

Bölüm 13

PARAPROTEİNEMİK VE PARANEOPLASTİK NÖROPATİLER

Aysel ÇOBAN TAŞKIN¹

PARAPROTEİNEMİK NÖROPATİLER

Plazma hücreleri antikör ya da immünglobulin (Ig) üretebilen matür B hücreleridir. İmmünglobulinler iki hafif (kappa ve lambda) ve iki ağır (IgG, IgA, IgM, IgD, IgE) zincirden oluşur. Her plazma hücresi tek tip ağır zincir ve özgün bir antijen bağlanma bölgesi içeren spesifik bir immünglobulin üretir (1).

Monoklonal gammopatiler, tek bir ağır zincir ve tek bir hafif zincir tarafından oluşturulan M-proteinlerinin veya paraproteinlerin çoğalması ve birikmesi ile karakterizedir (2). En yaygın monoklonal gammopati IgG'dir, bunu IgM ve IgA takip eder (1). Monoklonal gamopatinin varlığı serum veya idrar protein elektroforezi ile taranarak saptanır. Serum immünelektroforezi ve immünfiksasyon elektroforezi, paraproteinin monoklonal yapısını doğrulayabilen daha hassas ölçümlerdir (2). Monoklonal gamopati saptanması halinde malignite değerlendirmek için daha fazla araştırma gerekir. Bence-Jones proteini tespiti için idrar toplanması, Ig konsantrasyonu, tam kan sayımı, böbrek ve karaciğer fonksiyonları, kalsiyum, fosfor, eritrosit sedimentasyon hızı, C-reaktif protein, laktat dehidrojenaz değerlendirilmesi için kan tetkiki, kemik iliği aspiratı, organomegali saptamak için fizik muayene ve karın ve göğüs bilgisayarlı tomografisi (BT) ve biyopsi gerekir. Kemik lezyonlarının araştırılması için radyografi endikedir, bazı merkezlerde düşük doz BT taramaları kullanılmaktadır, tüm vücut manyetik rezonans görüntüleme (MRG) de tercih edilmektedir (3).

Monoklonal proteinler genellikle periferik nöropatilerle birlikte görülür. Hem periferik nöropati hem de monoklonal gamopati genel popülasyonda nispeten yaygındır: periferik nöropatinin genel prevalansı %1,66 ile %3,9 arasındadır (4), monoklonal proteinlerin insidansı 50 yaşından büyük bireylerde %3.2, 70 yaşın-

¹ Uzm. Dr., İzmir Tepecik Eğitim ve Araştırma Hastanesi, Nöroloji Kliniği, ayselcoban@hotmail.com

KAYNAKLAR

1. Naddaf E, Mauermann ML. Peripheral neuropathies associated with monoclonal gammopathies. *Continuum (Minneap Minn)*. 2020;26(5): 1369–1383.
2. Ramchandren S, Lewis RA. Monoclonal gammopathy and neuropathy. *Current Opinion in Neurology*. 2009; 22:480–485.
3. Lozeron P, Adams D. Monoclonal gammopathy and neuropathy. *Current Opinion in Neurology*. 2007; 20:536–541.
4. Hanewinkel R, Drenthen J, van Oijen M, et al. Prevalence of polyneuropathy in the general middle-aged and elderly population. *Neurology*. 2016;87(18):1892–1898.
5. Kyle RA, Therneau TM, Rajkumar SV, et al. Prevalence of monoclonal gammopathy of undetermined significance. *N Engl J Med*. 2006;354:1362–1369.
6. Chaudhry HM, Mauermann ML, Rajkumar SV. Monoclonal Gammopathy-Associated Peripheral Neuropathy: Diagnosis and Management. *Mayo Clin Proc*. 2017;92(5):838-850.
7. Mauermann ML. Paraproteinemic Neuropathies. *Continuum (Minneap Minn)*. 2014;20(5):1307–1322.
8. Raheja D, Specht C, Simmons Z. Paraproteinemic neuropathies. *Muscle Nerve*. 2015; 51: 1–13.
9. Kyle RA, Therneau TM, Rajkumar SV, et al. A long-term study of prognosis in monoclonal gammopathy of undetermined significance. *N Engl J Med* 2002;346(8):564-569.
10. Garcia-Santibanez R, Zaidman CM, Sommerville RB, et al. CANOMAD and other chronic ataxic neuropathies with disialosyl antibodies (CANDA). *J Neurol*. 2018;265(6):1402-1409.
11. Dispenzieri A. POEMS Syndrome: 2019 Update on diagnosis, risk-stratification, and management. *Am J Hematol*. 2019;94:812–827.
12. Gertz MA. Immunoglobulin light chain amyloidosis diagnosis and treatment algorithm 2018. *Blood Cancer J*. 2018; 23;8(5):44.
13. Darnell RB, Posner JB. Paraneoplastic syndromes involving the nervous system. *N Engl J Med* 2003;349(16):1543-1554.
14. Antoine JC, Camdessanche JP. Peripheral nervous system involvement in patients with cancer. *Lancet Neurol* 2007;6(1):75-86.
15. Graus F, Delattre JY, Antoine JC, et al. Recommended diagnostic criteria for paraneoplastic neurological syndromes. *nJ Neurol Neurosurg Psychiatry*. 2004;75(8): 1135-1140.
16. Muppidi S, Vernino S. Paraneoplastic Neuropathies. *Continuum (Minneap Minn)*. 2014;20(5):1359–1372.
17. Antoine JC, Camdessanche JP. Paraneoplastic neuropathies. *Curr Opin Neurol*. 2017; 30(5):513-520.
18. Graus F, Dalmau J. Paraneoplastic neuropathies. *Curr Opin Neurol*. 2013;26:489 – 495.

