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EC NEUROLOGY
Case Report

Case Report: GNE Myopathy in Hospital Kuala Lumpur

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Abstract

GNE myopathy is an ongoing muscle disease caused by mutation in the glucosamine (UDP-N-acetyl)-2-epimerase (GNE), a gene encoding for a single protein with key enzymatic activities in sialic acid biosynthetic pathway in which causing depletion of sialic acid in muscle cells [1]. It is extraordinary genetic (autosomal recessive) disorder, previous name include hereditary inclusion body myopathy, inclusion body myopathy type 2 (IBM 2) or Nonaka myopathy [2]. This rare muscle disease has a typical clinical and pathological characteristics that may be essential for its correct identification. We report a case of young woman with progressive muscle weakness of both lower limbs diagnosed as GNE myopathy.

Keywords: *GNE Myopathy; Distal Muscle Weakness; Sialic Acid; Inclusion Body Myopathy*

Introduction

GNE myopathy is a disorder that causes progressive skeletal muscle atrophy and weakness. The manifestation of the disease usually appears between 20 and 40 years of age and includes foot drop and difficulty walking [3]. The disease gradually affects other muscle of the arm and legs.

GNE myopathy occurs due to a mutation in a gene called GNE, which responsible for a step in the production of a sugar called sialic acid. GNE myopathy is diagnosed in patient presenting at the age 20 - 40 with foot drop and ongoing muscle weakness. Red - rimmed vacuoles (inclusions) are found on muscle biopsy and it is confirmed by sequencing of the GNE gene [1].

Case Report

A 28 year old woman who had no medical illnesses in the past, presented with progressive bilateral lower limb weakness for 3 years She had proximal muscle weakness that involved her both her thigh where she noticed she had difficulties to stands up after squatting down. She noticed to have imbalance in walking and experienced frequent fall. There were difficulties to climbing up the staircase where she need to hold on railing and less problem while descending the staircase. She also had difficulties while driving, where she need to drag both leg out of car and having trouble switching the paddles. There were no history of numbness, no speech or swallowing difficulties, no visual impairment, no urinary or bowel symptoms, no memory loss, no loss of appetite and no loss of weight. There were no similar history of similar complaints in the family and there were no history of consanguinity in family

Examination revealed Glasgow Coma Scale of 15/15, she had trendelenburg gait upon walking and cranial nerve examination was intact.

Power	Right (MRC)	Left (MRC)
Finger		
Flexion	5	5
Extension	4+	4+
APB	5	5
FDP	4	4
ADM	5	5
Elbow		
Flexion	5	5
Extension	4	4
Shoulder		
Adduction	5	5
Abduction	5	5
Hip		
Flexion	2	2
Extension	4-	4-
Abduction	5	5
Adduction	2	2
Knee		
Flexion	3	3
Extension	3	3
Dorsiflexion	4	4
Plantarflexion	4	4
Toe		
Flexion	4	4
Extension	4	4
Clonus	Absent	Absent
Babinski	Downward	Downward
Tone		
Upper limb	Normal	Normal
Lower limb	Normal	Normal
Reflexes		
Biseps	2+	2+
Triseps	2+	2+
Supinator	2+	2+
Knee	2+	2+
Ankle	2+	2+
Sensation	Intact	Intact
Fasciculus	Absent	Absent

There were no obvious muscle wasting seen. Nerve conduction study and Electromyography (EMG) show there were asymmetrical motor axonal polyneuropathy with EMG evidenced of proximal myopathy. Muscle biopsy revealed features of myopathy with rimmed vacuoles and clinic- pathological feature more in favour of GNE myopathy (hereditary inclusion myopathy).

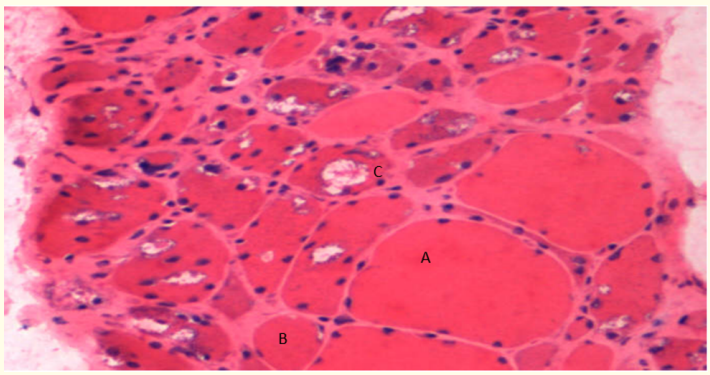

Figure: *Muscle biopsy of right thigh.*
A: Showing hypertrophic muscle fiber; B: Showing atrophic muscle fiber; C: Rimmed vacuole.

