

## Bölüm 8

# GASTROİNTESTİNAL STROMAL TÜMÖRLERDE ENDOSKOPIK TANI VE TEDAVİ YÖNTEMLERİ

Arif ATAY<sup>8</sup>

### GİRİŞ

Girişimsel endoskopi son dekatta cerrahideki doğal açıklıklardan translüminal endoskopik cerrahi (NOTES) alanının ortaya çıkmasıyla birlikte hızlı gelişme göstermiştir. Girişimsel gastrointestinal endoskopi uygulamaları bu doğrultuda genişlemekte ve gastrointestinal sistemin lümeninin önüne geçmektedir.

Gastrointestinal traktın subepitelyal lezyonları (SEL'ler), muscularis mukoza, submukoza veya muscularis propria kaynaklı tümörlerdir. Çoğu zaman rutin endoskopi ve kolonoskopi sırasında tesadüfen bulunurlar. Genellikle normal mukozaya sahip kitleler olarak tanımlanırlar. Çoğunlukla küçük (2cm çapından daha küçük) ve asemptomatiktirler; ancak, SEL'ler, tümörün büyüklüğüne, konumuna ve histopatolojisine bağlı olarak semptom verebilirler(1).

Üst gastrointestinal kanalda tespit edilen SEL'lerin çoğunluğu gastrointestinal stromal tümörlerdir. Daha az sıklıkta leiomyom, nöroendokrin tümörler, granüler hücre tümörleri gibi diğer patolojiler gözükmektedir. Rektumda tespit edilen SEL'lerin çoğunluğu SEL'i taklit eden epitelyal tümörler (adenokarsinom, skar) veya NET'tir (2). Kolon kaynaklı olanlar nadir gözükürler ve epidemiyolojileri hakkında kısıtlı bilgi mevcuttur.

### GASTROİNTESTİNAL STROMAL TÜMÖRLER

Gastrointestinal stromal tümörler(GIST), gastrointestinal sistemden kaynaklanan en yaygın mezenkimal tümörlerdir. Bu tümörler, gastrointestinal sistemin myenterik pleksusunda bulunan ve gastrointestinal sistem motilitesini ayarlayan Cajal'ın interstisyel hücrelerinden kaynaklanırlar(2,3). Genellikle 5-7 dekatta görülür. K/E

<sup>8</sup> Uzman Doktor., İKÇÜ Atatürk Eğitim Araştırma Hastanesi, atayarif@hotmail.com

## **ENDOSKOPIK REZEKSİYON SONRASI TAKİP**

Gastrointestinal stromal tümörler, endoskopik olarak rezeke edildikten sonra, yara iyileşmesine gözlemek, herhangi bir rezidüel tümör varlığını kontrol etmek için tedaviden 3-12 ay sonra kontrol endoskopi yapılması önerilir.

Orta ve yüksek riskli hastaların 3-4 ayda bir abdominal BT veya EUS ile , düşük riskli hastaların ise ilk 5 yıl için, 6 ayda bir BT veya EUS ile kontrolü önerilmektedir(58,59).

### **Sonuç**

Gastrointestinal stromal tümörler için, endoskopik mukozal rezeksiyon, endoskopik submukozal rezeksiyon gibi yöntemler küçük tümörler için minimal invaziv, konforlu, düşük komplikasyonlu, işe dönüş süreleri kısa işlemler olması karşın, derin yerleşimli tümörler için yetersiz kalabilen yöntemlerdir.

Submukozal tünel endoskopik rezeksiyon, Endoskopik tam kat rezeksiyon gibi daha invaziv yöntemler ise R0 rezeksiyon için daha avantajlıdır. Ancak tümör ekilmesi, kanama, enfeksiyon gibi komplikasyonlar daha sık görülebilir. Ayrıca bu teknikler ileri endoskopik beceri gerektiren deneyimle merkezler tarafından uygulanabilen özellikli işlemlerdir. EFTR'nin literatür verileri çoğunlukla Asya kaynaklı ve retrospektiftir. Ancak çalışmalarda lezyonların bir bütün olarak çıkarılma oranları net değildir. Takip süreleri kısadır. Yine STER'de benzer şekilde takip süreleri kısa ve genellikle retrospektif vaka serileridir. Ayrıca Çoğu GİST'in düşük riski ve yavaş büyümesi göz önüne alındığında bu tekniklerin uzun vadeli başarısını kanıtlamak zor olacaktır. Eş zamanlı endoskopik ve laparoskopik işlemlerinde kendine göre avantajları ve dezavantajları mevcuttur.

