Turk J Gastroenterol 2006; 17 (1): 20-24

Abdominal heterotopic tissues: Review of 24 cases diagnosed on postoperative histological evaluation

Abdominal heterotopik dokular; postoperatif dönemde tanınmış 24 olgunun gözden geçirilmesi

Taner YİĞİT[1], Cengizhan YİĞİTLER[1], Bülent GÜLEÇ[1], Cüneyt ATABEK[2], Ayhan ÖZCAN[3], Orhan KOZAK[1], Köksal ÖNER[1]

Departments of [1]General Surgery, [2]Pediatric Surgery, and [3]Pathology, Gülhane Military Medical Academy, Ankara

Background/aims: *Heterotopy is defined as abnormal localization of well-differentiated tissue. Heterotopic tissues usually tend to be asymptomatic and noncomplicated but sometimes may cause serious clinical problems. Malignancy potential is the most important issue in this clinical entity. In this study we reviewed medical records of 24 patients with heterotopic tissues.* ***Methods:*** *Between 1995-2004, 24 patients with heterotopic tissueswho were diagnosed during gastrointestinal system or abdominal wall surgery or upper gastrointestinal endoscopy were included in this study. Patients' medical data were retrospectively reviewed.* ***Results:*** *Sixteen patients with heterotopy were younger than 30 years and eight patients were older than 30 years. Nineteen (0.21%) heterotopic tissues were diagnosed in 8,945 patients who underwent gastrointestinal system surgery or upper gastrointestinal endoscopy, whereas five (0.21%) heterotopic tissues were diagnosed in 2,320 patients who underwent abdominal wall surgery. Overall, 24 (0.21%) heterotopic tissues were found in a total of 11,265 patients. The majority were pancreatic heterotopy, followed in decreasing order by gastric, adrenal and osseous heterotopy. In patients who underwent gastrointestinal surgery-endoscopy, pain was the main symptom (n=13)(68.4%), followed by dyspepsia (n=3)(15.7%) and vomiting-nausea (n=2)(10.5%). The main symptom in patients who underwent abdominal wall surgery was palpable mass. heterotopic tissues presented as wall thickening in 13, polypoid mass in five and whole solitary mass or intraparenchymal lesion in six patients.* ***Conclusion:*** *Although incidence of heterotopic tissues is low, in case of its suspicion or diagnosis, early treatment should be performed by surgical or endoscopic resection or patients must be followed up carefully due to risk of malignancy.*

Key words: Heterotopic tissue, carcinoma, intestinal heterotopy

Amaç: *Heterotopi iyi diferansiye olmuş bir dokunun anormal lokalizasyonudur. Genellikle asemptomatik kalma eğilimindedirler. Nadir de olsa yerleştikleri küçük çaplı bir kanalı tıkamaları, malignite gelişimi gibi bazı özel durumlarda, önemli klinik problemlere neden olabilirler. Malign hastalık gelişim riski heterotopik dokunun en önemli komplikasyonudur. Bu çalışmada postoperatif dönemde heterotopik doku tespit edilmiş 24 hastanın tıbbi verileri literatür eşliğinde gözden geçirildi.* ***Yöntem:*** *1995-2004 yılları arasında gastrointestinal sistem ve karın ön duvarı cerrahisi geçirmiş ve postoperatif dönemde heterotopik doku tespit edilmiş 24 hasta calışmaya dahil edildi.* ***Bulgular:*** *Heterotopi tespit edilen hastaların 16'sı 30 yaşın altında, 8'i ise 30 yaşın üzerinde idi. Gastrointestinal sistem cerrahisi veya üst gastrointestinal sistem endoskopisi uygulanmış olan toplam 8945 hastanın 19(%0.21)'unda, karın duvarı cerrahisi geçirmiş 2320 hastanın ise 5(%21)'inde heterotopik doku tespit edildi. Toplamda ise 11265 hastanın 24 (%0.21)'inde heterotopik doku tanısı konuldu. Heterotopik dokuların büyük bölümü pankreatik heterotopi idi. Bunu sırası ile gastrik, adrenal ve kemik heterotopileri izledi. Abdominal cerrahi-üst gastrointestinal sistem endoskopisi uygulanmış hastalarda ana semptom abdominal ağrıydı (n=13, 68%). Dispepsi (n=3, 16%) ve bulantı-kusma (n=2, 10%) takip eden diğer semptomlardı. Karın ön duvarı cerrahisi geçirmiş hastalarda ise ana bulgu operasyon alanında ele gelen şişlikti. Heterotopik doku 13 hastada yerleştiği dokuda duvar kalınlaşması, 5 hastada polipoid kitle lezyonu ve 6 hastada ise intraparankimal lezyon ya da soliter kitle lezyonu olarak ortaya çıktı.* ***Sonuç:*** *Heterotopik doku seyrek görülen klinik bir olgudur. Buna rağmen tanısı konulmuş ya da şüphelenilen olgularda malign hastalık gelişim riski gözününe alınarak cerrahi ya da endoskopik rezeksiyon ile erken tedavi gerçekleştirilerek, hastalar yakın takip edilmelidirler.*

