BÖLÜM 60

NÖROKÜTANÖZ HASTALIKLARIN DERMATOLOJİK BULGULARI VE YÖNETİMİ

Erdal PALA[1]

GİRİŞ

Nörokütanöz hastalıklar fakomatosis veya genodermatozlar olarak ta bilinen kutanea, nörolojik ve onkolojik bulgularla karakterize konjenital heterojen bir hastalık grubudur. Nörokütanöz hastalıkların prevalansı 1/700–1/1250 olarak tahmin edilir. Fakomatozlarda, "phakos" doğum işareti veya lekesi anlamındadır. 1920 yılında Alman göz doktoru van der Hoeve, "phakoma" kelimesini iki farklı benign göz lezyonu için kullanmıştır. Santral sinir sistemi (SSS) ve periferik sinirler sık tutulan yerlerdir. Göz, deri ve bağ dokuları tutulumu da olmaktadır. Fakomatozların klinikleri değişkenlik göstermekte olup en sık beyin ve cilt tutulumları görülmektedir. Epileptik nöbetler bazı nörokütanöz hastalıklarda klinik tablonun temel bulgusu olabilir. Tüm bu patolojiler çoğunlukla proto-onkogenler ve tümör süpresör genlerdeki defektler sonucunda oluşur.

NÖROFİBROMATOZİS (NF)

Nörofibromatozis Tip 1 (NF 1) (Von Recklınghausen Hastalığı):

Nörofibromatosiz (NF) çok sayıda konjenital anomali, tümör ve hamartomun bir arada olduğu, çoğunlukla otozomal dominant olarak geçiş gösteren hastalıktır. Vakaların %50'de aile öyküsü yoktur ve bunların somatik mutasyonlar sonucu oluştuğu düşünülmektedir.

Tablo 1 'de Riccardi[1] NF için klinik deri bulgularına göre bir sınıflandırma önermiştir.

Tablo 1: Nörofibromatosiz alt grupları[1]

NÖROFİBROMATOSİZ ALT TİPLERİ	
Katagori	**Tanımlama**
NF1	Von Recklinghausen
NF2	Akustik Schwannom
NF3	Mikst
NF4	Değişken
NF5	Segmental kahve lekeleri veya nörofibromlar veya her ikisi; bir veya birden çok dermatomda
NF6	Sadece kahve lekeleri
NF7	Geç başlangıç
NF-NOS	Diğer tiplere uymayan tanımlanamamış

Hastalığın prevalansı 1/3000 olgu olarak bildirilmiştir. NF-1'e, 17. Kromozomdaki (17q11.2 NF1 geni) mutasyon sonucunda oluşan defektif nörofibromin proteini neden olur.

[1] Dr. Öğr. Üyesi, Atatürk Üniversitesi Tıp Fakültesi Deri ve Zührevi Hastalıkları AD., erdalpala2525@gmail.com

de ortaya çıkarlar fakat tanısal değeri oldukça yüksektir. Saçlı deriye yerleşen lezyonlar skatrisyel alopesiye yol açabilir. Ses boğukluğu, göz kapağı papülleri, yaygın skatrisler ve intrakranial kalsifikasyonlar tanıya gitme açısından oldukça önemlidir. Lezyonların etkin bir tedavisi bulunmamaktadır. Atrofik skatrisler için dermabrazyon, kimyasal peeling ve CO2lazer tedavileri uygulanabilir. Hastalık yaşam süresini genellikle etkilemez, fakat infantil dönemde solunum yetmezliği, erişkin dönemde larinks obstrüksiyonu ve nörolojik komplikasyonlar yaşamsal risk oluşturabilir.