Hastanın genel durumu, tümörün lokalizasyonu, boyutu, cerrahın deneyimi göz önünde tutularak multidisipliner bir yaklaşımla en doğru tedavi seçeneği tercih edilmelidir. Gastroenteroloji, medikal onkoloji, genel cerrahi, radyoloji ve moleküler biyoloji gibi birçok branş bu disiplinin bir parçasıdır(1).

## **KAYNAKLAR**

1. Humphris JL, Jones DB. Subepithelial mass lesions in the upper gastrointestinal tract. J. Gastroenterol Hepatol 2008;23:556-66.
2. Demetri GD, Von Mehren M, Antoescu CR, et al. NCCN Task Force report: Update on the management of patients with gastrointestinal stromal tumors. J Natl Compr Canc Netw 2010;8 Suppl 2:S1-41; quiz S2-4
3. Joensuu H, Hohenberger P, Corless CL. Gastrointestinal stromal tumour. Lancet 2013;382:973-83.
4. Harlan LC, Eisenstein J, Russell MC, Stevens JL, Cardona K. Gastrointestinal Stromal Tumors: Treatment patterns of a population based sample. J. Surg. Oncol. 2015;111:702-707.

5. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. *Ann Surg.* 2000;231(1):51-58.
6. Chak A, Canto MI, Rösch T, et al. Endosonographic differentiation of benign and malignant stromal cell tumors. *Gastrointest Endosc.* 1997; 45:468-73
7. Soreide K, Sandvik OM, Soreide JA, , Giljaca V, Jureckova A, Bulusu VR. Global epidemiology of gastrointestinal stromal tumours (GIST): A systematic review of population-based cohort studies. *Cancer Epidemiol.* 2016;40:39-46.
8. Nilsson B, Bümbling P, Meis-Kindblom JM, Odén A, Dortok A, Gustavsson B, Sablinska K, Kindblom LG. Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era--a population-based study in western Sweden. *Cancer.* 2005;103(4):821-9.
9. Ma GL, Murphy JD, Martinez ME, Sicklick JK. Epidemiology of gastrointestinal stromal tumors in the era of histology codes: results of a population-based study. *Cancer Epidemiol Biomarkers Prev.* 2015;24(1):298-302.
10. Cassier PA, Ducimetière F, Lurkin A, et al. A prospective epidemiological study of new incident GISTs during two consecutive years in Rhône-Alpes region: incidence and molecular distribution of GIST in a European region. *Br J Cancer.* 2010;103(2):165-170.
11. Kawanowa K, Sakuma Y, Sakurai S, Hishima T, Iwasaki Y, Saito K, Hosoya Y, Nakajima T, Funata N. High incidence of microscopic gastrointestinal stromal tumors in the stomach. *Hum Pathol.* 2006;37(12):1527-35
12. Agaimy A, Wünsch PH, Hofstaedter F, Blaszyk H, Rümmele P, Gaumann A, Dietmaier W, Hartmann A. Minute gastric sclerosing stromal tumors (GIST tumorlets) are common in adults and frequently show c-KIT mutations. *Am J Surg Pathol.* 2007;31(1):113-20.
13. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, Miettinen M, O'Leary TJ, Remotti H, Rubin BP, Shmookler B, Sobin LH, Weiss SW. Diagnosis of gastrointestinal stromal tumors: A consensus approach. *Hum Pathol.* 2002;33(5):459-65.
14. Sircar K, Hewlett BR, Huizinga JD, Chorneyko K, Berezin I, Riddell RH. Interstitial cells of Cajal as precursors of gastrointestinal stromal tumors. *Am J Surg Pathol.* 1999;23(4):377-89.
15. West RB, Corless CL, Chen X, Rubin BP, Subramanian S, Montgomery K, Zhu S, Ball CA, Nielsen TO, Patel R, Goldblum JR, Brown PO, Heinrich MC, van de Rijn M. The novel marker, DOG1, is expressed ubiquitously in gastrointestinal stromal tumors irrespective of KIT or PDGFRA mutation status. *Am J Pathol.* 2004;165(1):107-13.
16. Kang GH, Srivastava A, Kim YE, Park HJ, Park CK, Sohn TS, Kim S, Kang DY, Kim KM. DOG1 and PKC- $\theta$  are useful in the diagnosis of KIT-negative gastrointestinal stromal tumors. *Mod Pathol.* 2011;24(6):866-75.
17. Rubin BP. Gastrointestinal stromal tumours: an update. *Histopathology.* 2006;48(1):83-96.
18. Miettinen M, Makhlof H, Sobin LH, Lasota J. Gastrointestinal stromal tumors of the jejunum and ileum: a clinicopathologic, immunohistochemical, and molecular genetic study of 906 cases before imatinib with long-term follow-up. *Am J Surg Pathol.* 2006;30(4):477-89.
19. Miettinen M, Sobin LH, Lasota J. Gastrointestinal stromal tumors of the stomach: a clinicopathologic, immunohistochemical, and molecular genetic study of 1765 cases with long-term follow-up. *Am J Surg Pathol.* 2005;29(1):52-68.
20. Sepe PS, Brugge WR. A guide for the diagnosis and management of gastrointestinal stromal cell tumors. *Nat Rev Gastroenterol Hepatol.* 2009;6(6):363-71.
21. Hedenbro JL, Ekelund M, Wetterberg P. Endoscopic diagnosis of submucosal gastric lesions. The results after routine endoscopy. *Surg Endosc.* 1991;5(1):20-3.
22. Menon L, Buscaglia JM. Endoscopic approach to subepithelial lesions. *Therap Adv Gastroenterol.* 2014; 7(3): 123-130.

