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CASE REPORT

A vasculitic neuropathy case related to cryoglobulinaemic vasculitis

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ABSTRACT

Vasculitis are a group of autoimmune disease which cause inflammation on vessel wall and vessel damage that leads to ischemia and necrotic damage in affected organs [1]. Vasculitic and autoimmune connective tissue disease can be a reason of peripheric neuropathy which will be hard to diagnose but also can be treatable [1]. Acute or sub-acute, painful, multifocal sensorial or sensorimotor polyneuropathy or asymmetric distal polyneuropathy may be the first sign of vasculitic disorder [1,2].

Acute motor sensorial axonal neuropathy (AMSAN) is a rare form of Guillain-Barre Syndrome which peripheral neurons has axonal damage and presenting with both motor and sensorial symptoms [3].

In this case report we will discuss the diagnostic period of a 76 years old patient who first evaluated as AMSAN in his polyclinic examination, tests and imaging's than hospitalized for further investigation and detailed evaluation which ends up with diagnosed as Cryoglobulinemic Vasculitis.

Keywords: acute motor sensorial axonal neuropathy, cryoglobulinemia, cryoglobulinemic vasculitis, neuropathy, vasculitis, vasculitic neuropathy.

INTRODUCTION

Cryoglobulinemic Neuropathy is a type of vasculitic neuropathy caused by increased cryoglobulins in blood and damage to the vessel walls ends up with ischemic and necrotic tissue damage [4,5]. Cryoglobulins are immunoglobulins that can be precipitated under 37 degrees [5]. Also, cryoglobulinemia can be asymptomatic it can affect small vessels and cause immuno-complex-related vasculitis [4]. Most cases are related to hepatitis C. Most hepatitis C patients will develop cryoglobulin but only %15 of patients can be shown clinical presentations of vasculitic disease [5]. Most cases presented with mononeuritis multiplex or symmetrical sensory-motor neuropathy [2]. In rare cases, it can be seen as ganglionopathy-like sensorial involvement [3].

The symptoms typically begin with distal paresthesias resembling sensory neuropathy. Distal symmetric muscle weakness follows paresthesias. Usually, the weakness starts mild and affects the extensor muscles of the foot. In rare severe cases supported ambulation will be needed. Deep tendon reflexes are often diminished or absent. Nerve conduction studies mostly show sensorial and motor fibers affected by axonal neuropathy [4].

CASE PRESENTATION

A 76-year-old male patient applied to the clinic with progressing symptoms which are numbness, pain, and weakness in his hands this complaint

was shown in his legs and caused difficulties in walking. The patient defined his symptoms started 2,5 months ago with numbness, pain, and weakness in his right hand, and after 20 days spread to his left hand, arm, and legs. There was no significant history of infectious diseases before his complaints. The patient stated that he had applied to outpatient clinics and had no results before. Thus the patient came to the neuromuscular clinic of our hospital and for further investigation, diagnosis, and treatment he was hospitalized.

In the patient's history, he had benign prostate hyperplasia and chronic kidney disease with an unknown etiology. Thus he had been using 0,4 mg tamsulosin, 500 mg anti-acidosis, and 5 mg prednisolone daily. When asked for the patient's family history it was learned that two of his brothers passed away because of malignant diseases.

In the patient's neurological examination, there was no significant loss of consciousness or orientation. No pathological exam findings in the cerebellar system and cranial nerve had been determined. The patient was right-hand dominated. In muscle force examination both upper limb's proximal muscle force was 4/5, 3/5 in distal; both low limbs proximal was 4/5, right ankle dorsiflexion 3/5, plantar flexion 4+/5, left ankle dorsiflexion 2+/5, plantar flexion 4+/5. There was atrophy in the patient's thenar and hypothenar muscles. There was glove-sock-type hypoesthesia. Both brachioradialis and Achill reflexes are absent bilaterally.

The laboratory tests of the hospitalized patient resulted in a creatine level of 3,04 mg/dL (high), parathyroid hormone level of 25,7 ng/L (normal); thyroid stimulating hormone level of 3,03 mIU/L (normal); vitamin B12 level of 954 ng/L (high). The first nerve conduction study performed by the patient hospitalized first in motor nerves compound muscle action potentials (CMAP) was achieved low or could not be achieved symmetrically. In sensorial conduction study, sensorial nerve action potentials (SNAP) could not be achieved. When studies were performed with a concentric needle there were denervation potentials in both the tibialis anterior muscle, right gastrocnemius medialis muscle, right extensor digitorum muscle, and right first dorsal interosseos muscle. This study's results are shown in Tables 1 and 2.