KAYNAKLAR

1. Riccardi VM. Mast-cell stabilization to decrease neurofibroma growth. Preliminary experience with ketotifen. Arch Dermatol. 1987;123:1011–6.
2. Pivnick EK, Riccardi VM. The Neurofibromatosis. In: Freedberg IM, Eisen AZ, Wolff K, et al. Fitzpatrick's Dermatology in General Medicine. 6 th edn. New York. McGraw-Hill, 2003: 1825–33.
3. Storm FK, Eilber FR, Mirra J, Morton DL. Neurofibrosarcoma. Cancer. 1980; 45:126–9
4. Zvulunov A, Barak Y, Metzker A. Juvenile xanthogranuloma, neurofibromatosis, and juvenile chronic myelogenous leukemia. World statistical analysis. Arch Dermatol. 1995;131(8): 904-8.
5. Kajimoto A, Oiso N, Fukai K, Ishii M. Bilateral segmental neurofibromatosis with gastric carcinoma. Clin Exp Dermatol. 2007;32(1):43-4.
6. Kaymak Y, Başsoy BÖ. Becker Nevüs ve Hamartomun Eşlik Ettiği Bir Nörofibromatoz Tip 1 Olgusu. Turkiye Klinikleri J Dermatol. 2015;25(3):108–12.
7. Neurofibromatosis-conference statement. National Institutes of Health consensus Development Conference. Arch Neurol. 1988;45: 575–8
8. DeBella K, Szudek J, Friedman JM. Use of the national institutes of health criteria for diagnosis of neurofibromatosis 1 in children. Pediatrics. 2000; 105: 608-14.
9. Gutmann DH, Aylsworth A, Carey JC, et al. The Diagnostic evaluation and multidisciplanry management of neurofibromatosis 1 and neurofibromatosis 2. JAMA. 1997;278:51-7
10. Méni C, et al. Treatment of neurofibromas with a carbon dioxide laser: a retrospective cross-sectional study of 106 patients. Dermatology. 2015;230(3):263–268.
11. Kriechbaumer LK, Susani M, Kircher SG, Distelmaier K, Happak W. Comparative study of CO2 and Er: YAG laser ablation of multiple cutaneous neurofibromas in von Recklinghausen's disease. Lasers in Medical Science. 2014;29: 1083–1091
12. Verma SK, et al. Considerations for development of therapies for cutaneous neurofibroma. Neurology. 2018;91(2 suppl 1):S21–S30
13. Allaway RJ, Gosline SJC, La Rosa S, et al. . Cutaneous neurofibromas in the genomics era: current understanding and open questions. Br J Cancer 2018; 118: 1539-48.
14. Riccardi VM. Ketotifen suppression of NF1 neurofibroma growth over 30 years. Am J Med Genet A. 2015;167:1570-7.
15. Chamseddin BH, et al. Management of cutaneous neurofibroma: current therapy and future directions. Neurooncol Adv. 2019 Dec 16;2 (Suppl 1):i107-i116.
16. Jimbow K. Tuberous sclerosis and guttate leukodermas. Semin Cutan Med Surg. 1997;16:30-5
17. Hurwitz S, Braverman IM. White spots in tuberous-sclerosis. J Pediatr. 1970;77:587-94
18. Schaffer JV, Gohara MA, McNiff JM, Aasi SZ, Dvoretzky I. Multiple facial angiofibromas: a cutaneous manifestation of Birt-Hogg-Dubé syndrome J Am Acad Dermatol. 2005; 53: pp. S108
19. Curatolo P, Bombardieri R, Jozwiak S. Tuberous sclerosis. Lancet. 2008;372(9639):657-68.
20. Webb DW, Clarke A, Fryer A, Osborne JP. The cutaneous features of tuberous sclerosis: a population study. Br J Dermatol. 1996;135: 1-5
21. Northrup H, Krueger DA, International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 international tuberous sclerosis complex consensus conference. Pediatr Neurol. 2013; 49: 243-54.
22. Wood BJ, Ramkaransingh JR, Fojo T, et al. Percutaneous tumor ablation with radiofrequency. Cancer. 2002;94:443-51.
23. Gomes AA, Gomes YV, Lima FB, Pessoa SG. Multiple facial angiofibromas treated with high-frequency equipment. An Bras Dermatol. 2011; 86: pp. S186-S189
24. Schepis C, Siragusa M. Cryosurgery: an easy and cheap therapy for facial angiofibromas in tuberous sclerosis. Eur J Dermatol. 2010; 20: pp. 506-507
25. Capurro S, Fiallo P. Timed surgery for treatment of angiofibromas in tuberous sclerosis Dermatol Surg. 2001; 27: pp. 486-488
26. Hori K, Soejima K, Nozaki M, Sakurai H, Takeuchi M, Yamaki T, et al. Treatment of facial angiofibroma of tuberous sclerosis using cultured epithelial autografts. Ann Plast Surg. 2006; 57: pp. 415-417
27. Janniger CK, Goldberg DJ. Angiofibromas in tuberous sclerosis: comparison of treatment by carbon dioxide and argon laser. J Dermatol Surg Oncol. 1990;16: pp. 317-320
28. Belmar P, Boixeda P, Baniandres O, Fernandez-Lorente M, Arra-zola JM. Long-term follow up of angiofibromas treated with CO2laser in 23 patients with tuberous sclerosis. Actas Dermosifiliogr.2005;96:498-503

