A study of the clinical, laboratory and imaging findings of Wilson Disease among children presenting with extrapyramidal abnormal movements

Areef Ramadan Ibrahim¹, Omneya Afify¹, Walaa Mohamed Hassan Elnaggar¹

¹Department of Pediatrics, Faculty of medicine, Cairo University, Cairo, Egypt.

Abstract

Wilson disease (WD) is a rare autosomal recessive inherited disorder of copper metabolism that is characterized by excessive deposition of copper in the liver, brain, and other tissues. WD is often fatal if not recognized and treated. The most commonly affected structures in the brain include the putamen, globus pallidus, nucleus caudatus, thalamus, and brain stem, neurological symptoms are present in approximately 15% of the children with WD, usually manifesting with movement disorders.

Objective: study the prevalence of WD among children presenting with extrapyramidal abnormal movements, frequency of the clinical presentations, hepatic manifestation, abnormal laboratory findings, abnormal MRI findings, the prevalence of presymptomatic cases of WD among family members and frequency of neurological deterioration with D penicillamine.

Patients and methods: We recruited 40 patients presenting with extrapyramidal abnormal movements. All cases were subjected to full history taking, complete
neurological examination, full liver function, serum ceruloplasmin, 24 urinary Cu before and after using D penicillamine, slit lamp examination and brain MRI.

**Results:** The study included 40 patients, divided into 3 groups. The tremors group included 22 patients (55 %) with a mean age at onset of symptoms was 9.5± 1.36 years. Eighteen patients (80%) had kinetic tremors while 4 patients (20%) had postural tremors; none of them fulfilled the diagnostic criteria of WD. The chorea group included 3 patients (7.5%) with the mean age of onset of symptoms was 6.5 ± 2 years; none of them fulfilled the diagnostic criteria of WD. The dystonia included 15 patients (37.5%) with a mean age of onset of symptoms was 11.6 ± 1.65 years. Among this group, two patients were diagnosed as WD ( both had mildly increased GGT, low serum ceruloplasmin, increased 24 urinary Cu excretion after D penicillamine, Kayser Fleischer rings and abnormal MRI brain hyperintense signals detected in basal ganglia and brain stem). Another patient presenting with dystonia was diagnosed by genetic analysis as Niemann Pick disease type C (NPC).

**Conclusion:** neurologic WD commonly presents with dystonia and dysarthria in children. All family members for cases with WD should be screened for early detection of the presymptomatic cases. NPC should be considered in the differential diagnosis of pediatric movement disorders.

**Keywords:** Extrapyramidal abnormal movements- Wilson disease- Children.
I. Introduction

Wilson disease (WD) is an autosomal recessive condition with an estimated prevalence of one in every 40,000 people. It is caused by a mutation of the ATP7B gene which is located on chromosome 13. The mutation reduces both the quantity of copper excreted via the biliary system and the quantity of copper bound in ceruloplasmin, which is a glycoprotein that transports the metal around the body\(^1\).

Deposition of copper occurs in liver, brain, kidney and Descemet’s membrane of the cornea. The majority of patients of WD present with either hepatic involvement (Hepatic Wilson) or neuropsychiatric manifestations known as Neuro-Wilson disease\(^2\).

The most commonly affected structures in the brain in patients with WD include the putamen, globus pallidus, nucleus caudatus, thalamus and brain stem\(^3\), neurological symptoms are present in approximately 15% of the children with WD\(^4\), with mean age at onset of symptoms nine years\(^5\), the neurological findings of WD are usually manifested with movement disorders in accordance with brain involvement\(^6\), the most frequent neurological manifestations observed are dysarthria, gait disturbance, risus sardonicus, dystonia, rigidity, tremor and dysphagia. Less frequent manifestations include chorea and athetosis. Rare neurological presentations include seizures, and pyramidal signs\(^7\).

Kayser Fleischer rings are seen in 50 to 60 % of patients with isolated Hepatic Wilson and in over 90 % of patients with clinical neurologic involvement\(^8\).
Brain MRI findings may be normal or show abnormal signal changes in patients with WD with neurological findings. Abnormal MRI findings in WD include hyper intense signal changes in T2-weighted images in the basal ganglia. These signal changes may be related with oedema, gliosis, loss of myelination and necrosis of the nerve cells or cystic degeneration as a result of the harmful effects of copper on the brain tissues.

