ΓΥΝΑΙΚΑ 60 ΕΤΩΝ ΜΕ ΒΡΑΔΕΩΣ ΕΞΕΛΙΣΣΟΜΕΝΗ ΔΙΑΤΑΡΑΧΗ ΒΑΔΙΣΗΣ

Συντήλα Στυλιανή-Αγγελική, Αφράντου Θεοδώρα, Παρίσης Δημήτριος, Ιωαννίδης Πάνος

Β' Νευρολογική Κλινική, Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης, Νοσοκομείο ΑΧΕΠΑ

Περίληψη

Η δυσχέρεια βάδισης αποτελεί σύμπτωμα πολλών νευρολογικών νοσημάτων. Η διαφορική διάγνωση είναι ευρεία και περιλαμβάνει εκτός των άλλων τις μιτοχονδριακές παθήσεις, το σύνδρομο CADASIL (αυτοσωματική υπολειπόμενη αρτηριοπάθεια με υποφλοιώδη έμφρακτα και λευκοεγκεφαλοπάθεια), την ισχαιμική λευκοεγκεφαλοπάθεια, νευροεκφυλιστικά νοσήματα και διαταραχές των μυών (μυοπάθειες). Παρουσιάζουμε ένα περιστατικό που αφορά σε μία γυναίκα μέσης ηλικίας η οποία νοσηλεύτηκε στην Κλινική μας για διερεύνηση προϊούσας εγκατάστασης δυσχέρειας στάσης-βάδισης αρχόμενης από 7ετίας. Λαμβάνοντας υπόψη το ατομικό και οικογενειακό ιστορικό, τα ευρήματα της νευρολογικής εξέτασης (εγγύς μυϊκή αδυναμία στα άνω και κάτω άκρα, παρουσία μυοτονικού φαινομένου στα άνω άκρα) και τα απεικονιστικά ευρήματα (μαγνητική τομογραφία εγκεφάλου), έγινε γονιδιακός έλεγχος (έλεγχος μεταλλάξεων στο γονίδιο DMPK στο χρωμόσωμα 19 – πρωτεϊνική κινάση της μυοτονικής δυστροφίας). Ο έλεγχος ανέδειξε >150 επαναλήψεις του τρινουκλεοτιδίου CTG στο ένα αλληλόμορφο γονίδιο, εύρημα συμβατό με μυοτονική δυστροφία τύπου 1.

Λέξεις ευρετηρίου: δυσχέρεια βάδισης, εγγύς μυϊκή αδυναμία, μυοτονικό φαινόμενο, μιτοχονδριακές παθήσεις, ισχαιμική λευκοεγκεφαλοπάθεια

A 60-YEAR-OLD WOMAN WITH SLOWLY PROGRESSIVE WALKING DIFFICULTY

Syntila Styliani-Aggeliki, Afrantou Theodora, Parissis Dimitrios, Ioannidis Panos

B΄ Department of Neurology, Aristotle University of Thessaloniki, AHEPA Hospital

Abstract

Walking difficulty is a symptom attributed to multiple neurological etiologies. The differential diagnosis is broad and includes mitochondrial disorders, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), ischemic leukoencephalopathy and myopathies. We present the case of a middle-aged woman who was admitted to our clinic complaining about slowly progressive difficulty in stance and walking that started 7 years ago. Taking into consideration her past medical history, the neurological examination (proximal weakness in the upper and lower limbs, myotonic response elicited in her hands) and the brain magnetic resonance imaging we proceeded to exam the DMPK gene that revealed more than 150 CTG repeats in one allele compatible with DM1.

Key words: walking difficulty, proximal weakness, myotonic response, mitochondrial disorders, ischemic leukoencephalopathy

1. Clinical background

A 60-year-old woman was admitted for evaluation of gait disturbance that started 7 years ago. She experienced difficulty in stance and walking that slowly progressed. Regarding her past medical history, she suffered from diabetes mellitus type I, sensorineural deafness from the age of fifties and bilateral cataracts. She also complained for migraines with aura, multiple episodes per month the last 6 years. She mentioned positive family history (two brothers suffering from cataracts and sensorineural deafness and two nephews suffering from cataracts).

