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Case Report / Olgu Sunumu

Motor polyneuropathy might be the presenting feature of acute intermittent porphyria

Akut intermittent porfiri motor polinöropati kliniği ile başlayabilir

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ABSTRACT

Acute intermittent porphyria (AIP) is a rare metabolic disorder that is the most common of the acute porphyries. Peripheral neuropathy occurs in 10%–40% of patients during an acute attack. A 25-year-old female presented with progressive quadriparesis for the last two weeks. Appendectomy and cholecystectomy operations were recorded in her past medical history because of abdominal pain attacks. She had acute motor polyneuropathy electroneuromyographic findings. Fluctuations in her liver function tests, tachycardia, high blood pressure, and hyponatremia were observed when she was staying in the hospital. She had a 24-hour urine porphobilinogen value of 48.4 mg, and a high-calorie diet with general nutritional support was started. During follow-up in the hospital, the patient's clinical symptoms improved gradually. AIP should be kept in mind in cases presenting with motor polyneuropathy even if the diagnosis was not done previously.

Keywords: Acute intermittent porphyria; motor polyneuropathy, progressive quadriparesis, peripheral nervous system

ÖZ

Akut intermitant porfiri (AIP), akut porfiriler arasında en sık görülen nadir bir metabolik hastalıktır. Periferik nöropati, akut atak sırasında hastaların %10-40'ında görülür. 25 yaşında kadın son iki haftada olan ilerleyici kuadriparezi ile başvurdu. Özgeçmişinde karın ağrısı ataklarından dolayı apendektomi ve kolesistektomi operasyonu öyküsü saptandı. Elektronöromiyografik bulgularına göre akut motor polinöropati tespit edildi. Hastane yatışı sırasında karaciğer fonksiyon testlerinde dalgalanma, taşikardi, yüksek kan basıncı ve hiponatremi gözlemlendi. 24 saatlik idrarda porfobilinojen değeri 48,4 mg geldi. Genel beslenme desteği ile yüksek kalorili diyet başlandı. Hastane takibi boyunca hastanın klinik semptomları giderek düzeldi. AIP, tanı daha önce konulmamış olsa bile motor polinöropati ile başvuran vakalarda akılda tutulmalıdır.

Anahtar kelimeler: Akut intermitant porfiri, motor polinöropati, ilerleyici kuadriparezi, periferik sinir sistemi

INTRODUCTION

The human porphyries indicate a wide variety of clinical symptoms according to the specific subtype and underlying enzymatic defect. Acute intermittent porphyria (AIP) is a rare metabolic disorder that is the most common of the acute porphyries and is characterized by enzymatic defect of porphobilinogen deaminase with depot and increased excretion of porphyrins and their precursors (1). AIP is the form that is most commonly associated with neurological disease, and it typically represents with autosomal dominant inheritance (2, 3). Both the central and peripheral nervous systems might be affected, and peripheral neuropathy occurs in 10%–40% of patients during an acute attack (4).

CASE PRESENTATION

A 25-year-old female presented with progressive quadriparesis for the last two weeks. She did not have shortness of breath, difficulty in swallowing, sensory disturbances, or urine-fecal incontinence. Appendectomy and cholecystectomy operations were recorded in her past medical history, and family history was unremarkable. In the physical examination, her pulse was 132/min and blood pressure was 166/110 mmHg, and scar marks were observed where she had undergone surgery in the abdominal area. Motor examination revealed quadriparesis to be more prominent in the upper extremities, and deep tendon reflexes were decreased bilaterally. No other physical or neurological abnormalities were observed. The patient was admitted with a diagnosis of acute motor polyneuropathy that was also supported by electroneuromyographic (ENMG) findings. The first ENMG evaluation was performed within 15 days of the patient's complaints, and motor nerve conduction study showed decreased amplitudes of the left ulnar, right tibial, and right peronealis nerve compound muscle action potentials (CMAPs) (Table 1). Sensory nerve conduction studies and needle ENMG did not detect any abnormalities. In the second ENMG (repeated 12 days later), motor nerve conduction studies of the CMAPS of the

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right median, right ulnar, tibial, and peroneal nerves showed bilaterally severe decreases in amplitude (Table 1), and the ENMG needle in the right upper extremity on the right triceps, right biceps, and right deltoid muscles showed denervation potentials and the presence of only sporadic neurogenic motor unit potentials. There were no pathological findings with the ENMG needle in the lower limbs. In control ENMG (one month after the second ENMG), bilateral tibial and bilateral peroneal nerve CMAP amplitudes were found to be lower, and this finding was compatible with motor neuropathy characterized by axonal degeneration was (Table 1).

Laboratory and radiological tests that are required for the differential diagnosis of the etiological cause were planned, and methylprednisolone pulse therapy was started after which the first examinations were performed to observe any contraindications.