Diagnosis of WD has a great impact because a specific treatment of proven efficacy exists and because without this treatment the disease is invariably fatal. Early treatment averts severe complications. Diagnosis may be difficult because there is no single test with adequate sensitivity and manifestations are not always typical, especially among children, and so it is dependent on a high index of clinical suspicion when presented with a patient with liver and/or neuropsychiatric disease.

Diagnosis is based on laboratory results such as: low ceruloplasmin and elevated 24-hour urine copper, free copper and copper in hepatic tissue. Observation of KF rings in an ophthalmological examination further supports the diagnosis.

D-penicillamine, zinc, triethylenetetramine and ammonium tetratiomolibdate are used in treatment of WD. D-penicillamine is substantially efficient because it causes a negative copper balance by increasing urinary copper excretion (Bandmann et al., 2015), however, it may worsen the neurological picture in initial treatment in patients with neurological involvement.
II. Patient and Methods

All cases will be subjected to the following:

A) Thorough history taking with stress on:

- Pattern of abnormal movements
- Symptoms onset, course and duration
- Associated hepatic symptoms (jaundice, organomegaly, ascites, loss of weight, coma, and hematemesis)
- Family history: consanguinity and family history of extrapyramidal abnormal movements and/or liver disease

B) Full clinical examination including:

Full detailed neurological examination:
1- General look: Conscious level, alertness, orientation, and intelligence.
2- Speech: particularly dysarthria
3- Gait: particularly ataxia
4- Cranial nerves examination
5- Motor system examination
6- Sensory system examination
7- Coordination:
8- Examination of the back and the cranium

Full detailed abdominal examination:
1- Inspection
2- Palpation (superficial and deep palpation)
3- Percussion
4- Auscultation

C) Ocular examination:

Assessment of anterior eye segment by slit lamp to detect KF rings.

D) Laboratory testing:
- Complete blood count
- Liver functions (total and direct bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), serum albumin and coagulation profile)
- Serum ceruloplasmin concentration.
- Serum copper and 24 urinary copper concentration before and with D penicillamine
- Liver biopsy (whenever possible)

E) Imaging:

Brain MRI with detailed description of any abnormality detected (hyperintense signal changes in T2-weighted images in the basal ganglia).
III. Results

We recruited 40 patients in the present study. They were presenting with extrapyramidal abnormal movements with an age of onset between 5-15 years. According to the type of presenting abnormal movements, the patients were subdivided into three main groups;

*Table 1: Characteristics of patients presenting with extrapyramidal abnormal movements.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremors group:</td>
<td></td>
</tr>
<tr>
<td>Total number of patients (%)</td>
<td>22(52%)</td>
</tr>
<tr>
<td>Mean age ± SD (in years)</td>
<td>10 ± 1.4</td>
</tr>
<tr>
<td>Mean age of onset ± SD (in years)</td>
<td>9.5 ± 1.36</td>
</tr>
<tr>
<td>Chorea group:</td>
<td></td>
</tr>
<tr>
<td>Total number of patients (%)</td>
<td>3(7.5%)</td>
</tr>
<tr>
<td>Mean age ± SD (in years)</td>
<td>7± 2.1</td>
</tr>
<tr>
<td>Mean age of onset ± SD (in years)</td>
<td>6.5 ± 2</td>
</tr>
<tr>
<td>Dystonia group:</td>
<td></td>
</tr>
<tr>
<td>Total number of patients (%)</td>
<td>15(37.5%)</td>
</tr>
<tr>
<td>Mean age ± SD (in years)</td>
<td>12.5 ± 1.65</td>
</tr>
<tr>
<td>Mean age of onset ± SD (in years)</td>
<td>11.6 ± 1.65</td>
</tr>
</tbody>
</table>
The tremors group:

This group included 22 patients (55%) with an age range from 8-13 years (mean age 10 ± 1.4 years); the mean age at onset of symptoms was 9.5 ± 1.36 years. Sixteen patients (72%) were males.

Seven patients (32%) were born to consanguineous parents while only 8 patients (36%) had a positive family history for tremors in their first degree relatives.

None of the patients in this group had a family history of liver disease.