23. Hunt GC, Smith PP, Faigel DO. Yield of tissue sampling for submucosal lesions evaluated by EUS. *Gastrointest Endosc.* 2003;57(1):68-72.
24. Eriksson M, Reichardt P, et al. Needle biopsy through the abdominal wall for the diagnosis of gastrointestinal stromal tumour - Does it increase the risk for tumour cell seeding and recurrence? *Eur J Cancer.* 2016;59:128-133.
25. Miettinen M, Lasota J. Gastrointestinal stromal tumors. *Gastroenterol Clin North Am.* 2013;42(2):399-415.
26. Palazzo L, Landi B, Cellier C, Cuillerier E, Roseau G, Barbier JP. Endosonographic features predictive of benign and malignant gastrointestinal stromal cell tumours. *Gut.* 2000;46(1):88-92.
27. Rösch T, Kapfer B, et al. Accuracy of endoscopic ultrasonography in upper gastrointestinal submucosal lesions: a prospective multicenter study. *Scand J Gastroenterol.* 2002;37(7):856-62.
28. Brand B, Oesterhelweg L, Binmoeller KF, Sriram PV, Bohnacker S, Seewald S, De Weerth A, Soehendra N. Impact of endoscopic ultrasound for evaluation of submucosal lesions in gastrointestinal tract. *Dig Liver Dis.* 2002;34(4):290-7.
29. Kim GH, Park DY, Kim S, Kim DH, Kim DH, Choi CW, Heo J, Song GA. Is it possible to differentiate gastric GISTs from gastric leiomyomas by EUS? *World J Gastroenterol.* 2009;15(27):3376-81.
30. Shah P, Gao F, Edmundowicz SA, Azar RR, Early DS. Predicting malignant potential of gastrointestinal stromal tumors using endoscopic ultrasound. *Dig Dis Sci.* 2009;54(6):1265-9.
31. Jeon SW, Park YD, Chung YJ, Cho CM, Tak WY, Kweon YO, Kim SK, Choi YH. Gastrointestinal stromal tumors of the stomach: endosonographic differentiation in relation to histological risk. *J Gastroenterol Hepatol.* 2007;22(12):2069-75.
32. Kai F, Mohamad A, et al. Diagnosis of gastrointestinal stromal tumor by endoscopic ultrasound-guided fine needle aspiration biopsy - a potential pitfall. *Annals of Diagnostic Pathology* 2002;6(5):294-301
33. Akahoshi K, Sumida Y, Matsui N, Oya M, Akinaga R, Kubokawa M, Motomura Y, Honda K, Watanabe M, Nagaie T. Preoperative diagnosis of gastrointestinal stromal tumor by endoscopic ultrasound-guided fine needle aspiration. *World J Gastroenterol.* 2007 Apr 14;13(14):2077-82.
34. Na HK, Lee JH, et al. Yields and Utility of Endoscopic Ultrasonography-Guided 19-Gauge Trucut Biopsy versus 22-Gauge Fine Needle Aspiration for Diagnosing Gastric Subepithelial Tumors. *Clin Endosc.* 2015;48(2):152-7
35. Polkowski M, Gerke W, Jarosz D, et al. Diagnostic yield and safety of endoscopic ultrasound-guided trucut [corrected] biopsy in patients with gastric submucosal tumors: a prospective study. *Endoscopy.* 2009;41(4):329-34
36. ESMO/European Sarcoma Network Working Group. Gastrointestinal stromal tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2014 Sep;25 Suppl 3:iii21-6
37. Dumonceau JM, Deprez PH, et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline - Updated January 2017. *Endoscopy.* 2017;49(7):695-714.
38. Chen QL, Pan Y, Cai JQ, Wu D, Chen K, Mou YP. Laparoscopic versus open resection for gastric gastrointestinal stromal tumors: an updated systematic review and meta-analysis. *World J Surg Oncol.* 2014;12:206.
39. Honda M, Hiki N, Nunobe S, Ohashi M, Kiyokawa T, Sano T, Yamaguchi T. Long-term and surgical outcomes of laparoscopic surgery for gastric gastrointestinal stromal tumors. *Surg Endosc.* 2014;28(8):2317-22
40. Joo MK, Park JJ, Kim H, et al. Endoscopic versus surgical resection of GI tumors in the upper GI tract. *Gastrointest Endosc* 2016;83:318-26
41. Rajan E, Wong Kee Song LM. Endoscopic full thickness resection. *Gastroenterology.* 2018;154(7):1925-37.

