

# GASTROİNTESTİNAL HASTALIKLARIN NÖROLOJİK BULGULARI

Elif DİDİNMEZ TAŞKIRDI<sup>1</sup>

Pınar GENÇPINAR<sup>2</sup>

## GİRİŞ

---

Bu bölüm gastrointestinal hastalıkların bir sonucu olarak ortaya çıkan nörolojik semptomlara odaklanmaktadır. Bu semptomlar nöropati, miyopati, ataksi, baş ağrısı ve nöbet dahil olmak üzere geniş bir yelpazede olup gastrointestinal ve nörolojik semptomların birbirleriyle ilişkilendirilmesi bu hastalıkların erken teşhisi açısından önem arz etmektedir. Aşağıda ekstraintestinal nörolojik belirtileri sık görülen bazı gastrointestinal hastalıklara yer verilmiştir.<sup>1</sup>

## MALABSORBSİYON SENDROMLARI

---

### Çölyak Hastalığı

Çölyak hastalığı, genetik olarak yatkın bireylerde (HLA sınıf II haplotipleri DQ2 veya DQ8) çevresel koşullarla birlikte enteropatiye yol açan gluten duyarlılığı olarak tanımlanır.<sup>2</sup> Tipik olarak diyare, karın ağrısı gibi gastrointestinal semptomlarla prezente

<sup>1</sup> Uzm. Dr., İzmir Sağlık Bilimleri Üniversitesi Tepecik Eğitim ve Araştırma Hastanesi, Çocuk Nörolojisi Kliniği, edidinmez@hotmail.com

<sup>2</sup> Prof. Dr., İzmir Katip Çelebi Üniversitesi Çocuk Nöroloji BD., İzmir Katip Çelebi Üniversitesi Sınır Bilim ve Uygulama Araştırma Merkezi, pinargencpinar@gmail.com

## SONUÇ

---

Gastrointestinal sistemi ilgilendiren birçok hastalığa nörolojik bulgular eşlik edebilir. Nöropati, miyopati, ataksi, baş ağrısı ve nöbetler dahil olmak üzere birçok nörolojik semptom bu hastalıklarda hem tanı anında hem izleminde karşımıza çıkabilir. Erken tanı ve tedavi hem komplikasyonların önlenmesi hem de hastaların yaşam kalitelerinin artırılması açısından önemlidir. Tanı, tedavi ve izlem süreçleri bölümlerin multidisipliner yaklaşımı ile devam ettirilmelidir.

## KAYNAKLAR

---

1. Swaiman KF, Ashwal S, Ferriero DM, Schor NF, Finkel RS, Gropman AL, et al. Swaiman's pediatric neurology e-book: Principles and practice: Elsevier Health Sciences; 2017.
2. Guandalini S, Assiri A. Celiac disease: a review. *JAMA Pediatr.* 2014;168(3):272-8.
3. Luostarinen L, Pirttilä T, Collin P. Coeliac disease presenting with neurological disorders. *Eur Neurol.* 1999;42(3):132-5.
4. Zelnik N, Pacht A, Obeid R, Lerner A. Range of neurologic disorders in patients with celiac disease. *Pediatrics.* 2004;113(6):1672-6.
5. Ruggieri M, Incorpora G, Polizzi A, Parano E, Spina M, Pavone P. Low prevalence of neurologic and psychiatric manifestations in children with gluten sensitivity. *J Pediatr.* 2008;152(2):244-9.
6. Lahat E, Broide E, Leshem M, Evans S, Scapa E. Prevalence of celiac antibodies in children with neurologic disorders. *Pediatr Neurol.* 2000;22(5):393-6.
7. Gabrielli M, Cremonini F, Fiore G, Addolorato G, Padalino C, Candelli M, et al. Association between migraine and Celiac disease: results from a preliminary case-control and therapeutic study. *Am J Gastroenterol.* 2003;98(3):625-9.
8. Diaconu G, Burlea M, Grigore I, Anton DT, Trandafir LM. Celiac disease with neurologic manifestations in children. *Rev Med Chir Soc Med Nat Iasi.* 2013;117(1):88-94.
9. Hadjivassiliou M, Rao DG, Grinewald RA, Aeschlimann DP, Sarrigiannis PG, Hoggard N, et al. Neurological Dysfunction in Coeliac Disease and Non-Coeliac Gluten Sensitivity. *Am J Gastroenterol.* 2016;111(4):561-7.
10. Bürk K, Bösch S, Müller CA, Melms A, Zühlke C, Stern M, et al. Sporadic cerebellar ataxia associated with gluten sensitivity. *Brain.* 2001;124(Pt 5):1013-9.
11. Cavusoglu D, Olgac Dundar N, Oztekin O, Arican P, Gencpinar P, Baran