Table 1. Nerve Conduction Study performed in first hospitalized

Motor CV				
Stimulation size	Lat. ms	Ampl. mV	Dur. ms	Vel. m/s
R, Abductor digiti minimi, Ulnaris, C8 T1				
Wrist	4,6	**0,08**	2,68	
L, Abductor digiti minimi, Ulnaris, C8 T1				
Wrist		**0**		
R, Abductor pollicis brevis, Medianus, C8 T1				
Wrist	3,8	**0,16**	3,44	
L, Abductor pollicis brevis, Medianus, C8 T1				
Wrist	3,2	**0,7**	6,04	
Elbow	7,2	**0,5**	6,64	53,0
R, Tibialis anterior, Peroneus, L4 L5 S1				
Head of fibula	3,0	0,7	9,96	
Popliteal fossa	4,1	0,7	8,25	56,1
R, Abductor hallucis, Tibialis, L4 L5 S1				
Medial malleolus	4,1	**0,21**	5,0	
L, Abductor hallucis, Tibialis, L4 L5 S1				
Medial malleolus	4,7	**0,35**	5,14	
R, Extensor digitorum brevis, Peroneus, L5-S1				
Sole of the foot		**0**		
L, Extensor digitorum brevis, Peroneus, L5-S1				
Sole of the foot		**0**		

* Sensorial Nerve Action Potentials (SNAP) could not be achieved

Table 2. Needle EMG

Site	Fibrill.	PSW	Fascicul.	MUP ampl	MUP dur	MUP polyphasicity	Interf. Pattern type	Comment
R, Deltoideus, Axillaris, C5 C6	No	No	No	Normal	Normal	No	Not examined	Normal
R, Biceps brachii, Musculocutaneus, C5 C6	No	No	No	Normal	Normal	No	Not examined	Normal
R, Interosseus I, Ulnaris, C8 T1	+++	+++	No				No contraction	
R, Rectus femoris, Femoralis, L2-L4	No	No	No	Normal	Normal	No	Not examined	Normal
R, Tibialis anterior, Peroneus, L4-L5-S1	+++	+++	No	Normal	Normal	+	Not examined	
R, Gastrocnemius, Tibialis, S1-S2	+	+	No	Normal	Normal	No	Not examined	
R, Ekstansor digitorum	++	++	No	Normal	Normal	+	Not examined	
L, Tibialis anterior, Peroneus, L4-L5-S1	++	++	No				No contraction	

With the lights of this electrophysiological study, the outcomes are coherent with significant symmetric sensory-motor axonal polyneuropathy in an acute period which is defined as AMSAN at first sight.

With these findings, we performed cerebrospinal fluid (CSF) testing. CSF protein was 217 mg/L (N: 150-450 mg/L) and there were no leukocytes.

Since the patient had chronic kidney disease, it was decided to perform plasmapheresis as the primary treatment option.

After 5 cycles of plasmapheresis, there was no significant clinical progression or improvement in neurological examination.

For the maintenance treatment, 48 mg of methyl-prednisolone daily was started. Because the patient had a chronicle kidney disease in which aetiology was unknown we performed further laboratory investigations. The levels of C-reactive protein (CRP), rheumatoid factor, Anti Hbc total were high and the level of C4 Complement was found low. Moreover, Myeloperoxidase (MPO)-Elisa (p-ANCA), Anti Hbs, and cryoglobulin were found positive. In the Immune fixation electrophoresis investigation, the kappa band was found dense.

These outcomes returned with a doubt of vasculitis thus we referred the patient to rheumatology and nephrology. After these consultations, new investigations were requested. These investigations were thorax Computed Tomography (CT) and abdominal ultrasonography (USG), immunofixation electrophoresis, blood cryoglobulin level, hepatitis markers, and beta 2 microglobulins.

In abdominal USG investigation, both renal parenchyma's EKO was increased as Grade 0-1.

In thorax CT there were millimetric densities in the right lung middle lobe, left lung lingular segment, and bilateral inferior lobes peribronchovascular zones were attracted attention and these lesions suggested clinical tracing as infectious progress.

In renal biopsy, the rate of global sclerosis was very high (%85) so it was not helpful for differential diagnosis.

For vasculitic assessment, the other systems were also investigated but there were no significant findings.

We performed a second EMG study 3 months after the first one and as well as the first study CMAP was symmetrically low or absent. Like the first investigation, SNAP's could not be achieved. There was no denervation potential in the concentric needle study. This study's results are shown in Tables 3 and 4.

These electrophysiological findings defined a chronicle severe axonal mainly distal polyneuropathy which affected both sensorial and motor fibres. Sural nerve biopsy had no help for diagnosis.