Routine blood tests showed anemia and hyponatremia, elevated levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), and increased erythrocyte sedimentation rate. ANA IFA showed a granular pattern, and anti-SSA was positive. Schirmer's test revealed dry eyes, but the salivary gland biopsy was reported to be normal. Methylprednisolone pulse therapy was started. Fluctuations in Aspartate aminotransferase and ALT values were observed during hospitalization (the highest valueswere AST 384 U/L and ALT 620 U/L). Ahigh creatine kinase level (1516 U/L) was observed on the fourteenth day of hospitalization. Hyponatremia, tachycardia, and high blood pressure continued for a few weeks after admission to hospital. Tachycardia and hypertension responded only to esmolol infusion.

Even though valid reasons for previous attacks of abdominal pain were reported, the absence of skın lesions or any features in her family history meant that acute motor polyneuropathy was likely the cause of admission to hospital. She had undergone repeated abdominal operations, but she said that she had been having an abdominal pain attack when asked again in detail. Fluctuations in her liver function tests, tachycardia, high blood pressure, and hyponatremia were observed during her stay in the hospital, and her 24-hour urine (total 2900 mL urine) porphobilinogen value was found to be 48.4 mg (reference value <1.6 mg). Taken together, AIP was diagnosed due to the clinical and laboratory findings and high urine porphobilinogen level (Table 2). The time period until the high porphobilinogen levels suggested that the attack began to decline and thus hematin could not be easily obtained. A high-calorie diet with general nutritional support was started, including 200 g per day IV glucose, amino acids, and vitamins, and trace elements support was given.

During follow-up in the hospital, the patient's clinical symptoms improved gradually. The serum AST and ALT levels fell and the hyponatremia, tachycardia, and high blood pressure disappeared. Muscle strength of the four extremities improved markedly in her motor examination, and she began to walk unassisted.

Table 1. Nerve conduction study (during the application/12 days later/1 month later)

Motor nerve	Latency (m/s)	Amp (mV)	CV (m/s)	F res.
Right median				
Wrist–APB	2.9/2.8	5.2/3.3		
Elbow–wrist	7.0/7.1	4.9/3.1	53.7/53.5	
Right ulnar				
Wrist–ADM	3.0/2.3/2.2	8.0/3.4/6.9		
Elbow–wrist	6.9/6.2/7.0	8.8/3.8/7.3	51.3/56.4/39.5	
Right tibialis				
Ankle–AH	3.4/5.0/5.1	6.5/3.5/0.5		
Poplitea–ankle	6.6/12.0/13.2	4.8/3.0/0.6	40.2/48.6/39.5	51.0/48.5/51.9
Left tibialis				
Ankle–AH	4.1/4.5/4.6	12/2.0/3.2		
Poplitea–ankle	12.1/13.0/15.0	8.5/1.4/2.2	43.6/40.0/31.7	
Right peroneus				
Ankle–EDB	3.6/3.3/4.3	3.1/1.6/2.1		
C. fibula–ankle	10.6/10.2/11.3	3.6/1.2/1.7	47.6/43.5/41.4	
Left peroneus				
Ankle–EDB	3.7/3.1/4.4	7.8/0.5/1.0		
C. fibula–ankle	1.5/10.5/11.1	6.9/0.4/1.0	44.1/41.9/41.8	

APB: abductor pollicis longus; ADM: abductor digiti minimi (hand); AH: abductor hallucis; EDB: extensor digitorum brevis; Amp: amplitude; mV: microvolt; C: caput; CV: conduction velocity

Table 2. Abnormal tests results

Test	Result	Reference value
Hemoglobin	10.2 g/dL	12.3–15.47 g/dL
ESR (erythrocyte sedimentation rate)	54 mm/h	1–20 mm/h
Total protein	5.75 g/dL	6.4–8.3 g/dL
Albumin	3.37 g/dL	3.5–5.2 g/dL
AST	139 U/L	5–32 U/L
ALT	133 U/L	5–33 U/L
Sodium mmoL/L	128 mmoL/L	136–145
Cholesterol	327 mg/dL	110–200 mg/dL
HDL cholesterol	103 mg/dL	45–65 mg/dL
LDL cholesterol	213 mg/dL	57–129 mg/dL
CA 125	203.7 U/mL	0.6–35 U/mL
CA 19–9	212.2 U/mL	0.61–7 U/mL
Vitamin D	<4 ng/mL	25–80 ng/mL
ANA IFA	Positive (+) granular pattern	
Anti–SSA	132(positive)	0–15
Porphobilinogen (total 2900 ml urine)	48.4 mg/24 hour	<1.6

AST: aspartat aminotransferaz; ALT: alanin aminotransferaz; ANA: anti–nükleer antikor; HDL: high density lipoprotein; LDL: low density lipoprotein; CA125: cancer antigen; ANA IFA: antinuclear antibody IFA; Anti–SSA: anti–Sjögren's syndrome A

