

Retrospective single center evaluation of endosonographic features of ectopic pancreas cases

EKTOPIK PANKREAS OLGULARININ ENDOSONOĞRAFİK ÖZELLİKLERİNİN RETROSPEKTİF TEK MERKEZ DEĞERLENDİRİLMESİ

 Ali ŞENKAYA¹,  Ferit ÇELİK¹,  İlkçe AKGÜN KURTULMUŞ²,  Fatih TEKİN¹,  Nevin ORUÇ¹,  Ahmet AYDIN¹

¹Ege University Medical Faculty Department of Internal Medicine, Division of Gastroenterology, Izmir, Turkey

²Ege University Medical Faculty Department of Internal Medicine, Izmir, Turkey

ABSTRACT

Objective: Ectopic pancreas is defined as pancreatic tissue located outside the normal pancreas. The aim of the present study was to determine the sonographic characteristics of lesions considered as ectopic pancreas via endoscopic ultrasonography (EUS) examination.

Materials and Methods: This retrospective single-center study included 53 patients diagnosed with ectopic pancreas by EUS between March 2014 and March 2020.

Results: In the study, 32 (60.4%) patients were female and mean age was 44.7 ± 12.1 years. Thirty seven (69.8%) lesions were detected at the antrum greater curvature side, 10 (18.9%) at the antrum posterior wall, three (5.7%) at the corpus, two (3.8%) at the bulbus. EUS examination revealed that all lesions exhibited a heterogeneous pattern, 52 (98.1%) lesions had a hypochoic appearance, 45 (85%) lesion borders were regular, and 45 (85%) showed central umbilication. The lesions were most frequently located in the submucosa (90.6%). The mean long axis was 10.7 ± 3.5 mm, the mean short axis was 4.8 ± 1.0 mm, and long/short axis ratio was 2.4 ± 0.9 . No significant difference was observed between the dimensions and size ratios of lesions and the presence or absence of umbilication ($p = 0.550, 1.000$ and 0.583 , respectively).

Conclusion: In cases where the endoscopic ultrasonography examination revealed subepithelial lesions of submucosal origin that are <2 cm in size, exhibiting a heterogeneous pattern and hypochoic appearance, anechoic duct-like structures, and a long/short axis ratio of >1.5 along with central umbilication, the diagnosis of ectopic pancreas should be prioritized.

Keywords: Ectopic pancreas, endoscopic ultrasonography, subepithelial lesion
ÖZ

Amaç: Ektopik pankreas, normal pankreas dışında kalan pankreas dokusudur.

Ali ŞENKAYA

Ege Üniveristesi Tıp Fakültesi, İç Hastalıkları Ana Bilim Dalı, Gastroenteroloji Bilim Dalı, Izmir
E-posta: dr.senkaya@gmail.com

 <https://orcid.org/0000-0002-5787-3422>

Bu çalışmanın amacı, endoskopik ultrason incelemesi ile ektopik pankreas olduğu düşünülen lezyonların sonografik özelliklerinin belirlenmesidir.

Gereç ve Yöntem: Çalışmamız Mart 2014–Mart 2020 tarihleri arasında endoskopik ultrason incelemesi ile ektopik pankreas tanısı konulan 53 olgunun retrospektif tek merkezli değerlendirilmesini içermektedir.

Bulgular: Çalışmamızdaki olguların 32(%60,4)'si kadın ve yaş ortalaması $44,7 \pm 12,1$ yıl saptanmıştır. Lezyonların 37'si (%69,8) antrum büyük kurvaturda, 10'u (%18,9) antrum posterior, üçü (%5,7) korpus, ikisi (%3,8) bulbusta saptanmıştır. Endoskopik ultrason incelemesinde, lezyonların tamamının heterojen paternde, 52'sinin (%98,1) hipoekoik görünümde, 45'inin (%85) sınırlarının düzenli olduğu ve 45'inde (%85) santral umbilikasyon varlığı saptanmıştır. Lezyonların en sık (%90,6) submukoza yerleşimli olduğu görülmüştür. Lezyonların uzun aks ortalaması $10,7 \pm 3,5$ mm, kısa aks ortalaması $4,8 \pm 1$ mm ve uzun aks / kısa aks oranı $2,4 \pm 0,9$ olarak saptanmıştır. Umbilikasyon varlığı ile lezyonların boyutları ve boyut oranları arasında anlamlı farklılık saptanmamıştır (sırasıyla $p = 0,550$, $1,000$ ve $0,583$).