Anahtar kelimeler: Heterotopik doku, karsinoma, intestinal heterotopi

Address for correspondence: Taner YİĞİT
GATA Genel Cerrahi Anabilim Dalı, 06018 Etlik, Ankara, Turkey
Phone: +90 312 304 50 18 • Fax: +90 312 304 50 02
E-mail: yigittaner@yahoo.com

Manuscript received: 25.07.2005 **Accepted:** 08.12.2005

INTRODUCTION

The term heterotopy, which is derived from the combination of "heteros" in Greek, meaning different, and "topos", meaning localization, refers to the abnormal localization of a well-differentiated normal tissue. Heterotopic tissues (HT) may arise anywhere from the mouth to rectum throughout the gastrointestinal tract. Since Egyedi (1) first reported HT on the gallbladder in 1934, various types of heterotopies in different tissue types such as polypoid lesions and thickening of the wall have been reported. Although many of the HT remain asymptomatic, in some certain conditions (i.e. obstruction of the duct where the HT present) HT may cause significant clinical conditions. The major clinical importance of heterotopies is the potential risk of malignancy. In the present study, the clinical presentation of HT is retrospectively reviewed in patients whose heterotopy was detected during pathological investigation.

MATERIALS AND METHODS

Between 1995 and 2004, hospital records of 24 patients diagnosed with heterotopy who underwent either gastrointestinal system (GIS)-abdominal wall (AW) surgery or upper gastrointestinal endoscopy (UGE) were retrospectively reviewed. Findings were evaluated in terms of incidence, symptomatology at presentation, the ratio of males to females, age, the relation of HT and target organ and shape of the lesion.

Mann-Whitney U test was used for statistical analysis. Statistical significance was established at $p<0.05$.

RESULTS

Heterotopic tissue was detected in 19 (0.21%) of 8, 945 patients who underwent GIS surgery or UGE, and in five (0.21%) of 2, 320 patients who underwent AW surgery. Overall, 24 heterotopies were detected in 11, 265 patients (0.21%). There were 11 (0.12%) pancreatic and eight (0.09%) gastric heterotopies in patients who underwent GIS surgery or UGE. In patients who underwent AW surgery, adrenal gland heterotopia was reported in four (0.17%) patients and osseous heterotopia in one (0.04%) patient.

Male/female ratio was 16/8. Mean age of the patients was 28.29 (range 1-87). There were 16 patients younger than 30 years and eight patients older than 30 years. Differences between gender and age were statistically significant ($p< 0.05$).

Thirteen (68.4%) of 19 patients who underwent GIS surgery or UGE had epigastric pain as the dominant symptom. Other remarkable symptoms were dyspeptic symptoms (heartburn, upper abdominal pain) in three (15.7%) patients and vomiting-nausea in two (10.5%) patients. One (5.2%) patient had no obvious symptoms in this group of patients. This asymptomatic patient's heterotopy was diagnosed with mesenteric lymph node biopsy material. The main symptom in patients who underwent AW surgery was swelling in the area (inguinal, umbilical) where the operation was considered.

