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CASE REPORT Open Access

Anti-Hu antibody seropositive neuropathy with large and small fiber involvement mimicking alcoholic neuropathy: a case report

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Abstract

Background Anti-Hu antibody neuropathy is considered a rare acquired peripheral neuropathy, but common among paraneoplastic syndromes. Typically, is described as subacute sensory neuronopathy and electrophysiological findings are usually suggestive of a sensory axonal neuropathy.

Case presentation We report the case of a 67-year-old man referred to our clinic with a 4-month history of progressive pain and paresthesias of distal lower limbs. He had a 30-year history of alcohol abuse and smoking. Alcoholic neuropathy was considered the most likely diagnosis, considering his history and evaluation. The patient's neurological examination revealed symmetric bilateral superficial and deep sensory loss in the lower extremities, reduced Achilles tendon reflexes and wide based gait. Electrophysiological testing was suggestive of axonal sensory-motor polyneuropathy and small fiber involvement. Even though alcohol consumption was discontinued, symptoms gradually worsened. Further testing was performed and the patient was found seropositive for anti-Hu antibody. Small-cell lung cancer was detected later, but patient passed away before treatment for cancer was administrated.

Conclusions The aim of our paper is to report a case of a rare paraneoplastic syndrome that can cause progressive sensory-motor neuropathy with large and small fiber involvement, which should be rapidly differentially diagnosed from other neuropathies, so that the underlying cause can be identified and, potentially, treated.

Keywords Anti-Hu, Neuropathy, Alcoholic, Paraneoplastic, Autoimmune, Small fiber

Background

Anti-Hu antibody neuropathy is considered a rare acquired peripheral neuropathy, but common among paraneoplastic syndromes. The most typical clinical presentation is described as subacute sensory neuronopathy [1], although several studies showed that motor involvement is not rare and also acute or progressive forms of the syndrome have also been described [2, 3]. Small fiber involvement is also described in some cases, with severe pain presenting as the prominent symptom [1, 4]. Cancer is not always detected in patients who present the syndrome and, in some cases, it may be detected later within months or years [1, 5]. Small-cell lung cancer appears to be the most common cause in the majority of the cases, while other tumors have been related to paraneoplastic anti-Hu neuropathy, such as prostate carcinoma, neuroblastoma, and chondromyxosarcoma [5]. Electrophysiological pattern of motor-sensory nerve conduction abnormalities and axonal degeneration is the prominent feature [2, 3], even though cases of pure sensory neuronopathy and demyelinating degeneration have also been described [2, 3, 6].

The aim of our paper is to report a case of a rare paraneoplastic syndrome that can cause progressive

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sensory-motor neuropathy with large and small fiber involvement, which should be rapidly differentially diagnosed from other neuropathies, so that the underlying cause can be identified and, potentially, treated.

Case presentation

A 69-year-old man was referred to our Clinic with a 4-month history of progressive pain and paresthesias of distal lower limbs. No other cognitive, systemic or autonomic symptoms were reported before his admission to our Clinic. Patient's body mass index (BMI) was 23,66 and he had a 30-year history of alcohol abuse and smoking (38 pack years). He initiated drinking red wine at the age of 27 and his daily alcohol consumption was 160 g for the last 30 years. His family history was negative for neurological diseases and he reported no other medical issues.

Nerve conduction studies performed up to one month before his reference to our Clinic (Table 1) were suggestive of a sensory axonal neuropathy of the lower limbs (Fig. 1a). The patient had already undergone extensive laboratory testing (blood sugar, urea, creatinine, ferritin, liver enzymes, vitamin B12, thiamine, folate, TSH, protein and immune electrophoresis, anti-nuclear antibody, serology for hepatitis B virus, hepatitis C virus and human immunodeficiency virus), as well as Magnetic Resonance Imaging (MRI) of the cervical and lumbosacral spine; None of the above revealed any abnormalities. Our differential diagnosis included toxic causes, systemic and autoimmune diseases, infections, and cancer. Alcoholic neuropathy was considered the most likely diagnosis, due to his medical history of alcohol abuse and no other reported possible cause of neuropathy, as well as due to his clinical and neurophysiological evaluation, compatible with a length- and dose-dependent toxic neuropathy.

The patient's neurological examination revealed distally pronounced symmetric superficial and deep sensory loss

Table 1 Nerve conduction studies performed one month before his admission to our clinic and upon his admission