Sonuç: Endoskopik ultrason incelemede; 2cm'den küçük, submukoza orijinli, heterojen ve hipoekoik paternli, anekoik kanal benzeri yapıların olduğu, santral umbilikasyonun eşlik ettiği, uzun aks / kısa aks oranı 1,5'den büyük olan subepitelyal lezyonların saptanması durumunda ektopik pankreas teşhisi ön planda tutulmalıdır.

Anahtar Sözcükler: Ektopik pankreas, endoskopik ultrasonografi, subepitelyal lezyon

Ectopic pancreas (EP), also known as pancreatic rest or aberrant pancreas, is defined as pancreatic tissue located outside the normal pancreas and containing its own duct and vascular supply (1). EP is typically located in the upper gastrointestinal (GI) tract adjacent to the pancreas, and in 90% of the cases, it is located in the stomach, duodenum, or proximal part of the jejunum (2). The frequency of EP is reportedly 0.6% – 13% in autopsies, 0.5% in laparoscopy, and 1% in panendoscopy (3, 4). Although EP is typically asymptomatic, it can infrequently cause dyspeptic complaints, abdominal pain, upper or lower GI bleeding, or acute abdomen (5). Typically, EP is detected as a subepithelial lesion (SEL) of <2 cm in size, which is incidentally found in the stomach antrum during endoscopy (6). Central umbilication, which is generally considered the location of a drainage channel, is observed in lesions of >5 mm in size (7). Although it is difficult to diagnose EP via endoscopic examination, EP can be defined as a hard, round SEL with central umbilication and depression that allows its distinction from normal submucosal tissue (8, 9) (Figure 1). However, central umbilication is not the definitive diagnostic marker for EP,

and it can be difficult to distinguish EP from leiomyoma, which is the most common SEL of the stomach (10). The most common endoscopically detected location of EP in the stomach is the posterior wall and greater curvature including the antrum and prepyloric region (11).



Figure 1: Endoscopic view of the ectopic pancreas. Submucosal lesion with central umbilication in the antrum, proximal to the pylorus, covered with normal mucosa.

There are two theories regarding the development of EP. The misplacement theory suggests that during rotation of the foregut, several elements of the primitive pancreas become separated and eventually form mature pancreatic tissue along the length of the GI tract (12). The metaplasia theory states that EP arises from areas of pancreatic metaplasia of the endoderm that migrate to the submucosa during embryogenesis (13).

The pathological diagnosis of EP is typically unachievable for two reasons. First, obtaining adequate tissue samples using endoscopic biopsy forceps is generally difficult; second, surgery or endoscopic resection is usually unnecessary for most asymptomatic patients (14). Conversely, imaging techniques assist in making an early and definitive differential diagnosis. Correlations between the sonographic and histopathological patterns of EP have previously been established in the literature (15, 16). It combines endoscopic ultrasonography (EUS), GI endoscopy, and ultrasonography and ensures a clear and nonsurgical visualization of various SELs in the upper GI tract (17-21). EUS has been used in several studies to evaluate EP, and sonographic characteristics can distinguish EP from other SELs (15, 22-28). The aim of the present study was to determine the endosonographic characteristics of lesions considered as EP via EUS examination.

MATERIAL AND METHODS

The present study includes a retrospective single-center evaluation of patients diagnosed with EP by EUS at the Gastroenterology & Endoscopy Unit between March 2014 and March 2020. Patients whose EUS reports were obtained following a search for the terms “ectopic pancreas” and “aberrant pancreas” from the endoscopy unit registry system were included. Patients aged <18 years were excluded. Age, sex, EUS characteristics of EP (localization, size, echogenicity, homogeneity, origin, borders, and presence of umbilication) of the patients were recorded in the case report form.