Neurological examination revealed weakness of the facial muscles, proximal weakness in the upper and lower limbs, increased deep tendon reflexes of the lower limbs and percussion myotonia in her right hand. Hematological, biochemical (including thyroid function, serum B12 and folic acid) tests and a full screen for autoimmune disorders were all normal except for slightly elevated CPK. Electromyography, nerve conduction studies and examination of the cerebrospinal fluid were all unremarkable.

Brain magnetic resonance imaging (MRI) showed periventricular leukoencephalopathy (figure 1), high MRI T2-FLAIR signal in the anterior part of both temporal lobes (figure 2) and mild frontal hyperostosis (figure 3).

Figure 2. Axial axial T2W MRI showing high signal lesions in the anterior part of both temporal lobes

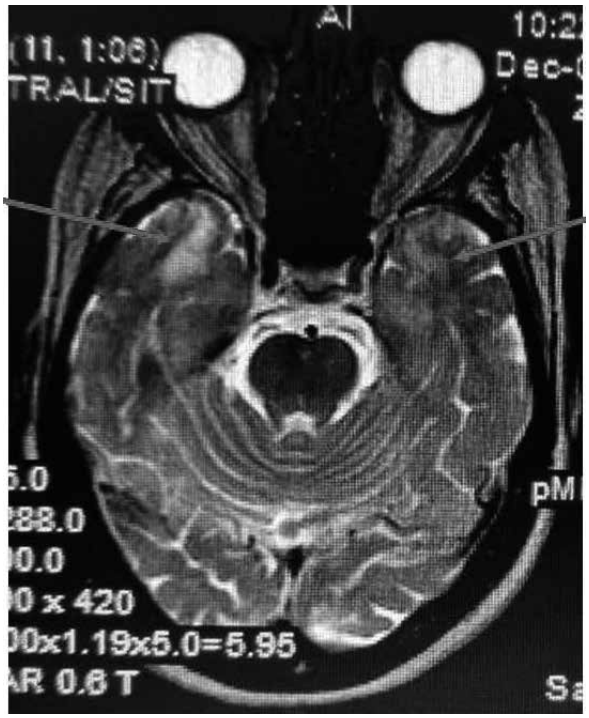


Figure 1. Axial fluid-attenuated inversion recovery MRI showing periventricular leukoencephalopathy

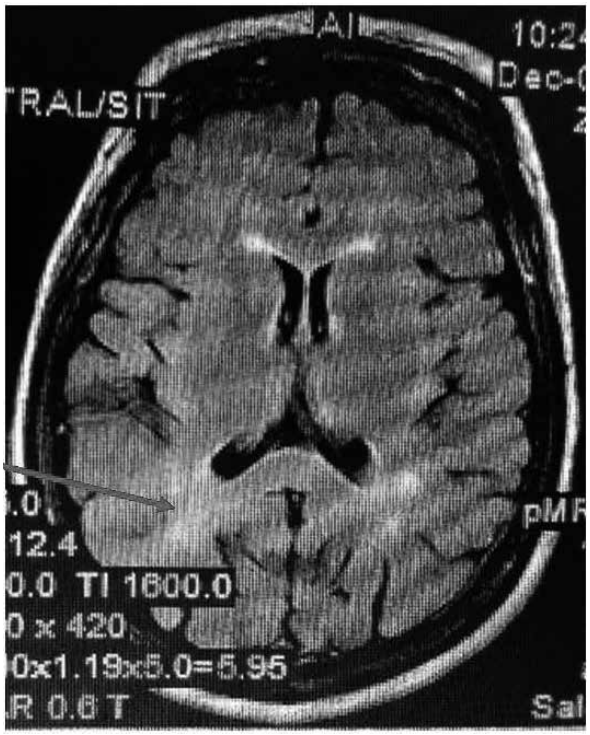
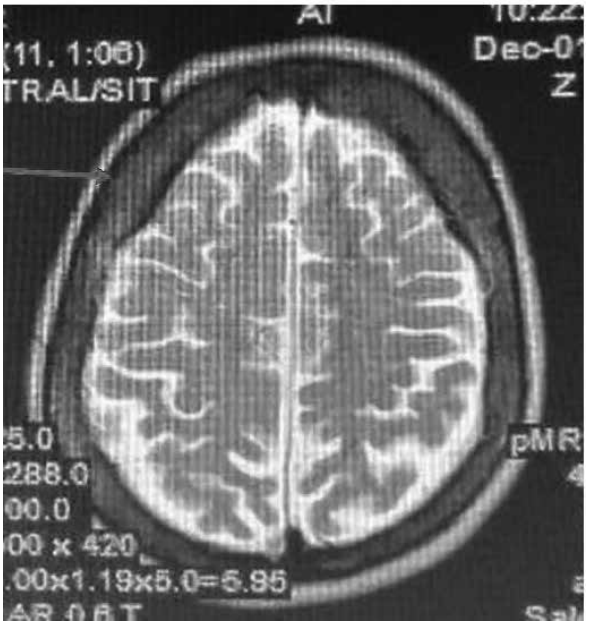