- M. A Neurological Appearance of Celiac Disease: Is There Any Associated Factor? *Pediatr Emerg Care*. 2021;37(6):303-7.
12. Luostarinen LK, Collin PO, Peräaho MJ, Mäki MJ, Pirttilä TA. Coeliac disease in patients with cerebellar ataxia of unknown origin. *Ann Med*. 2001;33(6):445-9.
  13. Kieslich M, Errázuriz G, Posselt HG, Moeller-Hartmann W, Zanella F, Boehles H. Brain white-matter lesions in celiac disease: a prospective study of 75 diet-treated patients. *Pediatrics*. 2001;108(2):E21.
  14. Henri-Bhargava A, Melmed C, Glikstein R, Schipper HM. Neurologic impairment due to vitamin E and copper deficiencies in celiac disease. *Neurology*. 2008;71(11):860-1.
  15. Ludvigsson JF, Zingone F, Tomson T, Ekbom A, Ciacci C. Increased risk of epilepsy in biopsy-verified celiac disease: a population-based cohort study. *Neurology*. 2012;78(18):1401-7.
  16. Gobbi G, Bouquet F, Greco L, Lambertini A, Tassinari CA, Ventura A, et al. Coeliac disease, epilepsy, and cerebral calcifications. The Italian Working Group on Coeliac Disease and Epilepsy. *Lancet*. 1992;340(8817):439-43.
  17. Fois A, Balestri P, Vascotto M, Farnetani MA, Di Bartolo RM, Di Marco V, et al. Progressive cerebral calcifications, epilepsy, and celiac disease. *Brain Dev*. 1993;15(1):79-82.
  18. Magaudda A, Dalla Bernardina B, De Marco P, Sfaello Z, Longo M, Colamaria V, et al. Bilateral occipital calcification, epilepsy and coeliac disease: clinical and neuroimaging features of a new syndrome. *J Neurol Neurosurg Psychiatry*. 1993;56(8):885-9.
  19. Thawani SP, Brannagan TH, 3rd, Lebowhl B, Green PH, Ludvigsson JF. Risk of Neuropathy Among 28,232 Patients With Biopsy-Verified Celiac Disease. *JAMA Neurol*. 2015;72(7):806-11.
  20. Alaedini A, Green PH, Sander HW, Hays AP, Gamboa ET, Fasano A, et al. Ganglioside reactive antibodies in the neuropathy associated with celiac disease. *J Neuroimmunol*. 2002;127(1-2):145-8.
  21. Hadjivassiliou M, Chattopadhyay AK, Davies-Jones GA, Gibson A, Grünewald RA, Lobo AJ. Neuromuscular disorder as a presenting feature of coeliac disease. *J Neurol Neurosurg Psychiatry*. 1997;63(6):770-5.
  22. Hadjivassiliou M, Sanders DS, Grünewald RA, Woodroffe N, Boscolo S, Aeschlimann D. Gluten sensitivity: from gut to brain. *Lancet Neurol*. 2010;9(3):318-30.
  23. Ludvigsson JF, Reichenberg A, Hultman CM, Murray JA. A nationwide study of the association between celiac disease and the risk of autistic spectrum disorders. *JAMA Psychiatry*. 2013;70(11):1224-30.
  24. Ghalichi F, Ghaemmaghami J, Malek A, Ostadrahimi A. Effect of gluten free diet on gastrointestinal and behavioral indices for children with autism spectrum disorders: a randomized clinical trial. *World J Pediatr*. 2016;12(4):436-42.
  25. Prosperi M, Santocchi E, Balboni G, Narzisi A, Bozza M, Fulceri F, et al. Be-