All patients had normal neurological examination apart from tremors which were of kinetic type in 18 patients (80%) while 4 patients (20%) had postural tremors

All patients had tremors involving both hands, sparing the head and legs. No effect on voice was noted in all of them. Tremors were bilateral, rhythmic, fast, and fine amplitude in all patients. The amplitude of the tremors increased with stress, fatigue and with certain voluntary activities, such as holding a cup.

All patients had normal CBC, thyroid profile, liver profile, serum ceruloplasmin, and 24 hours urinary Cu before and after D penicillamine test. None of the patients had KFR.

All patients had normal nerve conduction velocity test (NCV).

Brain MRI was normal for all patients; no T2/FLAIR hyperintense signals were detected in the basal ganglia, thalami or the brain stem.

According to the clinical, laboratory, and imaging investigations among this group; no patients fulfilled the diagnostic criteria of WD.
Table 2: Characteristics of the patients who presented with tremors.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of patients presenting with tremors (N=22): N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>16 (72)</td>
</tr>
<tr>
<td>Females</td>
<td>6 (28)</td>
</tr>
<tr>
<td>Consanguineous parents</td>
<td>7 (32)</td>
</tr>
<tr>
<td>Positive family history for tremors</td>
<td>8 (36)</td>
</tr>
<tr>
<td>Kinetic tremors</td>
<td>18 (80)</td>
</tr>
<tr>
<td>Postural tremors</td>
<td>4 (20)</td>
</tr>
</tbody>
</table>

The chorea and choreoathetosis group:

This group involved only 3 patients (7.5%). With an age range from 5-10 years (mean age 7±2.1 years) the mean age of onset of symptoms was 6.5±2 years. Two patients were females. None of the patients was born to consanguineous parents. The three patients had no family history of a similar condition. No family history of liver disease was noted.

Neurological examination revealed choreiform movements of all limbs (bilateral), tongue (darting), and lips. The patients alternately squeezed and released their hands when gripping an object (milkmaid sign). They had distal choreic movements occurring in the fingers, resembling piano-playing movements. Choreic movements were incorporated into apparently purposeful movements and worsened by attempts at movement and stress. The remainder of their neurological examination, including tone, power, reflexes, coordination, and sensation was normal. There was no history of fever, skin rash, or subcutaneous nodules preceding or coinciding with the development of the choreic movements.
All patients had normal CBC, liver profile, serum ceruloplasmin and 24 hours urinary Cu before and after D penicillamine test. None of the patients had KFR.

Brain MRI was normal in all patients; no T2/FLAIR hyperintense signals were detected in the basal ganglia, thalami or the brain stem.

According to the clinical, laboratory, and imaging investigations among this group; no patients fulfilled the diagnostic criteria of WD.

In an attempt the reach the possible underlying etiology; the following investigations were done:

- Echocardiography
- ECG
- ESR
- ASOT

All results came back normal apart from an abnormal echocardiographic finding in one patient. This patient was a female, her ECG, ESR, and ASOT were normal, but echocardiography revealed abnormal findings in the form of mitral regurge suggesting possible underlying rheumatic etiology; Sydenham’s chorea. The patient improved dramatically on oral steroids and haloperidol. Prophylactic long-acting penicillin was prescribed.

**Table 3: Characteristics of the patients who presented with chorea.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of patients presenting with chorea: (N=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%).</td>
</tr>
<tr>
<td>Males</td>
<td>1(33)</td>
</tr>
<tr>
<td>Females</td>
<td>2(66)</td>
</tr>
<tr>
<td>Consanguineous parents</td>
<td>0</td>
</tr>
<tr>
<td>Positive family history for tremors</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal echocardiographic findings</td>
<td>1(33)</td>
</tr>
</tbody>
</table>
The dystonia group:

This group included 15 patients (37.5%) with an age range from 10-15 years (mean age 12.5 ± 1.65 years) the mean age of onset of symptoms was 11.6 ± 1.65 years. Nine patients (60%) were females.

Three patients (20%) of the patients were born to consanguineous parents while only 2 patients (13%) had a positive family history of dystonia in their first-degree relatives. Only one patient in this group had a family history of liver disease (sister).