Five (26%) pancreatic heterotopies in stomach, one (5%) gastric and one (5%) pancreatic in gall bladder, seven (37%) gastric in Meckel's diverticulum, four (22%) pancreatic in small intestine and one (5%) pancreatic in mesenteric lymph node were detected in patients who underwent GIS surgery or UGE. In patients who underwent AW surgery, four (100%) adrenal gland heterotopies in mass lesion localized at inguinal canal and one osseous heterotopy in mass lesion localized at abdominal wall muscles were detected. Overall, 11 (45.8%) pancreatic, eight (33.3%) gastric, four (16.6%) adrenal and one (4.1%) osseous heterotopies were diagnosed in 24 patients.

Heterotopic tissue was in the form of wall thickening in 13 (54.1%), polypoid lesion in five (20.8%) and isolated mass lesion or intraparenchymal lesion in six (24%) cases. The relations between patient-heterotopy and the target organ are outlined in Table 1. Some of the heterotopic and host tissue samples are presented in Figure 1.

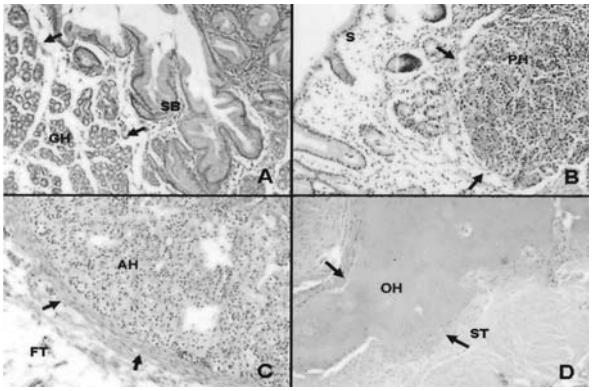

Figure 1. Some of the heterotopic and host tissue samples

A: Gastric heterotopy in small bowel, B: Pancreatic heterotopy in stomach, C: Adrenal heterotopy in inguinal canal, D: Osseous heterotopia in soft tissue, GH: Gastric heterotopy, SB: Small bowel, PH: Pancreatic heterotopy, S: Stomach, AH: Adrenal heterotopy, FT: Fatty tissue, OH: Osseous heterotopy, ST: Soft tissue

Table 1. The relations between patient-heterotopy and the target organ

No	Group	Age	Sex	Performed Procedure/ Diagnosis	Target Tissue	Type of HT	Shape of HT	Symptom on Admission
1	GIS+E	27	F	Endoscopy	Stomach	Pancreas	Polypoid	Dyspepsia
2	GIS+E	19	F	Endoscopy	Stomach	Pancreas	Polypoid	Dyspepsia
3	GIS+E	25	F	Endoscopy	Stomach	Pancreas	Polypoid	Dyspepsia
4	GIS+E	45	M	Cholecystectomy	GB	Gastric	Polypoid	Abdominal pain
5	GIS+E	55	F	IR+Cholecystectomy	Jejunum	Pancreas	Polypoid	Abdominal pain
6	GIS+E	21	M	App+Meckel's resection	MD	Gastric	Wall Thickening	Ileus
7	GIS+E	50	M	Gastrectomy	Stomach	Pancreas	Wall Thickening	Abdominal pain
8	GIS+E	78	M	Gastrectomy	Stomach	Pancreas	Wall Thickening	Gastric obstr.
9	GIS+E	50	M	IR+Gastrectomy	Jejunum	Pancreas	Wall Thickening	Gastric obstr.
10	GIS+E	59	F	Cholecystectomy	GB	Pancreas	Wall Thickening	Abdominal pain
11	GIS+E	87	F	IR	Ileum	Pancreas	Wall Thickening	Ileus
12	GIS+E	20	M	App+Meckel's resection	MD	Gastric	Wall Thickening	Abdominal pain
13	GIS+E	20	M	IR	Ileum	Pancreas	Wall Thickening	Abdominal pain
14	GIS+E	8	F	IR	MD	Gastric	Wall Thickening	Abdominal pain
15	GIS+E	3	M	App+Meckel's resection	MD	Gastric	Wall Thickening	Abdominal pain
16	GIS+E	4	M	App+Meckel's resection	MD	Gastric	Wall Thickening	Abdominal pain
17	GIS+E	10	F	App+Meckel's resection	MD	Gastric	Wall Thickening	Abdominal pain
18	GIS+E	8	M	Meckel's resection	MD	Gastric	Wall Thickening	Abdominal pain
19	GIS+E	20	M	MLN excision	MLN	Pancreas	Parenchymal Lesion	No symptom
20	AWS	59	M	Incisional herniorrhaphy	AW	Osseous	Parenchymal Lesion	AW swelling
21	AWS	1	M	Inguinal excisional biopsy	Inguinal	Adrenal	Parenchymal Lesion	Inguinal mass
22	AWS	1	M	Cryptorchidism	Inguinal	Adrenal	Parenchymal Lesion	Empty scrotum
23	AWS	3	M	Hydrocele	Scrotum	Adrenal	Parenchymal Lesion	Scrotal swelling
24	AWS	6	M	Inguinal herniorrhaphy	Inguinal	Adrenal	Parenchymal Lesion	Inguinal swelling