29. Weinberger CH, Endrizzi B, Hook KP, Lee PK. Treatment of angiofibromas of tuberous sclerosis with 5-aminolevulinic acid blue light photodynamic therapy followed by immediate pulsed dye laser. Dermatol Surg. 2009;35:1849-51
30. Wang L, Gao L, Abe T, Mizoguchi M. Effects of tranilast on angiofibromas of tuberous sclerosis. Pediatr Int. 1999;41:701-3
31. Turkmen M, Ertam I, Unal I, Dereli T. Facial angiofibromas of tuberous sclerosis: successful treatment with podophyllin. J EurAcad Dermatol Venereol. 2009;23:713-4
32. Dabora SL, Franz DN, Ashwal S, et al. Multicenter phase 2 trial of sirolimus for tuberoussclerosis: kidney angiomyolipomas and other tumors regress and VEGF- D levels decrease. PLoS One. 2011; 6: e23379
33. Haemel AK, O'Brian AL, Teng JM. Topical rapamycin: a novel approach to facial angiofibromas in tuberous sclerosis. Arch Dermatol. 2010;146:715-8
34. Wataya-Kaneda M, Tanaka M, Nakamura A, Matsumoto S, Katayama I. A topical combination of rapamycin and tacrolimus for the treatment of angiofibroma due to tuberous sclerosis complex (TSC): a pilot study of nine Japanese patients with TSC of different disease severity. Br J Dermatol. 2011;165:912–6
35. Wataya-Kaneda M, Tanaka M, Nakamura A, Matsumoto S,Katayama I. A novel application of topical rapamycin formulation, an inhibitor of mTOR, for patients with hypomelanotic macules in tuberous sclerosis complex. Arch Dermatol.2012;148:138-9.
36. Ho VCY, McLean DI. Benign epithelial tumors. In: Fitz patrick JB, Eisen AZ, Wolff K, Freedberg I, Austen KF, eds. 4th ed. New York: McGraw Hill; Q Rev Med. 1993. p.855-72.
37. Alonso-CL, Boixeda P, Reig I, de Daniel RC, Fleta-Asín B, P. Olasolo J. Carbon Dioxide Laser Treatment of Epidermal Nevi: Response and Long-Term Follow-Up. Actas Dermosifiliogr. 2012; 103 (10): 910-918
38. Park JH, Hwang ES, Kim SN, Kye YC. Er: YAG Laser Treatment of Verrucous Epidermal Nevi. J Dermatol Surg. 2004; 30(3): 378-381
39. MAR Osman, AN Kassab. Carbon dioxide laser versus erbium: YAG laser in treatment of epidermal verrucous nevus: a comparative randomized clinical study. J Dermatolog Treat. 2017; 28 (5): 452-457
40. Alkhalifah A, Fransen F, Le Duff F, Lacour JP, Wolkerstorfer A, Passeron T. Laser treatment of epidermal nevi: A multicenter retrospective study with long-term follow-up. J Am Acad Dermatol. 2020; 83(6): 1606-1615
41. Attia A, Elbasiouny MS. Treatment of Verrucous Epidermal Nevus Using Long Pulsed Nd: YAG Laser. Egyptian Dermatology Online Journal. 2010 6 (1): 2
42. Baba T, Narumi H, Hanada K, Hashimoto I. Successful Treatment of Dark-colored Epidermal Nevus with Ruby Laser. J Clin Dermatol. 1995; 22(8): 567-570