Seven patients (46%) had focal dystonia. Five patients (33%) had segmental dystonia. Two patients (13%) had multifocal dystonia and only one patient (6%) had hemidystonia. The patients with focal dystonia had dystonic posturing of the involved limb with downward wrist flexion and hyperextension of the fingers when the arm is stretched. The patient with hemi dystonia had a unilateral disabling dystonic gait. Two patients had prominent dysarthria. One patient had dysphagia and one patient had aphasia. No patients had cervical dystonia, blepharospasm, or writer’s cramp. Only one patient had an abnormal forced smile.

Examination for muscle tone revealed rigidity in the involved limbs with normal reflexes apart from one patient who had exaggerated deep tendon reflexes. No other abnormalities were detected on neurological examination.

The liver panel was normal for all cases except for two patients who had a mild increase in serum GGT (33 mg/dl, 27 mg/dl), decreased serum ceruloplasmin (9 mg/dl, 14mg/dl) and increased 24hour urinary Cu before and after D-penicillamine challenge test (423mcg/ 1367mcg; 380mcg/1228mcg) respectively (both cases were diagnosed as WD).
Table 1: Characteristics of the patients who presented with dystonia.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of patients presenting with dystonia (N=15): N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>6 (40)</td>
</tr>
<tr>
<td>Females</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Consanguineous parents</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Positive family history for dystonia</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Focal dystonia</td>
<td>7 (46)</td>
</tr>
<tr>
<td>Segmental dystonia</td>
<td>5 (33)</td>
</tr>
<tr>
<td>Multifocal dystonia</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Hemidystonia</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Aphasia</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Increased GGT</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Low serum ceruloplasmin</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Increased 24 hours urinary Cu</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Abnormal MRI brain</td>
<td>4 (26)</td>
</tr>
</tbody>
</table>

Analysis of the total 40 cases recruited in the present study, only two patients were diagnosed as WD and they presented with dystonia. And one patient was diagnosed genetically as Neiman Pick disease presented with dystonia and choreoform abnormal movements.

IV. Discussion

Wilson disease is a multisystem disorder that results from excessive accumulation of copper in various tissues. Thus, in addition to the affection of liver and brain, involvement of other tissues as kidney and Descemét’s membrane of the cornea is being increasingly recognized. The majority of patients of WD present with either hepatic involvement (Hepatic Wilson) or neuropsychiatric manifestations known as Neurologic Wilson.
In the present study, we recruited 40 patients presenting with extrapyramidal abnormal movements. All cases were subjected to full history taking, complete neurological examination, full liver function, serum ceruloplasmin, 24 urinary CU before and after using D penicillamine, slit lamp examination, and brain MRI. Two cases were diagnosed as WD. The sister of one of the patients was diagnosed as WD during the screening of family members without neurological manifestations.

We recruited 22 patients with tremors; the mean age of onset of symptoms was 9.5± 1.36 years. Similar results were reported by Lakhotia (2018), who reported that the age of onset for tremors in children was 9.71± 1.83 years in a case series that involved 211 children with tremors. Keller and Dure, (2009) concluded that tremor is one of the most common movement disorders seen in clinical practice, but it is an uncommon reason to seek medical attention during childhood, accounting for just 10%–20% of pediatric movement disorders.

According to our observation, tremors were more common in males than females. Male children represented 72% of patients with tremors. Similarly, Tan et al., (2006) reported that tremors were more common in males representing 73% of their study group. The reason for this male gender preponderance is unclear. Perhaps boys are more commonly brought to medical attention, or there may be a biological vulnerability in which males manifest the symptoms earlier than females.

Family history for tremors was positive in 8 children representing 36% of patients in the tremors group. Similar results were reported by Ghosh et al., (2016) who stated that 37% of children in their study group had a positive family history of tremors. These findings were inconsistent with results reported by Jankovic et al., (2004) that family history was positive in 79% of patients presenting with tremors. Louis et al., (2001) also reported that family history was positive in 79% of patients presenting with tremors. Our explanation for this may be related to the smaller number of patients recruited in our study. Also, other studies were addressing mainly essential tremors that had a genetic predisposition. In our study, all children who presented with tremors were recruited regardless of the possible etiology.
In the current study, none of the patients who presented with tremors was diagnosed as WD despite their relatively large number, as all patients had isolated tremors with normal MRI brain. Consistent with our findings, Alam et al., (2014) reported that tremors encountered in WD are commonly associated with lesions in the globus pallidus, the head of the caudate nucleus, and the substantia nigra.