Nerve (left side)	Amplitude (sensory uV – motor mV)	Velocity (m/s)	Latency (ms)	F wave latency (ms)
Laboratory references				
Sural sensory	*> 10*	> 45	< 3.5	–
Radial sensory	*> 25*	> 50	< 3.0	–
Median sensory	*> 18*	> 50	< 3.5	–
Ulnar sensory	*> 17*	> 50	< 3.7	–
Peroneal motor	*> 3*	> 42	< 6.0	< 47
Tibial motor	*> 5*	> 41	< 6.5	< 50
Median motor	*> 7*	> 51	< 3.5	< 32
Ulnar motor	*> 6*	> 51	< 4.0	< 35
Before admission				
Sural sensory	8.2	46.2	2.3	–
Radial sensory	26.3	54.0	2.1	–
Median sensory	21.1	53.5	2.8	–
Ulnar sensory	20.1	57.2	1.7	–
Peroneal motor	3.8	44.3	4.5	41.2
Tibial motor	5.7	45.0	3.1	43.8
Median motor	11.7	56.2	2.7	28.6
Ulnar motor	9.0	54.0	2.5	25.3
Upon admission				
Sural sensory	1.2	45.5	2.1	–
Radial sensory	25.7	54.2	2.1	–
Median sensory	20.0	53.0	2.8	–
Ulnar sensory	19.8	57.0	1.6	–
Peroneal motor	0.6	42.1	5.1	41.1
Tibial motor	1.1	44.0	5.2	43.9
Median motor	11.0	53.5	2.8	28.5
Ulnar motor	8.8	53.7	2.5	23.9

Nerves of both sides have been studied with similar findings

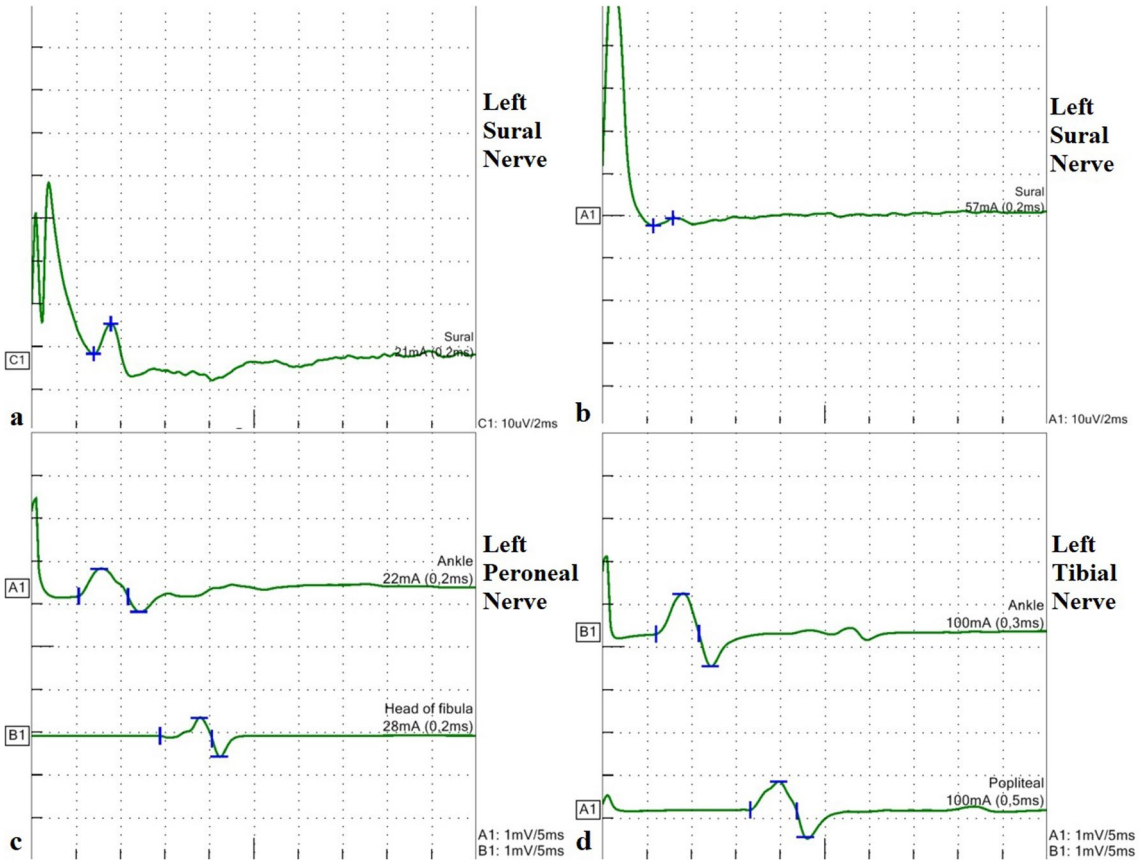

Fig. 1 Nerve conduction studies: sensory nerve action potentials in sural nerve. **a** One month before his admission to our clinic, **b** upon his admission. Compound motor nerve action potentials in **c** peroneal, and **d** tibial nerve, upon his admission. Motor and sensory distal latencies were measured from the onset of the potentials

in the lower extremities, reduced Achilles tendon reflexes and wide based gait. No motor, autonomic or systemic symptoms and signs were reported, at that time. A new electrophysiological testing was performed (Table 1), with nerve conduction studies revealing markedly reduced sensory nerve action potentials in sural nerves (Fig. 1b), and mildly reduced compound motor nerve action potentials in peroneal (Fig. 1c) and tibial motor nerves (Fig. 1d), suggesting axonal sensory-motor polyneuropathy. The patient was also tested for small fiber involvement. Sympathetic skin response (SSR) could not be recorded from the left plantar surface and thermal threshold (TT) was abnormal, with heat and cold threshold (HT and CT) values exceeding the mean control data, suggesting also small fiber neuropathy [7].