43. Kim JJ, Chang MW, Shwayder T. Topical tretinoin and 5-fluorouracil in the treatment of linear verrucous epidermal nevus. J Am Acad Dermatol 2000;43:129-32.
44. Sandoval KR, Machado MCR, Oliveira ZNP, Nico MMS. CHILD syndrome: successful treatment of skin lesions with topical lovastatin and cholesterol lotion. An Bras Dermatol. 2019 Jul 26;94(3): 341-343.
45. Pascual-Castroviejo I, Pascual-Pascual SI, Velázquez-fragua R, Lapunzina P. Oculocerebrocutaneous (Delleman) syndrome: report of two cases. Neuropediatrics. 2005; 36: 50–4.
46. Nguyen D, Turner JT, Olsen C, et al. Cutaneous manifestations of Proteus syndrome: correlations with general clinical severity. Arch Dermatol 2004; 140: 947–53.
47. Busch RM, Chapin JS, Mester J, et al. Cognitive characteristics of PTEN hamartoma tumor syndromes. Genet Med. 2003 15:548–53.
48. Reddy KVK, Anusha A, Maloth KN, Sunitha K, Thakur M. Mucocutaneous manifestations of Cowden's syndrome. Indian Dermatol Online J. 2016; 7(6): 512–515.
49. Cnudde F, Boulard F, Muller P, Chevallier J, Teron-Abou B. Cowden disease: treatment with acitretine. Ann Dermatol Venereol. 1996, 123(11):739-741
50. Tallman B, Tan OT, Morelli JG, et al. Location of port-wine stains and the likelihood of ophthalmic and/or central nervous system complications. Pediatrics 1991; 87: 323–7.
51. Brightman LA, Geronemus RG, Reddy KK. Laser treatment of port-wine stains. Clin Cosmet Investig Dermatol. 2015; 8: 27–33.
52. Pascual-Castroviejo I, Viaño J, Moreno F, et al. Hemangiomas of the head, neck and chest with associated vascular and brain anomalies: a complex neurocutaneous syndrome. AJNR Am J Neuroradiol. 1996; 17: 461–71.
53. Joerger M, Koberle D, Neumann HP, Gillosen S Von Hippel–Lindau disease—a rare disease important to recognize. Onkologie. 2005; 28: 159–63.
54. Abdalla SA, Letarte M Hemorrhagic telangiectasia: current views on genetics and mechanisms of disease. J Med Genet 2006; 43: 97–110.
55. Legierse CM, Canninga-Van Dijk MR, Bruijnzeel-Koomen CA, Kuck-Koot VC Sneddon syndrome and the diagnostic value of skin biopsiesthree young patients with intracerebral lesions and livedo racemosa. Eur J Dermatol 2008; 18: 322–8.
56. Eiris-Puñal J, Picon-Cotos M, Viso-Lorenzo A, Castro-Gago M. Epileptic disorder as the first neurologic manifestation of blue rubber bleb nevus syndrome. J Child Neurol. 2002; 17: 219–22.
57. Alomari AI, Orbach DB, Mulliken JB, Bisdorff A, Fishman SJ, Norbash A, et al. Klip pel-Trenaunay syndrome and spinal arteriovenous malformation: an erroneous associati on. Am J Neuro radiol. 2010; 31(9): 1608-12.