EUS examination was performed in patients with or without umbilication in whom SEL was detected and were accordingly referred. EUS examination was performed by

the gastroenterology faculty members of the same center, who are experienced in EUS, using the GU-UE160 Olympus (Tokyo, Japan) device. The local ethics committee approval was obtained for the study (Approval number: 20-11T/11).

The compliance of the variables to normal distribution was examined using visual (histogram) and analytical (Kolmogorov–Smirnov test) methods. Numerical data collected in the study were expressed as mean, median, standard deviation, and maximum–minimum value. Categorical data were expressed as ratio and percentage. The comparison of sizes of EP based on the presence of umbilication was performed using Mann–Whitney U test. The correlation between age and dimensions of EP was evaluated using the Spearman correlation test. A p-value of <0.05 was considered statistically significant. All statistical analysis and calculations were performed using the SPSS Statistics Ver. 22.0.

RESULTS

In the present study, 32 (60.4%) patients were female and the mean age was 44.7 ± 12.1 years. The detected EP cases were present at endoscopically different locations: 37 (69.8%) lesions were at the antrum greater curvature side, 10 (18.9%) at the antrum posterior wall, three (5.7%) at the corpus, two (3.8%) at the bulbus, and one (1.9%) at the antrum anterior wall. All lesions exhibited a heterogeneous pattern, 52 (98.1%) lesions had a hypoechoic appearance, 45 (85%) lesion borders were regular, and 45 (85%) showed central umbilication (Figure 2). The lesions were most frequently (90.6%) located in the submucosa. The presence of thin tubular structures was observed in all lesions. EUS examination of EP cases revealed that the mean long axis was 10.7 ± 3.5 mm, mean short axis was 4.8 ± 1 mm, and long/short axis ratio was 2.4 ± 0.98 (Table 1). There was no significant difference between the EP dimensions and size ratios in patients with or without umbilication ($p = 0.550$; 1.000 and 0.583, respectively) (Table 2). No significant correlation was observed between age and EP long axis, short axis, and long/short axis ratio (Spearman ρ : -0.221 , $p = 0.111$; ρ : -0.212 , $p = 0.127$; and ρ : 0.019 , $p = 0.895$, respectively).

Table 1. Demographic and endoscopic ultrasonographic characteristics of patients

	n (%)
Sex	
Female	32 (60.4)
Male	21 (39.6)
Age (mean ± SD) (min–max) (years)	44.7 ± 12.1 (19–68)
Lesion location	
Antrum greater curvature	37 (69.8)
Antrum posterior	10 (18.9)
Corpus	3 (5.7)
Bulbus	2 (3.8)
Antrum anterior	1 (1.9)
Echogenicity	
Hypoechoic	52 (98.1)
Isoechoic	1 (1.9)
Homogeneity	
Heterogeneous	53 (100)
Layer	
Submucosa	48 (90.6)
Submucosa + muscularis propria	5 (9.4)
Borders	
Regular	45 (85)
Irregular	8 (15)
Presence of umbilication	
No	8 (15)
Yes	45 (85)
EUS long axis (mean ± SD) (min–max) (mm)	10.7 ± 3.5 (5–25)
EUS short axis (mean ± SD) (min–max) (mm)	4.8 ± 1 (2.3–10)
Long/short axis ratio (mean ± SD) (min–max)	2.4 ± 0.9 (1.4–8.3)

EUS: Endoscopic ultrasonography

DISCUSSION

The present study retrospectively evaluated the characteristics of 53 EP cases who underwent esophagogastroduodenoscopy for any reason and were incidentally detected to have SEL in the EUS examination.