Patient was referred to a 3-week program in a Detoxification Clinic and was administrated vitamin B complex supplements.

He was reevaluated 1 month later, and even though he had not consumed any alcoholic beverage, his gait impairment had worsened and he reported postural dizziness. His examination revealed slight overall worsening compared to his last evaluation as regards pain and numbness of distal lower limbs and, in addition, bilateral plantar dorsiflexion weakness and postural hypotension. Diagnosis of alcoholic neuropathy was reconsidered due to his clinical worsening and a lumbar puncture was performed at that time. Cerebrospinal fluid (CSF) contained slightly elevated protein at 52 mg/dl without pleocytosis. Further examinations, including cryoglobulins, antineutrophil cytoplasmic antibodies (ANCA), angiotensin converting enzyme (ACE), IgM and IgG antibodies for herpes simplex virus 1 and 2, varicella zoster virus, cytomegalovirus, West Nile virus, Epstein–Barr virus, enterovirus, adenovirus, influenza, echovirus, mumps, measles, rubella, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* and *Borrelia burgdorferi*, anti-CRMP5 and anti-Yo antibodies, were negative. Testing for serum anti-Hu antibody, however, was positive with a titer of 1:6400. Full body computerized tomography (CT) with contrast and positron emission tomography (PET-SCAN) scanning were performed according to EFNS proposal for

tumor screening [8], without malignancy findings. Treatment with prednisone, plasma exchange and intravenous immunoglobulin (IVIg) showed no benefit and symptoms gradually worsened, with pronounced muscle weakness of lower limbs.

Repeated evaluation for cancer detection was performed 3 months later, and chest CT revealed an 8 mm nodule at the left lower lobe of lungs. PET-SCAN confirmed CT's findings, revealing diseased tissue and peribronchial nodules at the left lower lobe. Bronchoscopy was performed soon after PET-SCAN, and biopsy results were indicative for small cell lung cancer. The patient died of respiratory infection 2 weeks after bronchoscopy.

Conclusions

Alcoholic neuropathy remains up to now an exclusion diagnosis. There are no pathognomonic findings to prove the diagnosis, which is based on medical history, clinical and electrophysiological findings, and exclusion of other possible causes of neuropathy.

Clinically, it is a progressive length-dependent neuropathy with primary sensory features, reduced or absent tendon reflexes and less frequently motor involvement. Electrophysiological studies demonstrate abnormalities in sensory and motor nerves with axonal loss. Small fiber involvement is common in alcoholic neuropathy, with pain being usually present in most patients. Alcohol abstinence and administration of vitamin B complex supplements stabilize and improve neuropathy symptoms within days or weeks [9].

As seen in our case, clinical and neurophysiological worsening of neuropathy was reported, even though alcohol abstinence and diagnosis of alcoholic neuropathy was questioned. Other causes of axonal sensorimotor neuropathy needed to be investigated. Due to his negative extensive laboratory testing before his admission to our Clinic and his medical history of 38 pack years smoking, paraneoplastic and autoimmune neuropathies were considered a possible cause. Small fiber neuropathy is also rarely reported in paraneoplastic neuropathies, so a screening for cancer and paraneoplastic antibodies needed to be performed. Even though in our patient only serum was tested for antibodies titer, we suggest that both CSF and serum should be tested, if a CSF specimen is available [10].

Due to its atypical clinical and electrophysiological features, alcoholic neuropathy is difficult to be distinguished from other causes of neuropathy sharing similar features, and overlapping disease can be a challenge for physicians. Clinical course, response to alcohol abstinence and absence of other abnormalities in patients' diagnostic evaluation still remain essential features in diagnosis. Patients should be closely followed-up by physicians so that other potentially reversible causes of neuropathy are early identified and treated if possible.

Abbreviations

MRI	Magnetic resonance imaging
SSR	Sympathetic skin response
TT	Thermal threshold
CSF	Cerebrospinal fluid
CT	Computerized tomography
PET SCAN	Positron emission tomography
IVIg	Intravenous immunoglobulin
ANCA	Antineutrophil cytoplasmic antibodies
ACE	Angiotensin converting enzyme

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Author contributions

MP: design and conceptualized manuscript, collecting the data, drafted the manuscript for intellectual content. TZ: data collection and revision of manuscript. MR: data collection and revision of manuscript. DK: designing, drafting and revision of manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The corresponding author takes full responsibility for the data, has full access to all the data, and has the right to publish any or all data separate and apart from any sponsor.

Declarations

Ethics approval and consent to participate

Publication of this manuscript is complying with the specific requirements of Scientific Committee of Evangelismos and Eginition Hospitals.

Consent for publication

Written informed consent was obtained from the patient's wife for publication of this case report and any accompanying images.

Competing interests

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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