The MRI finding of thigh and leg show

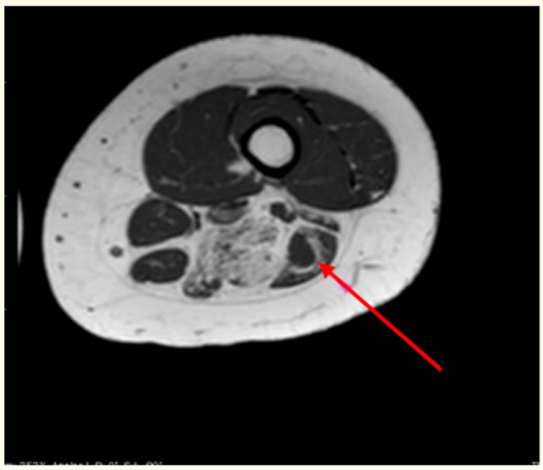

Figure 1A

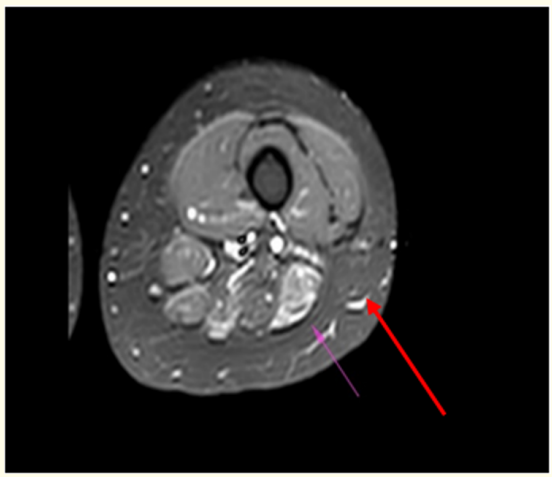

Figure 1B

Figure 1: *Left thigh imaging showing atrophy with fatty infiltration at posterior compartment with arrow showing oedematous lesion medial compartment (Figure 1A: T1 images, Figure 1B stir image).*

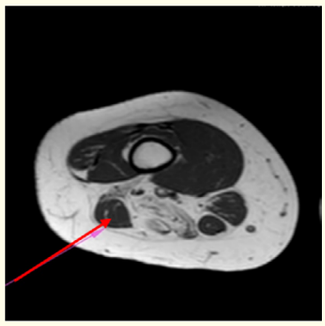

Figure 2A

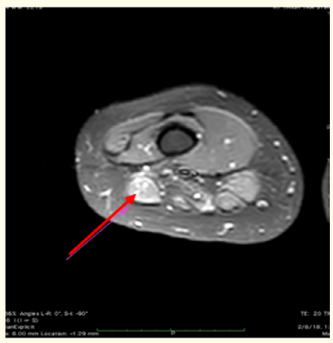

Figure 2B

Figure 2: *Show right thigh which show muscle atrophy with fatty infiltration at posterior compartment. Arrow show oedematous at medial compartment of right thigh (Figure 2A: T1 Image, Figure 2B: Stir image). Both right and left show generalized muscle atrophy with fatty infiltration in posterior compartment, sparing the biceps femoris. The medial compartment is also affected, except for the gracilis muscle. Rectus femoris in anterior compartment is also affected, the rest of muscle are spared.*

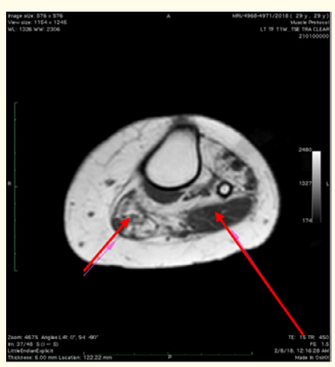

Figure 3A

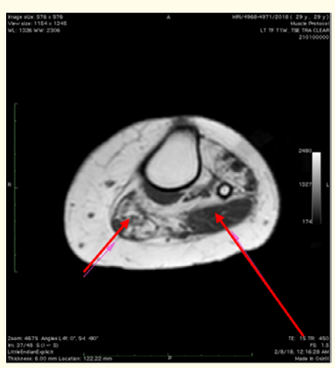

Figure 3B

Figure 3: *Short arrow showing generalized muscle atrophy with fatty infiltration involving all compartment of left leg. Long arrow showing residual muscle fibre that left (Figure 3A: T1 image. Figure 3B: Stir image).*

