

## Bölüm 15

### Paraneoplastik Hipoglisemi

Merve DİRİKOÇ<sup>1</sup>

#### GİRİŞ

Açlık plazma glukozunun normal değerinin alt sınırı  $70\text{mg/dl}$ 'dır ( $3,9\text{mmol/L}$ ) (1). Daha düşük değerler hipoglisemi olarak adlandırılır. Hipogliseminin tanısı düşük plazma glukozu, hipoglisemi işaret ve semptomları, hipoglisemi düzeltilince semptomların geri çekilmesinden oluşan Whipple Triadı ile deteklenir. Hipoglisemiye yol açan bir tedavi olmaksızın spontan ve tekrarlayıcı hipogliseminin medikal olarak çözümü zorlayıcı olup birçok sebepten kaynaklanmaktadır: postprandiyal hipoglisemi, insülinoma, otoimmün hipoglisemi, adrenal yetmezlik veya kritik hastalık (2). Nadiren pankreastan kaynaklanmayan bazı tümörler paraneoplastik hipoglisemiye sebep olur ve bu durum adacak hücresinden kaynaklanmayan tümör hipoglisemisi (NICTH) olarak adlandırılır (3,4).

#### NICTH

NICTH birçok malign ve benign tümörün seyrinde görülebilen nadir bir paraneoplastik sendromdur (5). Literatürde mezotelyoma, hemangioperistom, adrenokortikal karsinom, pankreatik kanser, medüller tiroid kanseri, lenfoma/lösemi, fibrosarkom, karsinoid sendrom, gastrointestinal stromal tümör, renal hücreli kanser, prostat kanseri, meme kanseri, mesane kanseri ve soliter fibröz tümörlerin seyrinde görüldüğü vakalar raporlanmıştır (2,3,6). NICTH ilişkili tümörler Tablo 1'de gösterilmiştir (7). NICTH ilk olarak 1929'da Nadler ve arkadaşları tarafından metastatik hepatoselüler karsinomlu bir hastada tespit edilmiştir (h). Toraks yerleşimli soliter fibröz tümörlerde tespit edilen

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## KAYNAKLAR

1. Gardner DG, Shoback D. *Greenspan's basic & clinical endocrinology*. 9th ed. NY:McGraw-Hill;201:657.
2. Kandaswamy L, Raghavan R, Pappachan J: Spontaneous hypoglycemia: diagnostic evaluation and management. *Endocrine*. 2016, 53:47-57.
3. Garla V, Sonani H, Palabindala V, et al. Non-islet cell hypoglycemia: case series and review of the literature. *Front Endocrinology*. 2019, 10:316.
4. Hirai H, Ogata E, Ohki S, et al. Hypoglycemia associated with a gastrointestinal stromal tumor producing high molecular-weight insulin growth factor II: a case report and literature review. *Internal Medicine* 2016, 55:1309-1314.
5. De Groot JW, Rikhof B, Van Doorn J, et al. Non-islet cell tumour- induced hypoglycemia: a review of the literature including two new cases. *Endocrin Relat Cancer*. 2007;14:979–993.
6. Khowaja A, Johnson-Rabbett B, Bantle J, et al. Hypoglycemia mediated by paraneoplastic production of insulin like growth factor-2 from a malignant renal solitary fibrous tumor - clinical case and literature review. *BMC Endocrin Disorders*. 2014, 14:49.
7. Mohammed T, Ozcan G, Siddique, AS et al. Doege-Potter Syndrome with a benign solitary fibrous tumor: a case report and literature review. *Case Reports in Oncology*. 2021;14:470-476.
8. Nadler WH, Wolfer JA. Hepatogenic hypoglycemia associated with primary liver cell carcinoma. *Archives of Internal Medicine*. 1929;44(5):700-710.
9. Baldwin RS. Hypoglycemia with neoplasia (Doege-Potter Syn- drome). *Wisconsin Medical Journal*. 1965;64:185–189.
10. Wada Y, Okano K, Ando Y, et al. A solitary fibrous tumor in the pelvic cavity of a patient with Doege-Potter syndrome: a case report. *Surgery Case Reports*. 2019, 5:60.
11. Phillips LS, Robertson DG. Insulin-like growth factors and non-islet cell tumor hypoglycemia. *Metabolism*. 1993;42:1093–1101.
12. Rikhof B, Van Doorn J, Suurmeijer AJ, et al. Insulin-like growth factors and insulin-like growth factor-binding proteins in relation to disease status and incidence of hypoglycaemia in patients with a gastrointestinal stromal tumour. *Annals of Oncology*. 2009;20(9):1582–8.
13. Eghbali F, Karami R. Refractory hypoglycemia induced by a duodenal wall gastrointestinal stromal tumor: a case report. *Caspian Jounal of Internal Medicine*. 2021;12(supp 2):S447-450.
14. Marks V, Teale JD. Tumours producing hypoglycaemia. *Diabetes/Metabolism Research and Reviews*. 1991;7(2):79-91.
15. Bodnar TW, Acevedo MJ, Pietropolo M. Management of non-islet-cell tumor hypoglycemia: a clinical review. *Journal of Clinical Endocrinology and Metabolism*. 2013;99:713–722.
16. Dutta P, Aggarwal A, Gogate Y, et al. Non-islet cell tumor-induced hypoglycemia: a report of five cases and brief review of the literature. *Endocrinology, Diabetes and Metabolism Case Reports*. 2013;130046.
17. Khowaja A, Johnson-Rabbett B, Bantle J, et al. Hypoglycemia mediated by paraneoplastic production of Insulin like growth factor-2 from malignant renal solitary fibrous tumor – clinical case and literature review. *BMC Endocrine Disorders*. 2014;14:49.
18. Ullrich A, Gray A, Tam AW, et al. Insulin-like growth factor I receptor primary structure: comparison with insulin receptor suggests structural determinants that define functional specificity. *EMBO Journal*. 1986;5: 2503–12.
19. Puche JE, Castilla-Cortazar I. Human conditions of insulin-like growth factor-I (IGF-I) deficiency. *Journal of Translational Medicine*. 2012;10:224.
20. Thomas J, Kumar SC. Nonislet Cell Tumor Hypoglycemia. *Case Reports in Endocrinology*.