**Figure 2:** Endoscopic ultrasound view of the ectopic pancreas. Heterogeneous hypoechoic structure, approximately 10 × 4.5 mm in size, with submucosal localization and containing thin tubular structures.**Table 2.** Evaluation of the correlation between the presence of umbilication and the sizes of ectopic pancreas

	Presence of umbilication		p
	No (n = 8)	Yes (n = 45)	
EUS long axis (mm)	12.1 ± 6.3	10.5 ± 2.8	0.550
EUS short axis (mm)	5.1 ± 2.5	4.8 ± 1.8	1.00
Long/short axis ratio	2.8 ± 2.3	2.3 ± 0.5	0.583

EUS: Endoscopic ultrasonography

Varying results have been reported in the literature in terms of sex distribution of patients with EP. Research has reported the male/female ratio as 3/1 (29); however, some studies have reported no significant difference in terms of sex of the patient (26, 28). In the present study, 60.4% of the

patients were female. In the literature, the ages of the patients reportedly range from 40 to 70 years (30). The mean patient age in our study was 44.7 ± 12.1 (19–68) years, which is consistent with the literature.

Typically, EP is <2 cm in size (6). In the present study, the mean long axis measured by EUS was 10.7 ± 3.5 (5–25) mm and the long/short axis ratio measured by EUS was 2.4 ± 0.9 (1.4–8.3). In the literature, a long/short axis ratio of >1.5 reportedly supports the diagnosis of EP (31). A ratio of <1.5 is indicative of mesenchymal tumor and can be evaluated in terms of distinguishing it from EP in EUS examination (25). EP can be encountered in every area of the GI system—from the esophagus to the colon—and it is frequently localized in the stomach antrum, duodenum, and proximal jejunum (32). Furthermore, it can be localized in the anterior or posterior wall of the stomach and is often located in the greater curvature (11, 13). In the present study, 90.6% of the EP cases was detected at the antrum, 5.7% at the corpus, and 3.8% at the bulbus, which is consistent with the literature. EP cases were most frequently detected on the antrum greater curvature.

Central umbilication, which is typically considered as the location of a drainage channel, is observed in EP of >5 mm in size (7). The presence of central umbilication is a characteristic feature in endoscopic examination and has been described in 35%–90% of the cases in the literature (6, 26, 28, 33). In the present study, central umbilication was detected in 85% of the cases, which is consistent with the literature.

Mesenchymal tumors, including gastrointestinal stromal tumors, leiomyomas, and schwannomas, are predominantly composed of muscularis propria (34). EP may occur in all layers of the GI tract wall. The submucosal (15%–70%) and muscularis propria (11%–80%) localizations of lesions are the most common, whereas mucosal or serosal localizations are rare. In the present study, 90.6% of the lesions were located in the submucosa. However, the layer involvement of EP greatly varies between case series (6, 15, 25, 26, 28, 35). This discrepancy may be owing to the relatively small sample sizes evaluated or different inclusion criteria. However, the most important confounding factor is probably the interobserver variation

in the interpretation of EUS images. Chak et al. showed that the assessment of EUS characteristics greatly varied between different pairs of experts (36). Moreover, the characteristics related to EUS appearance of EP differed between studies. Reportedly, a heterogeneous pattern is observed in 47%–100% of EP lesions, and a hypoechoic appearance is observed in 69%–100% of EP lesions (6, 15, 28, 35). In the present case series, 98.1% of the EP lesions exhibited a heterogeneous pattern and 100% had a hypoechoic appearance. Moreover, thin tubular structures were observed in all lesions.

EUS-fine needle aspiration (FNA) biopsy was not performed in any patient in our study. In the literature, performing EUS-FNA for typical EP cases (submucosal origin, heterogeneous echogenicity, long/short axis ratio of >1.5, and central umbilication) was not recommended (31). The limitations of our study were the absence of EUS-FNA and that of a final histopathological diagnosis.

Consequently, if the EUS examination revealed SELs of submucosal origin that were <2 cm in size exhibiting a heterogeneous pattern and hypoechoic appearance, anechoic duct-like structures, and a long/short axis ratio of >1.5 along with central umbilication, the diagnosis of EP should be prioritized.