- havioral Phenotype of ASD Preschoolers with Gastrointestinal Symptoms or Food Selectivity. *J Autism Dev Disord.* 2017;47(11):3574-88.
26. Şahin Y, Durucu C, Şahin DA. Evaluation of hearing loss in pediatric celiac patients. *Int J Pediatr Otorhinolaryngol.* 2015;79(3):378-81.
  27. Lionetti E, Francavilla R, Pavone P, Pavone L, Francavilla T, Pulvirenti A, et al. The neurology of coeliac disease in childhood: what is the evidence? A systematic review and meta-analysis. *Dev Med Child Neurol.* 2010;52(8):700-7.
  28. Abenavoli L. Brain hypoperfusion and neurological symptoms in celiac disease. *Movement Disorders.* 2010;25(6):799-800.
  29. Gondim Fde A, Oliveira GR, Teles BC, Souza MH, Braga LL, Messias EL. A case-control study of the prevalence of neurological diseases in inflammatory bowel disease (IBD). *Arq Neuropsiquiatr.* 2015;73(2):119-24.
  30. Gondim FA, Brannagan TH, 3rd, Sander HW, Chin RL, Latov N. Peripheral neuropathy in patients with inflammatory bowel disease. *Brain.* 2005;128(Pt 4):867-79.
  31. Benavente L, Moris G. Neurologic disorders associated with inflammatory bowel disease. *Eur J Neurol.* 2011;18(1):138-43.
  32. Figueroa JJ, Loftus EV, Jr., Harmsen WS, Dyck PJ, Klein CJ. Peripheral neuropathy incidence in inflammatory bowel disease: a population-based study. *Neurology.* 2013;80(18):1693-7.
  33. Ohyagi M, Ohkubo T, Yagi Y, Ishibashi S, Akiyama J, Nagahori M, et al. Chronic inflammatory demyelinating polyradiculoneuropathy in a patient with Crohn's disease. *Intern Med.* 2013;52(1):125-8.
  34. García-Cabo C, Moris G. Peripheral neuropathy: an underreported neurologic manifestation of inflammatory bowel disease. *Eur J Intern Med.* 2015;26(7):468-75.
  35. Katsanos AH, Katsanos KH, Kosmidou M, Giannopoulos S, Kyritsis AP, Tsianos EV. Cerebral sinus venous thrombosis in inflammatory bowel diseases. *Qjm.* 2013;106(5):401-13.
  36. Lazzerini M, Bramuzzo M, Maschio M, Martellosi S, Ventura A. Thromboembolism in pediatric inflammatory bowel disease: systematic review. *Inflamm Bowel Dis.* 2011;17(10):2174-83.
  37. DeFilippis EM, Barfield E, Leifer D, Steinlauf A, Bosworth BP, Scherl EJ, et al. Cerebral venous thrombosis in inflammatory bowel disease. *J Dig Dis.* 2015;16(2):104-8.
  38. Karmody CS, Valdez TA, Desai U, Blevins NH. Sensorineural hearing loss in patients with inflammatory bowel disease. *Am J Otolaryngol.* 2009;30(3):166-70.
  39. Moris G, Milla A, Ribacoba R, González C. Acute deafness as an extraintestinal manifestation of ulcerative colitis. *Eur J Intern Med.* 2005;16(6):440-2.
  40. Ratzinger G, Sepp N, Vogetseder W, Tilg H. Cheilitis granulomatosa and Melkersson-Rosenthal syndrome: evaluation of gastrointestinal involvement and therapeutic regimens in a series of 14 patients. *J Eur Acad Der-*