DISCUSSION

Porphyria is a genetic disease caused by defects in heme biosynthesis. Porphyries are divided into acute and cutaneous categories based on their predominant symptoms. Patients with acute porphyries (i.e., neurovisceral porphyria) present with symptoms of abdominal pain, neuropathy, autonomic instability, and psychosis (5). Attacks might continue for days or weeks, and recurrent nausea, vomiting, and dehydration might occur (6). In our case, the patient had undergone appendectomy and cholecystectomy because of repeated pain attacks. Peripheral neuropathy can occur in 10%–40% of patients during an acute attack, and neuropathic symptoms can develop within 1 month of the onset of abdominal pain (4). Porphyric neuropathy remains a predominantly motor neuropathy, but cranial nerve involvement has also been described, most commonly affecting the facial nerve and vagus nerve. Because of the clinical similarities, it can mimic Guillain-Barré syndrome (GBS). Deep tendon reflexes are often preserved in the early stages, which might help in the differentiation from GBS (7). In contrast to most other metabolic neuropathies that have distal lower limb predominance, porphyric neuropathy often presents with proximal weakness (1).

Anti-SSA (Ro52/Ro60) auto-antibodies have been associated with systemic lupus erythema tosus, Sjögren's syndrome, subacute cutaneous lupus, neonatal lupus syndrome, systemic sclerosis, and myositis (8). The porphyries have been described in association with a variety of autoimmune disorders, and antinuclear antibodies (ANAs) were found in 8/15 (53%) of patients with AIP (9). In our case, ANA IFA showed a granular pattern, and anti-SSA was positive in laboratory tests.

Porphyries are autosomal dominant disorders, but in our case the patient history was unremarkable. It is unclear how reliable this information is, but it is known that 80% of patients can lead a biochemically and clinically normal life (10, 11).

CONCLUSION

We consider three important points in this case. AIP should be kept in mind in cases presenting with motor polyneuropathy even if the diagnosis was not done previously, AIP has various systemic findings that can lead to the diagnosis, and anti-SSA positivity might be seen in AIP, which is not wellknown among neurologists (10).

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REFERENCES

1. Lin CS, Park SB, Krishnan AV. Porphyric neuropathy. Handb Clin Neurol 2013; 115: 613-27. [CrossRef]
2. Solis C, Martinez-Bermejo A, Naidich TP, Kaufmann WE, Astrin KH, Bishop DF, et al. Acute intermittent porphyria: studies of the severe homozygous dominant disease provides insights into the neurologic attacks in acute porphyrias. Arch Neurol 2004; 61: 1764-70. [CrossRef]
3. Lin CS, Krishnan AV, Lee MJ, Zagami AS, You HL, Yang CC, et al. Nerve function and dysfunction in acute intermittent porphyria. Brain 2008; 131: 2510-9. [CrossRef]
4. Hift RJ, Meissner PN. An analysis of 112 acute porphyric attacks in Cape Town, South Africa: Evidence that acute intermittent porphyria and variegate porphyria differ in susceptibility and severity. Medicine (Baltimore) 2005; 84: 48-60. [CrossRef]

5. Foran SE, Abel G. Guide to porphyrias. A historical and clinical perspective. Am J Clin Pathol 2003; 119 Suppl: S86-93.
6. Gross U, Sassa S, Jacob K, Deybach JC, Nordmann Y, Frank M, et al. 5-Aminolevulinic acid dehydratase deficiency porphyria: a twenty-year clinical and biochemical follow-up. Clin Chem 1998; 44: 1892-6.
7. Albers JW, Fink JK. Porphyric neuropathy. Muscle Nerve 2004; 30: 410-22. [CrossRef]
8. Hervier B, Rimbert M, Colonna F, Hamidou MA, Audrain M. Clinical significance of anti-Ro/SSA-52 kDa antibodies: a retrospective monocentric study. Rheumatology (Oxford) 2009; 48: 964-7. [CrossRef]
9. Allard SA, Charles PJ, Herrick AL, McColl KE, Scott JT. Antinuclear antibodies and the diagnosis of systemic lupus erythematosus in patients with acute intermittent porphyria. Ann Rheum Dis 1990; 49: 246-8. [CrossRef]
10. Anderson KE, Bloomer JR, Bonkovsky HL, Kushner JP, Pierach CA, Pimstone NR, et al. Recommendations for the diagnosis and treatment of the acuteporphyrias. Ann Intern Med 2005; 142: 439-50. [CrossRef]
11. Michaels BD, Del Rosso JQ, Mobini N, Michaels JR. Erythropoietic protoporphyria: a case report and literature review. J Clin Aesthet Dermatol 2010; 3: 44-8.

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