REFERENCES

1. Trifan A, Târcoveanu E, Danciu M, Huțanașu C, Cojocariu C, Stanciu C. Gastric heterotopic pancreas: an unusual case and review of the literature. *J Gastrointest Liver Dis.* 2012;21:209–12.
2. Burke GW, Binder SC, Barron AM, Dratch PL, Umlas J. Heterotopic pancreas: gastric outlet obstruction secondary to pancreatitis and pancreatic pseudocyst. *Am J Gastroenterol.* 1989;84:52–5.
3. Gupta MK, Karlitz JJ, Raines DL, Florman SS, Lopez FA. Clinical case of the month. Heterotopic pancreas. *J La State Med Soc.* 2010;162:310–3.
4. DeBord JR, Majarakis JD, Nyhus LM. An unusual case of heterotopic pancreas of the stomach. *Am J Surg.* 1981;141:269–73.

5. Yuan Z, Chen J, Zheng Q, Huang XY, Yang Z, Tang J. Heterotopic pancreas in the gastrointestinal tract. *World J Gastroenterol.* 2009;15:3701-3.
6. Atwell A, Sams S, Fukami N. Diagnosis of ectopic pancreas by endoscopic ultrasound with fine-needle aspiration. *World J Gastroenterol.* 2015;21:2367-73.
7. Nebel OT, Farrell RL, Kirchner JP, Macionus RF. Aberrant pancreas: an endoscopic diagnosis. *Am J Gastroenterol.* 1973;60:295-300.
8. Sathyanarayana SA, Deutsch GB, Bajaj J, Friedman B, Bansal R, Molmenti E, et al. Ectopic pancreas: A diagnostic dilemma. *Int J Angiol.* 2012;21:177-80.
9. Elwir S, Glessing B, Amin K, Jensen E, Mallery S. Pancreatitis of ectopic pancreatic tissue: A rare cause of gastric outlet obstruction. *Gastroenterol Rep (Oxf).* 2017;5:237-40.
10. Perillo RP, Zuckerman GR, Shatz BA. Aberrant pancreas and leiomyoma of the stomach: indistinguishable radiologic and endoscopic features. *Gastrointest Endosc.* 1977;23:162-3.
11. Subasinghe D, Sivaganesh S, Perera N, Samarasekera DN. Gastric fundal heterotopic pancreas mimicking a gastrointestinal stromal tumour (GIST): a case report and a brief review. *BMC Res Notes.* 2016;9:185.
12. Armstrong CP, King PM, Dixon JM, Macleod IB. The clinical significance of heterotopic pancreas in the gastrointestinal tract. *Br J Surg.* 1981; 68:384-7.
13. Chandan VS, Wang W. Pancreatic heterotopia in the gastric antrum. *Arch Pathol Lab Med.* 2004;128:111-2.
14. Yoshida T, Sakamoto A, Kuroki K, Kojo A, Watanabe H, Tanaka K. Electrocoagulation biopsy of aberrant pancreas of the stomach. *Am J Gastroenterol.* 1976;66:554-8.
15. Matsushita M, Hajiro K, Okazaki K, Takakuwa H. Gastric aberrant pancreas: EUS analysis in comparison with the histology. *Gastrointest Endosc.* 1999;49:493-7.
16. Hase S, Nakazawa S, Yoshino J, Kojima Y, Niwa Y, Ohashi S. A study on gastric and small intestinal aberrant pancreas by endoscopic ultrasonography with special reference to comparison with histological appearance. *Jpn J Gastroenterol.* 1989;86:1684-91.
17. Geller A, Wang KK, Dimagno EP. Diagnosis of foregut duplication cysts by endoscopic ultrasonography. *Gastroenterology.* 1995;109:838-42.
18. Shen EF, Arnott IDR, Plevris J, Penman ID. Endoscopic ultrasonography in the diagnosis and management of suspected upper gastrointestinal submucosal tumors. *Br J Surg.* 2002;89:231-5.
19. Rosch T, Lorenz R, Dancygier H, Wichert AV, Classen M. Endosonographic diagnosis of submucosal upper gastrointestinal tract tumors. *Scand J Gastroenterol.* 1992;27:1-8.
20. Boyce GA, Sivak MV, Rosch T, Classen M, Fleischer DE. Evaluation of submucosal upper gastrointestinal tract lesions by endoscopic ultrasound. *Gastrointest Endosc.* 1991;37:449-54.
21. Zhou PH, Yao LQ, Zhong YS, He GJ, Xu MD, Qin XY. Role of endoscopic miniprobe ultrasonography in diagnosis of submucosal tumor of large intestine. *World J Gastroenterol.* 2004;10:2444-6.
22. Rösch T, Kapfer B, Will U, Baronius W, Strobel M, Lorenz R, et al. Accuracy of endoscopic ultrasonography in upper gastrointestinal submucosal lesions: a prospective multicenter study. *Scand J Gastroenterol.* 2002;37:856-62.
23. Karaca C, Turner BG, Cizginer S, Forcione D, Brugge W. Accuracy of EUS in the evaluation of small gastric subepithelial lesions. *Gastrointest Endosc.* 2010;71:722-7.