- matol Venereol. 2007;21(8):1065-70.
41. Lloyd DA, Payton KB, Guenther L, Frydman W. Melkersson-Rosenthal syndrome and Crohn's disease: one disease or two? Report of a case and discussion of the literature. *J Clin Gastroenterol.* 1994;18(3):213-7.
  42. Bernal W, Wendon J. Acute liver failure. *N Engl J Med.* 2013;369(26):2525-34.
  43. Shawcross DL, Wendon JA. The neurological manifestations of acute liver failure. *Neurochem Int.* 2012;60(7):662-71.
  44. Scott TR, Kronsten VT, Hughes RD, Shawcross DL. Pathophysiology of cerebral oedema in acute liver failure. *World J Gastroenterol.* 2013;19(48):9240-55.
  45. Dara N, Sayyari AA, Imanzadeh F. Hepatic encephalopathy: early diagnosis in pediatric patients with cirrhosis. *Iran J Child Neurol.* 2014;8(1):1-11.
  46. Amodio P, Montagnese S. Clinical neurophysiology of hepatic encephalopathy. *J Clin Exp Hepatol.* 2015;5(Suppl 1):S60-8.
  47. Huster D. Wilson disease. *Best Pract Res Clin Gastroenterol.* 2010;24(5):531-9.
  48. Lorincz MT. Neurologic Wilson's disease. *Ann N Y Acad Sci.* 2010;1184:173-87.
  49. Youn J, Kim JS, Kim HT, Lee JY, Lee PH, Ki CS, et al. Characteristics of neurological Wilson's disease without Kayser-Fleischer ring. *J Neurol Sci.* 2012;323(1-2):183-6.
  50. Denning TR, Berrios GE, Walshe JM. Wilson's disease and epilepsy. *Brain.* 1988;111 ( Pt 5):1139-55.
  51. Seniów J, Bak T, Gajda J, Poniatowska R, Czlonkowska A. Cognitive functioning in neurologically symptomatic and asymptomatic forms of Wilson's disease. *Mov Disord.* 2002;17(5):1077-83.
  52. Deguti MM, Tietge UJ, Barbosa ER, Cancado EL. The eye in Wilson's disease: sunflower cataract associated with Kayser-Fleischer ring. *J Hepatol.* 2002;37(5):700.
  53. Salari M, Fayyazi E, Mirmosayyeb O. Magnetic resonance imaging findings in diagnosis and prognosis of Wilson disease. *J Res Med Sci.* 2018;23:23.
  54. Schilsky ML. Treatment of Wilson's disease: what are the relative roles of penicillamine, trientine, and zinc supplementation? *Curr Gastroenterol Rep.* 2001;3(1):54-9.
  55. Wiggelinkhuizen M, Tilanus ME, Bollen CW, Houwen RH. Systematic review: clinical efficacy of chelator agents and zinc in the initial treatment of Wilson disease. *Aliment Pharmacol Ther.* 2009;29(9):947-58.
  56. Douglas EF, White PT. Abdominal epilepsy--a reappraisal. *J Pediatr.* 1971;78(1):59-67.
  57. Zinkin NT, Peppercorn MA. Abdominal epilepsy. *Best Pract Res Clin Gastroenterol.* 2005;19(2):263-74.
  58. Franzon RC, Lopes CF, Schmutzler KM, Morais MI, Guerreiro MM. Recurrent abdominal pain: when should an epileptic seizure be suspected?

- Arq Neuropsychiatr. 2002;60(3-a):628-30.
59. Dutta SR, Hazarika I, Chakravarty BP. Abdominal epilepsy, an uncommon cause of recurrent abdominal pain: a brief report. *Gut*. 2007;56(3):439-41.
  60. Kshirsagar VY, Nagarsenkar S, Ahmed M, Colaco S, Wingkar KC. Abdominal epilepsy in chronic recurrent abdominal pain. *J Pediatr Neurosci*. 2012;7(3):163-6.
  61. Siegel AM, Williamson PD, Roberts DW, Thadani VM, Darcey TM. Localized pain associated with seizures originating in the parietal lobe. *Epilepsia*. 1999;40(7):845-55.
  62. Nair DR, Najm I, Bulacio J, Lüders H. Painful auras in focal epilepsy. *Neurology*. 2001;57(4):700-2.
  63. Schade GH, Gofman H. Abdominal epilepsy in childhood. *Pediatrics*. 1960;25:151-4.
  64. Peppercorn MA, Herzog AG. The spectrum of abdominal epilepsy in adults. *Am J Gastroenterol*. 1989;84(10):1294-6.
  65. Scarpato E, Kolacek S, Jojkic-Pavkov D, Konjik V, Živković N, Roman E, et al. Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents in the Mediterranean Region of Europe. *Clin Gastroenterol Hepatol*. 2018;16(6):870-6.
  66. Mortimer MJ, Kay J, Jaron A. Clinical epidemiology of childhood abdominal migraine in an urban general practice. *Dev Med Child Neurol*. 1993;35(3):243-8.
  67. Kothare SV. Efficacy of flunarizine in the prophylaxis of cyclical vomiting syndrome and abdominal migraine. *Eur J Paediatr Neurol*. 2005;9(1):23-6.
  68. Symon DN, Russell G. Double blind placebo controlled trial of pizotifen syrup in the treatment of abdominal migraine. *Arch Dis Child*. 1995;72(1):48-50.
  69. Worawattanakul M, Rhoads JM, Lichtman SN, Ulshen MH. Abdominal migraine: prophylactic treatment and follow-up. *J Pediatr Gastroenterol Nutr*. 1999;28(1):37-40.
  70. Kakisaka Y, Wakusawa K, Haginoya K, Saito A, Uematsu M, Yokoyama H, et al. Efficacy of sumatriptan in two pediatric cases with abdominal pain-related functional gastrointestinal disorders: does the mechanism overlap that of migraine? *J Child Neurol*. 2010;25(2):234-7.
  71. Drossman DA, Hasler WL. Rome IV-Functional GI Disorders: Disorders of Gut-Brain Interaction. *Gastroenterology*. 2016;150(6):1257-61.
  72. Hasler WL, Levinthal DJ, Tarbell SE, Adams KA, Li BUK, Issenman RM, et al. Cyclical vomiting syndrome: Pathophysiology, comorbidities, and future research directions. *Neurogastroenterol Motil*. 2019;31 Suppl 2(Suppl 2):e13607.
  73. Li BU, Lefevre F, Chelimsky GG, Boles RG, Nelson SP, Lewis DW, et al. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition consensus statement on the diagnosis and management of cyclic vomiting syndrome. *J Pediatr Gastroenterol Nutr*. 2008;47(3):379-93.