Table 3. Second Nerve Conduction Study Results (performed 3 months later after the first one)

Motor CV				
Stimulation size	Lat. ms	Ampl. mV	Dur. ms	Vel. m/s
R, Extensor indicis, Radialis, C6 C7 C8				
Upper third of the forearm	3,0	0,9	7,32	
Middle third of the shoulder	6,1	0,46	7,6	56,8
R, Abductor digiti minimi, Ulnaris, C8 T1				
Wrist	4,1	**0,14**	4,0	
Elbow	7,5	**0,13**	4,84	50,0
Arm	10,3	**0,14**	5,09	50,0
L, Abductor digiti minimi, Ulnaris C8 T1				
Wrist		**0**		
R, Abductor pollicis brevis, Medianus C8 T1				
Wrist		**0**		
L, Abductor pollicis brevis, Medianus C8 T1				
Wrist	3,4	**0,7**	5,64	
Elbow	7,8	**0,8**	6,6	50,0
R, Tibialis anterior, Peroneus, L4 L5 S1				
Head of fibula	3,8	1,0	9,8	
Popliteal fossa	6,4	1,2	10,5	40,0
L, Tibialis anterior, Peroneus, L4 L5 S1				
Head of fibula	4,0	0,42	7,9	
Popliteal fossa	5,9	0,23	8,15	40,0
R, Abductor hallucis, Tibialis, L4 L5 S1				
Medial malleolus		**0**		
L, Abductor hallucis, Tibialis, L4 L5 S1				
Medial malleolus		**0**		
R, Extensor digitorum brevis, Peroneus, L4 L5 S1				
Sole of the foot		**0**		
L, Extensor digitorum brevis, Peroneus, L4 L5 S1				
Sole of the foot		**0**		

*Sensorial Nerve Action Potentials (SNAP) could not be achieved

Table 4. Needle EMG

Interpretation								
Site	Fibril.	PSW	Fascicul.	MUP ampl.	MUP dur.	MUP polyphasicity	Interf. Pattern type	Muscle pattern
R. Biceps brachii, Musculocutaneus, C5 C6	No	No	No	Normal	Normal	+	Not examined	Normal
R Interosseus I, Ulnaris, C8 T1	No	No	No				NO CONTRACTION	
R, Rectus femoris, Femoralis, L2-L4	No	No	No	Normal	Normal	No	Not examined	Normal
R, Tibialis anterior, Peroneus, L4 L5 S1	No	No	No	N-	+	+		

After new studies, the patient was evaluated multi-disciplinary and defined as having "cryoglobulinemia related vasculitic neuropathy". While the patient's follow-up was continuing the patient passed away because of sepsis after a lung infection.

DISCUSSION

Even though Vasculitic and connective tissue-related neuropathies are clinical cases that stay in the background during diagnosis, they are important to bring to mind because of their treatability [1]. Sometimes, peripheral neuropathies are the first symptom of vasculitic disease [2]. Underlying physiopathology is end-organ damage caused by vasculitis-related vessel wall damage, which leads to ischemia and necrosis [1].

Primary, secondary vasculitis or non-systemically localized vasculitis can cause neuropathy [2]. Neuropathies in systemic vasculitis are most common in Charge Strauss syndrome (%50-70), Poly Arthritis Nodosa (PAN), and Microscopic Poly Angitis. In secondary vasculitic causes, we can see clinical cases like Hepatitis B-related PAN (%80), Hepatitis C-related mixt cryoglobulinemia (~%60), and rheumatoid vasculitis (%45-50). No neuropathy is noticed in Kawasaki disease, Takayasu Arteritis, and anti-glomerular basal membrane disease, and very rare in Giant Cell Arteritis and Behchet disease [1,2].

Neuropathy can start in vasculitic cases as distal neuropathy or acute, sub-acute painful sensorial and sensorimotor neuropathy. Systemical symptoms may be together. Stepwise progression is typical. In some cases the symmetrical and slow progress will cause to be misidentified as idiopathic distal polyneuropathy. Rarely fulminant progression can mimic Gullian-Barre Syndrome [2-4].

Electrophysiological studies must be performed bilaterally on the suspect of vasculitis to show asymmetry [2,4]. Sometimes, symmetrical involvement can be seen in chronic cases. Nerve conduct studies are important for finding the nerve that will be chosen for biopsy [2,4].

In cryoglobulinaemic vasculitis, the cryoglobulins in the blood must be cleaned fast with plasmapheresis for good results [4]. Additionally, there are open studies that show rituximab may be helpful for poly-neuropathy symptoms [4]. Since it develops under the condition of hepatitis, antiretroviral drugs may be helpful for treatment [4]. At the same time, glucocorticoids and intravenous immunoglobulins can be useful [4].

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Conflict of interest

The authors declare that there is no conflict of interest.

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