GIS+E: Gastrointestinal+Endoscopy, AWS: Abdominal wall surgery, M: Male, F: Female, IR: Intestinal resection, MD: Meckel's diverticulum, GB: Gallbladder, MLN: Mesenteric lymph node, Obstr: Obstruction, App: Appendectomy

DISCUSSION

Two hypotheses have been asserted to explain the development of heterotopy. The first is metaplastic and the other is embryonal, which has become more commonly accepted. Many gastrointestinal organs arise from endoderm, while muscular and connective tissues arise from mesoderm (2). These multipotential cells, potential sequence of many mature organs, of endoderm and mesoderm have the ability to undergo changes, forming many different layers. HT arise as a result of this changing process somewhere outside the norm. They can be situated throughout the gastrointestinal tract and, due to their congenital origins, they are observed more frequently in younger patients. In our patients as well, heterotopy was seen more frequently in the younger age group.

In many cases, HT present as nodular-polypoid structures and wall thickening in the organ where they are localized (3, 4). In our series including 24 patients, the majority presented as a wall thickening. We believe that these two presentation features (wall thickening and polypoid lesions) are a unique clue in the diagnosis of HT in the preoperative period when the other malignant entities have been excluded. Diagnosis of these specifications usually impels the clinician to perform biopsy and this usually helps in diagnosis of the disease in the preoperative stage. Otherwise, the predominance of pancreatic heterotopy was striking in our study, followed in decreasing order of frequency by gastric, adrenal and ossseous heterotopies. Pancreatic heterotopies were mostly localized in stomach and small intestine while gastic heterotopies were concentrated in Meckel's diverticula. All of the adrenal heterotopies were localized in the inguinal canal.

Many heterotopies remain asymptomatic and are diagnosed incidentally after the examination of pathology specimen. Pain is the main symptom in symptomatic cases (5, 6). It usually arises due to the obstruction of passage or organ lumen. For instance, heterotopia localizing in the prepyloric area, the cystic canal or Wirsung's duct could cause incomplete or complete obstruction (7, 8). Dolan et al. (9) questioned the relation between HT and presentation of symptoms and found no marked correlation. Likewise, Hsia et al. (10) were not able to find a correlation between symptomatology and HT. However, Armstrong et al. (11) reported a direct relation between the symptoms and the number of lesions and the extent of submucosal involvement. When we retrospectively reviewed our patients' symptomatology, we thought that symp-

toms could relate to HT in only two of our patients. These included one patient who had perforated Meckel's diverticulum lined with heterotopic gastric mucosa and one patient who had a pyloric stenosis that originated from the heterotopic pancreatic tissue localized in the pylorus. Given these findings, we agree with the idea of Dolan et al. that alleges symptomatology is not always associated with HT. As in both pancreatic and gastric heterotopies, all pathologies presenting in the original tissue can be observed in HT. For instance, pancreatitis, pancreatic cyst and abscess formation and pancreatic cancer and islet tumor may develop in heterotopic pancreatic tissue (12). In addition, ulceration and inflammation may be observed in patients with gastric mucosal heterotopy (5, 13). In such a case, specific symptoms of the emerging pathology may be observed. If infection is present, the patient might experience fever and leukocytosis.