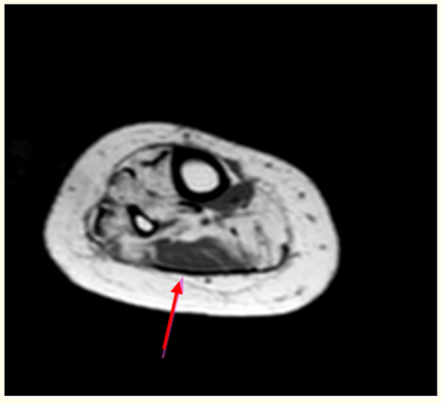

Figure 4A

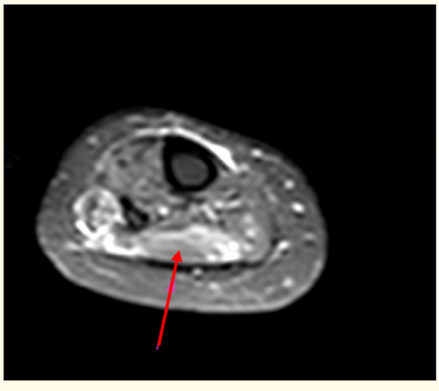

Figure 4B

Figure 4: *Short arrow show generalized muscle atrophy with fatty infiltration involving all compartment of right leg. Long arrow shows residual muscle fibre that left (Figure 4A: T1 image. Figure 4B: Stir image).*

Right and left leg: Generalized muscle atrophy with fatty infiltration involving all compartments of the leg. Residual fibres noted in extensor digitorum muscle in anterior compartment, peroneus longus and brevis muscle in lateral compartment, and posterior tibialis and soleus muscles in compartment. Mild oedema noted in both lateral and medial head of gastrocnemius and soleus muscle. Genetic testing was sent and results reported as mutation in GNE gene.

Discussion

My aim of writing this case report is to describe the clinical manifestation as well as the radiological, pathology and genetic finding in diagnosing GNE myopathy.

In most reported cases, patient with GNE myopathy usually present with weakness at the distal muscle and sparing of the quadriceps muscle as the illness progress [4]. Our patient presented with more distal weakness compared to proximal weakness. Clinical examination of her MRC of the proximal muscles were more affected than distal muscles. She had a waddling gait rather than foot drop which further confirmed her proximal weakness.

A review 9 cases of GNE in India revealed asymmetrical foot drop as initial presentation with preserved quadriceps muscle. Onset of illness was in the second and third decade, mean duration of illness was 1 - 14 years. As the disease progresses, patient will become wheelchair dependent [5].

Retrospectively, radiological imaging of 13 patients diagnosed with GNE myopathy were examined, and they found in early disease, severe fatty-fibrous replacement of the biceps femoris short head muscles, always accompanied by less severe involvement of the gluteus minimus, tibialis anterior, extensor hallucis and digitorum longus, soleus and gastrocnemius medialis, which represent a unique combination of muscle involvement. These findings were present in all patients including those with milder or atypical phenotypes. Therefore, such features are of diagnostic interest and potentially constitute an ''MRI signature'' of the disease in its initial stages. The involvement of the semitendinosus and tibialis posterior may represent an additional clue leading to a diagnosis of GNE myopathy [6]. In our case, the patient's MRI was done at 3rd year of illness, showing generalized muscle atrophy with fatty infiltration at posterior compartment of thigh with sparing of the biceps femoris muscle.

In case of histo-pathological finding, there will be presence of small angular fibres, formation of rimmed vacuoles and deposition of various proteins in muscle fibre. The hallmark will be Congo red positive deposition in vacuolated or non-vacuolated fibres [2]. These features were not seen in our case.

Conclusion

GNE myopathy had been typically described as progressive distal myopathy, with sparing of quadriceps muscle. Our patient had progressive proximal myopathy more compare to distal muscle weakness and there were no evidence of quadriceps sparing. We feel this could be due to a delay in imaging. The diagnosis was confirmed with histo-pathological and genetic sequencing.

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