In the present study, 3 cases with chorea were recruited. Choreic movements were exacerbated by stress and relieved by sleep. Similar results were obtained by Bhidayasiri and Truong, (2004) that chorea is usually worsened by anxiety and stress and subsides during sleep.

None of the three cases presented with chorea was diagnosed as WD. In contrast with our observation; Nouren and Rana, (2011) reported chorea in 24% of cases with WD. We relate the absence of WD among the chorea group to the relatively small number of patients and their young age.

According to our observation, one of the patients with chorea had valvular lesions in echocardiography raising the possibility of Sydenham’s chorea. The patient showed dramatic improvement on oral steroids. Similarly, Barash et al., (2005) reported five children diagnosed with Sydenham's chorea and treated with a short course of corticosteroids. Marked improvement of the involuntary movements was observed within 24-48 hours, with complete resolution within 7-12 days after commencement of treatment.

Dystonia group involved 5 patients with an age range from 10-15 years (mean age 12.5 ± 1.65 years). The mean age of onset of symptoms was 11.6 ± 1.65 years. Similar results were reported by Fernández-Alvarez and Nardocci, (2012) who stated that genetic dystonia typically starts in childhood or adolescence. The initial symptom is usually a focal action dystonia involving one limb.

According to our observation, dystonia was more common in females as they represented (60%) of patients with dystonia. Similar results were reported by Soland et al., (1996) about the higher prevalence of females to males in all categories of focal dystonia. Pekmezović et al., (2003) also reported that the crude prevalence of all studied types of dystonia (focal, segmental, and multifocal) in Belgrade was 13.6 per 100,000 populations (11.8 per 100,000 for males and 15.2 per 100,000 for females). In contrast with our observation; Bartolomé et al., (2003) reported that males were more commonly affected with focal dystonia.
Among the patients presented with dystonia, two patients were diagnosed with WD while none of the patients in the other two groups was diagnosed as WD despite a larger number of patients recruited. This should alert us about raising the suspicion index for WD in approaching children presenting with dystonia.

The ages of onset of symptoms for the two diagnosed cases were 11 and 14 years. Similar results were obtained by Bayram et al., 2016 who reported 12 cases of neurologic WD with a mean age at the time of diagnosis was 9.9±3.4 years\(^3\), and this supports our finding of the early onset of neurologic WD in the first and second decade of life which warrant the necessity of early diagnosis to avoid the development of fatal complications. In contrast to our observation; Merle et al., (2007) reported that patients with neurological symptoms were significantly older at the onset of symptoms than patients with hepatic symptoms (20.2 \(vs\) 15.5 years of age)\(^12\).

According to our observation; dysarthria was common in both cases with WD along with dystonia which means that dysarthria is a common presenting symptom in neurologic WD. Similar results were obtained by Kumar et al., (2013) who reported two cases of neurologic WD presented with dysarthria and dystonia\(^12\).
In the current study; one of the cases diagnosed with WD had a history of repeated fractures related to trivial traumas due to severe osteopenia complicating WD many years before diagnosis. Our observation was supported by case reports from the literature. Shin et al., 2016 reported a young patient who initially presented with an arm fracture, but a thorough investigation proved the diagnosis of WD\textsuperscript{7}. Verma et al., (2013) also reported a case of WD in 16 years old boy who initially presented with multiple pathological fractures\textsuperscript{11}. These data emphasize the importance of exclusion of WD in children presenting with unexplained osteopenia and pathological fractures.

According to our observation; both cases with WD had a mild elevation of GGT. Similar results were obtained by Pfeifer et al., (2016) who reported a case with WD that had an elevation in GGT and CPK\textsuperscript{5}.

