5
ADEM	14	14.4
Multiple sclerosis	4	4.1
Conversion	6	6.2
Encephalitis	5	5.2
Migraine	3	3.1
Miller Fisher syndrome	2	2.1
Neurometabolic disease	2	2.1
Epileptic ataxia	1	1.0
Kawasaki disease	1	1.0
Trauma	1	1.0
Total	97	100

ADEM: Acute disseminated encephalomyelitis, CNS: Central nervous system

Table 2. Distribution of recent infections of patients presenting with ataxia complaints

Infection	Number	Percentage (%)
None	42	43.3
Upper respiratory tract infection	30	30.9
Chickenpox	12	12.4
Acute gastroenteritis	9	9.3
Urinary tract infection	2	2.1
Acute otitis media	2	2.1
Total	97	100

Table 3. Comparison of acute postinfectious cerebellar ataxia patients with CNS demyelinating (ADEM, MS) and other etiology groups

Characteristics	Acute postinfectious cerebellar ataxia n=57	CNS demyelinating diseases n=18	Other n=22	p
Gender, number (%)				0.204
Male	36 (63.2%)	10 (55.6)	9 (40.9)	
Girl	21 (36.8%)	8 (44.4)	13 (59.1)	
Age, year, avg. (min./max.)	5 (1/15)	8 (2/16) B	7.75 (2/16)	**0.009** [a]**0.015** [b]0.219 [c]0.986
Prior infection history, number (%)	47 (82.5)	5 (27.8%)	3 (13.6)	**<0.001** [a]**<0.001** [b]**<0.001** [c]ns
History of previous drug use, number (%)	18 (33.3)	1 (5.6)	3 (13.6)	**0.027** [a]**0.020** [b]ns [c]ns
Hemoglobin, <11 gr, number (%)	10 (17.5)	3 (21.4)	1 (4.5)	0.881
Leukocytes <10000, number (%)	35 (61.4)	13 (64.3)	14 (63.6)	0.958
AST, high, number (%)	4 (7.0)	2 (11.1)	0 (0.0)	0.360
ALT, high, number (%)	2 (3.5)	3 (16.7)	0 (0.0)	0.058
CRP, high, number (%)	9 (15.8)	2 (11.1)	2 (9.1)	0.850
Sedimentation, >20, number (%)	20 (58.8)	5 (56.6)		0.436
Abnormal cranial MRI, number (%)	0/39	18/18 (100)	3 (15.0)	**<0.001** [a]**<0.001** [b]ns [c]**<0.001**

ADEM: Acute disseminated encephalomyelitis, MS: Multiple sclerosis, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CRP: C-reactive protein, MRI: Magnetic resonance imaging, ns: Not significant, n: Number, CNS: Central nervous system
[a]Pairwise comparison of patients with acute postinfectious cerebellar ataxia with patients with CNS demyelinating (ADEM, MS)
[b]Pairwise comparison of patients with acute postinfectious cerebellar ataxia with the other etiology group
[c]Pairwise comparison of CNS demyelinating (ADEM, MS) patients with the other etiology group

varicella vaccination has been included in the vaccination calendar since 2011 in our country and that vaccination is not routinely administered in those born before 2011.

In our study, acute ataxia was detected in 12 children after chickenpox. Nine of these patients were born before 2011, and three of them were after 2011. It was learned that two of the three patients who were born after 2011 and were not vaccinated against varicella belonged to families who had migrated from Syria, and one of them did not have any vaccine other than BCG vaccine. Many causes other than varicella virus, such as coxsackievirus, echovirus, enteroviruses, hepatitis A virus, herpes simplex virus, and rotavirus, may cause postinfectious cerebellar ataxia.[8,11] In our study, most of the patients had a history of various upper respiratory tract and gastrointestinal infections. The development of symptoms after vaccination in only one patient suggests that vaccination is less likely to be associated with acute ataxia than the viral diseases it prevents.

Typically, ataxia can be seen in 15% of GBS patients who cause ascending weakness due to inflammatory demyelinating polyneuropathy.[1,4] Ataxia may be the first clinical finding in Miller Fischer syndrome, which is a variant of GBS.[14] In our study, Miller Fischer syndrome was found in two patients with ataxia.