- 2013; 308086.
21. Dynkewich Y, Rother KI, Whitford I, et al. Tumors, IGF-2 and hypoglycemia: insights from the clinic, the laboratory and the historical archive. *Endocrine Reviews*. 2013;34:798–826.
  22. Tani Y, Tateno T, Izumiya H, et al. Defective expression of prohormone convertase 4 and enhanced expression of insulin-like growth factor II by pleural solitary fibrous tumor causing hypoglycemia. *Endocrine Journal*. 2008;55:905–11.
  23. Alkemade GM, Bakker M, Rikhof B, et al. Hypoglycemia in a Patient With a Big “Big”-IGF-II- Producing Tumor. *Journal of Clinical Endocrinology and Metabolism*. 2013; 98:3113–3114.
  24. Daughaday WH, Emanuele MA, Brooks MH, et al. Synthesis and secretion of insulin-like growth factor II by a leiomyosarcoma with associated hypoglycemia. *New England Journal of Medicine*. 1988;319:1434 –1440.
  25. Baxter RC. The role of insulin-like growth factors and their binding proteins in tumor hypoglycemia. *Hormone Research*. 1996;46:195–201.
  26. LeRoith D, Roberts CT Jr. The insulin-like growth factor system and cancer. *Cancer Letters*. 2003;195:127–137.
  27. Cryer PE, Axelrod L, Grossman AB, et al. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology and Metabolism*. 2009;94:709 –728.
  28. Livingstone C. Insulin-like growth factor-II and cancer. *Endocrine-Related Cancer*. 2013;20:321–339.
  29. Fukuda I, Hizuka N, Ishikawa Y, et al. Clinical features of insulin- like growth factor-II producing non-islet-cell tumor hypoglycemia. *Growth Hormone&IGF Research*. 2006;16:211–216.
  30. Teale JD, Marks V. Glucocorticoid therapy suppresses abnormal secretion of big IGF-II by non-islet cell tumours inducing hypoglycaemia (NICTH). *Clinical Endocrinology (Oxford)*. 1998;49:491– 498.
  31. Miraki-Moud F, Grossman AB, Besser M, et al. A rapid method for analyzing serum pro-insulin-like growth factor-II in patients with non-islet cell tumor hypoglycemia. *Journal of Clinical Endocrinology and Metabolism*. 2005;90:3819–3823.
  32. Bourcigaux N, Arnault-Ouary G, Christol R, et al. Treatment of hypoglycemia using combined glucocorticoid and recombinant human growth hormone in a patient with a metastatic non-islet cell tumor hypoglycemia. *Clinical Therapeutics*. 2005;27(2):246–51.
  33. Ishida S, Noda M, Kuzuya N, et al. Big insulin-like growth factor II-producing hepatocellular carcinoma associated with hypoglycemia. *Internal Medicine*. 1995;34:1201–1206.
  34. Tominaga N, Kawarasaki C, Kanemoto K, et al. Recurrent solitary fibrous tumor of the pleura with malignant transformation and non- islet cell tumor-induced hypoglycemia due to paraneoplastic over-expression and secretion of high-molecular-weight insulin-like growth Factor II. *Internal Medicine*. 2012;51:3267–3272.
  35. Kirkland LL, Kashiwagi DT, Brantley S, et al. Nutrition in the hospitalized patient. *Journal of Hospital Medicine*. 2013;8:52–58.
  36. Wagner S, Greco F, Hamza A, et al. Retroperitoneal malignant solitary fibrous tumor of the small pelvis causing recurrent hypoglycemia by secretion of insulin-like growth factor 2. *European Urology*. 2009;55:739–42.
  37. Mohammed K, Abi Khalil C, Olivier S, et al. Paraneoplastic hypoglycemia in a patient with a malignant solitary fibrous tumor. *Endocrinology, Diabetes&Metabolism Case Reports*. 2014;2014:140026.
  38. Jang JG, Chung JH, Hong KS, et al. A case of solitary fibrous pleura tumor associated with severe hypoglycemia: Doege–Potter syndrome. *Tuberculosis and Respiratory Disease (Seoul)*. 2015;78:120–4.