74. Spiri D, Rinaldi VE, Titomanlio L. Pediatric migraine and episodic syndromes that may be associated with migraine. *Ital J Pediatr.* 2014;40:92.
75. Hyman PE, Milla PJ, Benninga MA, Davidson GP, Fleisher DF, Taminiu J. Childhood functional gastrointestinal disorders: neonate/toddler. *Gastroenterology.* 2006;130(5):1519-26.
76. Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, van Tilburg M. *Functional Disorders: Children and Adolescents.* Gastroenterology. 2016.
77. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalgia.* 2013;33(9):629-808.
78. McAbee GN, Morse AM, Cook W, Tang V, Brosgol Y. Neurological Etiologies and Pathophysiology of Cyclic Vomiting Syndrome. *Pediatr Neurol.* 2020;106:4-9.
79. Carbonari G, Tonti G, Di Pisa V, Franzoni E, Cordelli DM. Pediatric epilepsies misdiagnosed as gastrointestinal disorders. *Epilepsy Behav.* 2018;83:137-9.
80. Chopra SS, Kulkarni SD, Hegde AU, Shah KN. Cyclical vomiting syndrome with bilateral epileptiform discharges. *Indian Pediatr.* 2011;48(2):143-5.
81. Puy H, Gouya L, Deybach JC. Porphyrrias. *Lancet.* 2010;375(9718):924-37.
82. Zaatreh MM. Levetiracetam in porphyric status epilepticus: a case report. *Clin Neuropharmacol.* 2005;28(5):243-4.
83. Wessels T, Blaes F, Röttger C, Hügens M, Hüge S, Jauss M. [Cortical amaurosis and status epilepticus with acute porphyria]. *Nervenarzt.* 2005;76(8):992-5, 7-8.
84. Asselbergs FW, Kremer Hovinga TK, Bouwsma C, van Ingen J. Acute intermittent porphyria as a cause of respiratory failure: case report. *Am J Crit Care.* 2009;18(2):180, 78-9.
85. Pischik E, Kauppinen R. Neurological manifestations of acute intermittent porphyria. *Cell Mol Biol (Noisy-le-grand).* 2009;55(1):72-83.
86. Linares DM, Ross P, Stanton C. Beneficial Microbes: The pharmacy in the gut. *Bioengineered.* 2016;7(1):11-20.
87. Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. *Cell.* 2014;157(1):121-41.
88. Nicholson JK, Holmes E, Kinross J, Burcelin R, Gibson G, Jia W, et al. Host-gut microbiota metabolic interactions. *Science.* 2012;336(6086):1262-7.
89. Rieder R, Wisniewski PJ, Alderman BL, Campbell SC. Microbes and mental health: A review. *Brain Behav Immun.* 2017;66:9-17.