42. Casali PG, Jost L, gastrointestinal stromal tumours:ESMO clinical recommendations for diagnosis, treatment and follow-up. *Annals of oncology* 2009;20:64-7
43. Mc Carter MD, Antonescu CR, Ballman KV, et al. Microscopically positive margins for primary gastrointestinal stromal tumors: analysis of risk factors and tumor recurrence. *J Am Coll Surg* 2012;215:53-9; discussion 59-60
44. Maranki J, stavropoulos SN. endoscopic full-thickness resection of subepithelial lesions of the GI tract. In: *Clinical gastrointestinal Endoscopy*. Third Edition. Elsevier. 510-6.e2.
45. Sun S, Ge N, Wang C, et al. Endoscopic band ligation of small gastric stromal tumors and follow-up by endoscopic ultrasonography. *Surg Endosc* 2007;21:574-8.
46. Nan G, Siyu S, Shiwei S, et al. Hemoclip-reinforced and EUS-assisted band ligation as an effective and safe technique to treat small GISTs in the gastric fundus. *Am J Gastroenterol* 2011;106:1560-1.
47. Kantsevov SV, Adler DG, et al. Endoscopic mucosal resection and endoscopic submucosal dissection. *Gastrointest endosc.*2008;68(1):11-8
48. Zhou P, Yao L, Qin XY. Endoscopic submucosal dissection for gastrointestinal stromal tumors: a report of 20 cases. *Zhonghua Wei Chang Wai Ke Za Zhi*. 2008;11:219-22
49. Suzuki H, İkedo K endoscopic mucosal resection and full thickness resection with complete defect closure for early gastrointestinal malignancies. *Endoscopy* 2001;33:437-9 .
50. Wang L, Ren W, et al. full-thickness endoscopic resection of non intracavitary gastric stromal tumors: a novel approach. *Surg Endosc* 2011;25:641-7
51. Schmidt A, Meier B, Caca K. Endoscopic full-thickness resection: Current status. *World J Gastroenterol*. 2015 Aug 21;21(31):9273-85.
52. Zhou PH, Yao LQ, Qin XY, et al. Endoscopic full-thickness resection without laparoscopic assistance for gastric submucosaltumors originated from the muscularis propria. *Surg Endosc.* 2011;25(9):2926-31.
53. Xu MD, Cai MY, Zhou PH, et al. Submucosal tunneling endoscopic resection: a new technique for treating upper GI submucosaltumors originating from the muscularis propria layer (with videos). *Gastrointest Endosc.* 2012;75(1):195-9.
54. Ye LP, Zhang Y, et al. Submucosal tunneling endoscopic resection for small upper gastrointestinal subepithelial tumors originating from the muscularis propria layer. *Surg Endosc.* 2014 Feb;28(2):524-30.
55. Tan Y, Tang X, et al. Comparison between submucosal tunneling endoscopic esection and endoscopic full-thickness resectiüon for gastric stromal tumors orginating from the muscularis propria layer. *Surg Endosc* 2017;31:3376-82.
56. Willingham F, Reynolds P, et al. Hybrid Push-Pull Endoscopic and Laparoscopic Full Thickness Resection for the Minimally Invasive Management of Gastrointestinal Stromal Tumors: A Pilot Clinical Study. *Gastroenterol Res Pract.* 2015; 2015: 618756.
57. Balde AI, Chen T, et al. Safety analysis of laparoscopic endoscopic cooperative surgery versus endoscopic submucosal dissection for selected gastric gastrointestinal stromal tumors: a propensity score-matched study. *Surg endsc* 2017;31:843-51.
58. Koo DH1, Ryu MH, et al. Asian Consensus Guidelines for the Diagnosis and Management of Gastrointestinal StromalTumor. *Cancer Res Treat.* 2016;48(4):1155-1166.
59. Blay JY, Bonvalot S, et al. Consensus meeting for the management of gastrointestinal stromal tumors. Report of the GIST Consensus Conference of 20-21 March 2004, under the auspices of ESMO. *Ann Oncol.* 2005;16(4):566-78.