19. Flanagan EP, Sandroni P, Pittock SJ, Inwards DJ, Jones LK Jr. Paraneoplastic lower motor neuronopathy associated with Hodgkin lymphoma. *Muscle Nerve*. 2012;46(5):823-7.
20. Viala K, Béhin A, Maisonobe T, et al. Neuropathy in lymphoma: a relationship between the pattern of neuropathy, type of lymphoma and prognosis? *J Neurol Neurosurg Psychiatry*. 2008;79(7):778-2.
21. Forsyth PA, Dalmau J, Graus F, et al. Motor neuron syndromes in cancer patients. *Ann Neurol* 1997; 41:722 – 730.
22. Camdessanché JP, Jousserand G, Ferraud K, et al. The pattern and diagnostic criteria of sensory neuronopathy: a case-control study. *Brain* 2009; 132:1723-1733.
23. Auger RG, Windebank AJ, Lucchinetti CF, Chalk CH. Role of the blink reflex in the evaluation of sensory neuronopathy. *Neurology* 1999;53(2):407Y408.
24. Molinuevo JL, Graus F, Serrano C, et al. Utility of anti-Hu antibodies in the diagnosis of paraneoplastic sensory neuropathy. *Ann Neurol* 1999; 44:976– 980.
25. Titulaer MJ, Soffietti R, Dalmau J, et al. Screening for tumours in paraneoplastic syndromes: report of an EFNS task force. *Eur J Neurol* 2011; 18:19.
26. Gwathmey KG. Sensory neuronopathies. *Muscle Nerve* 2016; 53:8. Amato AA, Ropper AH. Sensory Ganglionopathy. *N Engl J Med* 2020; 383:1657.
27. Winston N, Vernino S. Recent advances in autoimmune autonomic ganglionopathy. *Curr Opin Neurol* 2010; 23:514 – 518.
28. Koike H, Watanabe H, Sobue G. The spectrum of immune-mediated autonomic neuropathies: insights from the clinicopathological features. *J Neurol Neurosurg Psychiatry* 2013; 84:98 – 106.
29. Li Y, Jammoul A, Mente K, et al. Clinical experience of seropositive ganglionic acetylcholine receptor antibody in a tertiary neurology referral center. *Muscle Nerve* 2015; 52:386.
30. Gibbons CH, Vernino SA, Freeman R. Combined immunomodulatory therapy in autoimmune autonomic ganglionopathy. *Arch Neurol* 2008; 65:213.
31. Vighiani MC, Magistrello M, Polo P, et al. Risk of cancer in patients with Guillain-Barre syndrome (GBS). A population-based study. *J Neurol* 2004; 251:321.
32. Antoine JC, Honnorat J, Camdessanché JP, et al. Paraneoplastic anti-CV2 antibodies react with peripheral nerve and are associated with a mixed axonal and demyelinating peripheral neuropathy. *Ann Neurol* 2001; 49:214.
33. Kannan MA, Challa S, Kandadai RM, et al. Series of paraneoplastic vasculitic neuropathy: a rare, potentially treatable neuropathy. *Neurol India* 2015; 63:30.
34. Dubey D, David WS, Amato AA, et al. Varied phenotypes and management of immune checkpoint inhibitor-associated neuropathies. *Neurology* 2019; 93:e1093.
35. Mancone S, Lycan T, Ahmed T, et al. Severe neurologic complications of immune checkpoint inhibitors: a single-center review. *J Neurol* 2018; 265:1636.
36. Reynolds KL, Guidon AC. Diagnosis and Management of Immune Checkpoint Inhibitor-Associated Neurologic Toxicity: Illustrative Case and Review of the Literature. *Oncologist* 2019; 24:435.