24. Changchien CS, Hsiaw CM, Hu TH. Endoscopic ultrasonographic classification of gastric aberrant pancreas. *Chang Gung Med J.* 2000;23:600–7.
25. Kim JH, Lim JS, Lee YC, Hyung WJ, Lee JH, Kim MJ, et al. Endosonographic features of gastric ectopic pancreases distinguishable from mesenchymal tumors. *J Gastroenterol Hepatol.* 2008;23:e301–e307.
26. Chen SH, Huang WH, Feng CL, Chou JW, Hsu CH, Peng CY, et al. Clinical analysis of ectopic pancreas with endoscopic ultrasonography: an experience in a medical center. *J Gastrointest Surg.* 2008;12:877–81.
27. Watanabe K, Irisawa A, Hikichi T, Takagi T, Shibukawa G, Sato M, et al. Acute inflammation occurring in gastric aberrant pancreas followed up by endoscopic ultrasonography. *World J Gastrointest Endosc.* 2012;4:331–4.
28. Park SH, Kim GH, Park DY, Shin NR, Cheong JH, Moon JY, et al. Endosonographic findings of gastric ectopic pancreas: a single center experience. *J Gastroenterol Hepatol.* 2011;26:1441–6.
29. Mulholland KC, Wallace WD, Epanomeritakis E, Hall SR. Pseudocyst formation in gastric ectopic pancreas. *JOP.* 2004;5:498–501.
30. Christodoulidis G, Zacharoulis D, Barbanis S, Katsogridakis E, Hatzitheofilou K. Heterotopic pancreas in the stomach: a case report and literature review. *World J Gastroenterol.* 2007;13:6098–100.
31. Gottschalk U, Dietrich CF, Jenssen C. Ectopic pancreas in the upper gastrointestinal tract: Is endosonographic diagnosis reliable? Data from the German Endoscopic Ultrasound Registry and review of the literature. *Endosc Ultrasound.* 2018;7:270–8.
32. Erkan N, Vardar E, Vardar R. Heterotopic pancreas: Report of two cases. *JOP.* 2007;8:588–91.
33. Gottschalk U, Casper B, Boden G. Ectopic pancreas presenting as a large gastric antral papilla. *Endoscopy.* 2003;35:547.
34. Wiech T, Walch A, Werner M. Histopathological classification of nonneoplastic and neoplastic gastrointestinal submucosal lesions. *Endoscopy.* 2005;37:630–4.
35. Chou JW, Cheng KS, Ting CF, Feng CL, Lin YT, Huang WH. Endosonographic features of histologically proven gastric ectopic pancreas. *Gastroenterol Res Pract.* 2014;2014:160601.
36. Chak A, Canto MI, Rösch T, Dittler HJ, Hawes RH, Tio TL, et al. Endosonographic differentiation of benign and malignant stromal cell tumors. *Gastrointest Endosc.* 1997;45:468–73.