Figure 3. Axial T2W MRI showing frontal hyperostosis



2. What is the most likely cause?

A. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL).

B. ischemic leukoencephalopathy.

C. mitochondrial disease.

D. myotonic dystrophy type 1.

1. Answer

D. myotonic dystrophy type 1 (adult onset)

2. Discussion

Walking difficulty is a symptom attributed to multiple neurological etiologies. In our case, the differential diagnosis was broad and included mitochondrial disorders in the presence of sensorineural deafness, diabetes mellitus type 1 and facial weakness, CADASIL because of migraines with aura and typical MRI lesions in the temporal lobes and also ischemic leukoencephalopathy due to bilateral periventricular confluent lesions in the brain. Genetic testing for mutations in the Notch 3 gene was done in another neurology clinic and it was negative. After a careful evaluation of her history in combination with a thorough neurological examination (myotonic response-percussion myotonia was elicited in her right hand) and MRI findings, we proceeded to exam the DMPK gene that revealed more than 150 CTG repeats in one allele compatible with DM1.

It is worth mentioning that our patient presented with clinical myotonia without electrophysiogical findings.

Myotonic dystrophies are autosomal dominant multisystemic diseases that are characterized by both skeletal muscle and heart dysfunction and central nervous system (CNS) manifestations [1]. There are two types, myotonic dystrophy type 1 (DM1) and type 2 (DM2). Type 1 is caused by mutations in the gene that encodes for myotonic dystrophy protein kinase (DMPK) on chromosome 19q13.3. The mutation causes expansion of the CTG trinucleotide repeats in the gene. Patients with DM1 can be divided into five main categories: congenital, childhood-onset, juvenile, adult onset and late onset/asymptomatic [1]. The adult onset form of DM1 manifests with distal weakness, myotonia, cataracts, conduction defects, insulin resistance, respiratory failure and CNS symptoms (frontal dysexecutive syndrome, apathy, social interactions problems) [1]. Brain imaging in DM1 shows cranial vault abnormalities (hyperostosis) as well as widespread white and gray matter involvement throughout the brain (frontal, temporal, parietal and occipital lobar regions) [1,3].

References

1. Genevieve Gourdon, Giovanni Meola, *Myotonic Dystrophies: State of the Art of New Therapeutic Developments for the CNS Front.* Cell. Neurosci., 20 April 2017 doi.org/10.3389/fncel.2017.00101
2. Robert B. Darrof, Joseph Jankovic, John C. Mazziota, Scott L. Pomeroy Bradley's Neurology in Clinical Practice.
3. Kees Okkersen et al. *Brain imaging in myotonic dystrophy type 1 A systematic review Neurology* 2017;89:1-1.