In previous studies, a history of drug use was reported in up to 30% of the patients.[1,4] In our study, 21 of the patients who applied for ataxia had a history of drug use before the development of ataxia, but the drugs used in these patients were antibiotics and antipyretic drugs. In these patients, the cause of ataxia was thought to be an infection rather than the drugs used. It may not be determined whether ataxia developing in patients using drugs for infection is due to infection or drug. While ataxia that occurs during drug use is thought to be due to toxic exposure, ataxia that occurs a few days after infection and therefore drug use is defined as postinfectious cerebellar ataxia.

Migraine and benign paroxysmal vertigo can cause acute ataxia.[6] In our study, migraine was found to be the cause of ataxia in 3% of the patients.

Psychogenic causes were found in a significant portion of children presenting with ataxia. Similar to the previously reported rate of 5%, ataxia due to psychogenic causes was found in 6% of the patients in this study.[11] Before diagnosing psychogenic ataxia, especially life-threatening causes of ataxia should be excluded.

Trauma is one of the rare but serious causes of acute ataxia.[7] In our study, trauma-related ataxia was found in only one patient. However, trauma should be questioned in all children presenting with ataxia because it is associated with high mortality and morbidity.

Ataxia due to cerebrovascular causes is very rare in children.[10,11,15] The reason for this is that cerebrovascular events are much rarer in children than in adults. In parallel with this, stroke was not found as the cause of ataxia in any patient in our study.

In a previously published review, it was reported that 43% of lumbar punctures, 42% of EEG and 49% of toxic scans performed in patients presenting with acute ataxia had abnormal results, but most of these abnormal results were not diagnostic.[5] In patients presenting with ataxia emergency neuroimaging is recommended in the presence of changes in consciousness, signs of increased intracranial pressure, focal neurological signs, asymmetric ataxia, or a history of trauma.[1,6,16,17] However, there are researchers who recommend neuroimaging in all children who present with ataxia in order not to miss a serious underlying cause.[5] In our study, the diagnosis could be made in 70% of the patients by history, physical examination and routine laboratory tests. However, the diagnosis could be made with the help of cranial MRI in 18 patients (19%) who were diagnosed with ADEM and MS. Again, CSF examination was required in five patients diagnosed with encephalitis and in two patients diagnosed with Miller Fischer syndrome, EEG in one patient diagnosed with epilepsy, and further metabolic examinations in two patients diagnosed with metabolic disease. The following conclusions can be drawn from these results: most of the patients can be diagnosed with a careful history and detailed physical and neurological examination in children presenting with acute ataxia; lumbar puncture, EEG and metabolic examinations are not necessary in every patient and should be requested according to the history and physical examination findings and neuroimaging should be performed in all children whose exact cause of ataxia cannot be determined.

Study Limitations

The most important limitation of the study is that it is retrospective and limited to file information. Other limitations are that not every patient has been evaluated with the same algorithm, the time of evaluation by the pediatric neurologist is different, some patients have varicella vaccine and others do not.

Conclusion

The most common cause of acute ataxia in children is acute postinfectious cerebellar ataxia. In addition, ataxia may be the first symptom of diseases with high mortality and morbidity such as encephalitis, ADEM, MS, Miller Fisher syndrome and trauma. Therefore, differential diagnosis should be made based on a careful history and detailed physical and neurological examination findings.

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Ethics

Ethics Committee Approval: Approval for this study was obtained from the Local Ethics Committee of University of Health Sciences Turkey, Dr. Behçet Uz Children's Education and Research Hospital, and Surgery Training and Research Hospital (date: 30.03.2017, protocol no: 2016/119).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.Ç., Ü.Y., M.B., Design: T.Ç., Ü.Y., Data Collection or Processing: M.B., T.Ç., Analysis or Interpretation: T.Ç., Ü.Y., Literature Search: T.Ç., Ü.Y., M.B., Writing: T.Ç., Ü.Y.

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