Keiser Fleischer rings are widely reported in the literature in the case of neurologic WD and according to our observation; KFR was detected in both cases with WD. Keiser Fleischer ring was denser in the patient with more severe symptoms. Similar results were obtained by Sullivan et al., (2002) who mentioned that The KFR is the single most important diagnostic sign in WD; it was found in 95\% of patients. Virtually all patients with KFR have neurological manifestations. The density of a KFR correlates with the severity of Wilson's disease\textsuperscript{6}.
In the current study; both cases with WD had abnormal signal involving basal ganglia and midbrain which is consistent with the existing evidence in the literature. Singh et al., (2011), Salari et al., (2018), and Dusek et al., (2019) reported cases with WD who had T2 hyperintensity involving putamen, thalami, and brainstem\textsuperscript{10}. Kozić et al., (2003) reported the presence of high T1 signal intensity in the globus pallidus, putamen, and mesencephalon in association with hepatic WD and high T2 signal intensity in the striatum among patients with neurologic WD \textsuperscript{2}, this enforced our observation as both cases diagnosed with WD had isolated neurological manifestation with abnormally high T2 signal in basal ganglia and brain stem and normal T1 MRI brain.

It is highly recommended to perform family screening. In this study, we aimed to investigate the value of family screening of children with WD. By screening, the presymptomatic sister of one of our cases was diagnosed and treatment was initiated promptly. Similar results were obtained by Li et al., (2018) who reported diagnosing presymptomatic carriers by screening. They enrolled 20 children with WD and 50 family members of each of these patients (40 parents and 10 siblings), two new patients with presymptomatic WD (1 mother and 1 brother) in 2 families were found\textsuperscript{11}. 
There is considerable phenotypic variability in WD, even in the presence of an identical genotype. We report two sisters with probable same genetic mutation presenting with different phenotypic pictures, one of them had neurological manifestations only (dystonia and dysarthria) while her sister had pure hepatic involvement (liver cirrhosis). Similarly, Sapuppo et al., (2020) reported two Sicilian sisters carrying the same genotype for ATB7B gene \([c.3207C > A / c.3904-2A > G]\). Although both started to present signs at the age of 10 years, onset was characterized by neurological signs in the first (tremors, motor incoordination, language and cognitive impairment), while liver involvement has been the only sign in the other\(^8\)

According to our observation; both cases with WD didn’t have initial worsening in their neurological symptoms on starting treatment with D-penicillamine, we may relate this to the early diagnosis of our cases. In contrast with results; Serra et al., 2020 reported that in patients with Wilson's disease and neurological manifestations, treatment with D-penicillamine can cause worsening of neurological symptoms, usually in the first few weeks of treatment because the neurological damage can be severe and irreversible\(^8\).
Niemann-Pick Type C (NPC) is a progressive and life-limiting autosomal recessive disorder caused by mutations in either the *NPC1* or *NPC2* gene. Mutations in these genes are associated with abnormal endosomal-lysosomal trafficking, resulting in the accumulation of multiple tissue-specific lipids in the lysosomes. The clinical spectrum of NPC disease ranges from a neonatal rapidly progressive fatal disorder to an adult-onset chronic neurodegenerative disease. It is highly heterogeneous, and there is limited awareness of a substantial subgroup that has an attenuated adolescent/adult-onset disease. In these patients, psychiatric features, often a psychosis, may dominate the initial impression, although often there is associated ataxia and cognitive impairment.

We report a case of NPC presenting with unusual presentation in the form of abnormal movements (dystonia and choreoform movements) associated with seizures and dysarthria. Similar results were obtained by Koens et al., (2016) who reported that movement disorder was the initial neurological symptom in six patients with genetically confirmed NPC. Zavala et al., (2018) also reported unusual presentation in the form of progressive generalized choreic movements, hallucinations, and cognitive impairment. These different unusual presentations of NPC requires a high index of suspicion especially in managing children with abnormal movements for early detection and treatment of this devastating rather treatable disease.
Genetic analysis in our patient revealed homozygous missense mutation involving NPC 1 gene (p.Ser1197Phe). Esswai et al., (2020) reported the same mutation in an Egyptian child presenting with loss of speech and epilepsy starting at the age of 6 years, but no abnormal movements were noted\(^7\). This emphasizes the heterogeneous phenotypic presentations of NPC even among the patients with the same genetic mutations. It may also indicate the high prevalence of this type of mutation among Egyptian children with NPC.

**Conclusion**

Abnormal movements in children warrant thorough clinical examination and investigations for early detection of devastating and treatable conditions as WD and NPC especially in children presenting with dysarthria and dystonia.

**References**