58. Maramattom BV, Cohen-Gadol AA, Wijdicks EF, Kalmas D. Segmental cutaneous hemangioma and spinal arteriovenous malformation (Cobb syndrome). Case record and historical perspective. J Neurosurg Spine. 2005; 3: 249–52.
59. Pilarski R, Stephens JA, Noss R, et al. Predicting PTEN mutations: an evaluation of Cowden syndrome and Bannayan–Riley–Ruvalcaba syndrome clinical features. J Med Genet. 2011; 48: 505–12.
60. Garavelli L, Leask K, Zanacca C, et al. MRI and neurological findings in macrocephaly–cutis marmorata telangiectatica congenita syndrome: report of 10 cases and review of the literature. Genet Couns. 2005; 16: 117–28.
61. Chung EO, Bodensteiner JB, Noorani PA, Schochet SS. Cerebral white-matter changes suggesting leukodystrophy in ataxia telangiectasia. J Child Neurol. 1994; 9: 31–5.
62. Privette ED, Ram G, Treat JR, Yan AC, Heimall JR. Healing of Granulomatous Skin Changes in Ataxia-Telangiectasia After Treatment with Intravenous Immunoglobulin and Topical Mometasone 0.1% Ointment. Pediatr Dermatol. 2014; 31(6): 703-707
63. Hare McCoppin HH, Goldberg DJ. Laser treatment of facial telangiectases: An update. Dermatol Surg. 2010;36(8):1221-30.
64. Alikhan A, Lee AD, Swing D, et al. Vaccination as a probable cause of incontinentia pigmenti reactivation. Pediatr Dermatol. 2010; 27: 62–4.
65. Ardelean D, Pope E. Incontinentia pigmenti in boys: a series and review of the literature. Pediatr Dermatol. 2006; 23: 523-7.
66. Jessup CJ, Morgan SC, Cohen LM, Viders DE. Incontinentia pigmenti: treatment of IP with topical tacrolimus. J Drugs Dermatol. 2009, 8(10):944-946
67. Nagase T, Takanashi M, Takada H, Ohmori K. Extensive vesiculobullous eruption following limited ruby laser treatment for incontinentia pigmenti: A case report. Australas J Dermatol. 1997; 38(3): 155-157
68. Kaya TI, Tursen U, İkizoğlu G. Therapeutic use of topical corticosteroids in the vesiculobullous lesions of incontinentia pigmenti. Clin Exp Dermatol. 2009; 34(8): e611-e613
69. Hashimoto K, Yoshikawa K. A case of incontinentia pigmenti treated with short-term systemic corticosteroid. Skin research. 1992; 34(2): 206-211
70. Donati P, Muscardin L, Amantea A, Paolini F. Venuti a detection of HPV-15 in painful subungual tumors of incontinentia pigmenti: successful topical therapy with retinoic acid. Eur J Dermatol. 2009; 19: 243–247.
71. Barros B, Helm K, Zaenglein A, Seiverling E. Keratoacanthoma-Like Growths of Incontinentia Pigmenti Successfully Treated with Intralesional Methotrexate. Pediatr Dermatol. 2017; 34(4): e203-e204
72. Bodemer C, Diociaiuti A, Rabia SH, Robert MP, Desguerre I, Manière MC, et.al. Multidisciplinary consensus recommendations from a European network for the diagnosis and practical management of patients with incontinentia pigmenti. J Eur Acad Dermatol Venereol. 2020; 34(7): 1415-1424
73. Ito M. Studies on melanin XI. Incontinentia pigmenti achromians. A singular case of nevus depigmentosus systematicus bilateralis. Tohoku J Exp Med 1952; 55: 57-59.
74. Amal C, Litaiem N. " hypomelanosis of Ito." StatPearls [İnternet] (2020).
75. Sharma, P, Nicoli, E. R, Serra-Vinardell, J, Morimoto, M, Toro, C, Malicdan, MCV, & Introne, W. J. Chediak-Higashi syndrome: a review of the past, present, and future. Drug Discovery Today: Disease Models. Elsevier. 2020; 31: 31-36
76. Sarkozy A, Conti E, Digillio MC, et al. Clinical and molecular analysis of 30 patients with multiple lentigines LEOPARD syndrome. J Med Genet. 2004;41:68.
77. Ganemo A, Jagell S, Vahlquist A. Sjogren-larsson syndrome: a study of clinical symptoms and dermatological treatment in 34 Swedish patients. Acta Derm Venereol. 2009; 89:68–73.
78. Lambert WC, Gagna EC, and Lambert MW. "Trichothiodystrophy: Photosensitive, TTD-P, TTD, Tay Syndrome." Diseases of DNA Repair. Springer. 2010: 106-110.
79. Kiwilsza M, Tutak KS. Gorlin-Goltz syndrome – a medical condition requiring a multidisciplinary approach. Med Sci Monit. 2012; 18(9): 145–153.
80. Osiecka BJ, Nockowski P, Szepietowski JC. The use of the photodynamic method in the treatment of recurrent basal cell carcinoma on the example of Gorlin-Goltz syndrome-management algorithm. Dermatol Ther. 2020; 33 (6): e14499
81. Aydın H, Yologlu Z, Sargın H, Metin MR. Parry-Romberg syndrome Physical, clinical, and imaging features. Neurosciences . 2015; 20(4): 368–371.