There is no specific technique to detect HT in the preoperative period. Detection of polypoid lesions or wall thickening on the target organ with computed tomography, ultrasonography, UGE or colonoscopy and sampling of this tissue might diagnose the disease at the preoperative stage. It has been reported that Tc-99 pertechnetate scintigraphy may be used for the diagnosis of heterotopic gastric mucosa in children (14). In addition, some osseous heterotopies may be disclosed by direct radiographs or during bone scintigraphy (15, 16).

While many heterotopic tissues remain asymptomatic and are found incidentally in pathological investigation performed in the postoperative period, metaplastic changes may take place in heterotopic epithelium in the presence of chronic inflammation. As malignancies arising from HT have been reported in the literature, HT may be a cause of intestinal malignancies (17-21). Even if none of our patients had a history of malignancy since the diagnosis of heterotopy, we think that the potential risk of the development of malignancy is the most important issue for this group of patients, and therefore their enrollment in a surveillance program is important.

In conclusion, heterotopy may not be considered during the diagnostic process because of its rare occurrence. If a patient has inexplicable pain complaints and was diagnosed with some lesions in polypoid shape or wall thickening in the target organ, heterotopy should be kept in mind in the differential diagnosis, especially in young patients. In case of suspicion or diagnosis of heterotopy, the potential risk of malignancy should be taken into account and the lesion should be managed with early surgical or endoscopic resection or the patients must be followed up carefully.

REFERENCES

1. Egyedi L. Case of polyps of the gallbladder containing an aberrant gastric mucous membrane. Gyogyaszat 1934; 74: 596-9.
2. Langman J. Digestive system. In: Langman J, ed. Medical Embryology. 4th ed. Baltimore: Williams & Wilkins, 1981; 212-33.
3. Pradines P, Brauner M, Legrand I, et al. Heterotopic gastric mucosa in the gallbladder. AJR 1989; 152: 432.
4. Leyman P, Saint-Marc O, Hannoun L, et al. Heterotopic gastric mucosa presenting as gallbladder polyps. Acta Chir Belg 1996; 96: 128-9.
5. Lamont N, Winthrop AL, Cole FM, et al. Heterotopic gastric mucosa in the gallbladder: a cause of chronic abdominal pain in a child. J Pediatr Surg 1991; 26(11): 1293-5.
6. Hlavaty T, Lukac L, Vyskocil M, et al. Heterotopic pancreas in gastric antrum with macroscopic appearance of gastric polyp. Bratisl Lek Listy 2002; 103(3): 117-20.
7. Hazzan D, Peer G, Shiloni E. Symptomatic heterotopic pancreas of stomach. IMAJ 2002; 4: 388-9.
8. Obermaier R, Walch A, Kurtz C, et al. Heterotopic pancreatitis with obstruction of the major duodenal papilla – a rare trigger of obstructive orthotopic pancreatitis. Pancreatology 2004; 4: 244.
9. Dolan RV, ReMine WH, Dockerty MB. The fate of heterotopic pancreas. Arch Surg 1974; 109: 763-5.
10. Hsia CY, Wu CW, Lui WY. Heterotopic pancreas: a difficult diagnosis. J Clin Gastroenterol 1999; 28(2): 144-7.
11. Armstrong CP, King PM, Dixon JM, et al. The clinical significance of heterotopic pancreas in gastrointestinal tract. Br J Surg 1981; 68: 384-7.
12. Lee HY, Choi YH, Song S, et al. Lithiasis in a heterotopic pancreas of the stomach. J Comput Assist Tomogr 2003; 27(1): 85-7.
13. Larsen EH, Diedrich PJB, Sorensen FB. Peptic ulcer in the gallbladder. A case report. Acta Chir Scand 1985; 151: 575-6.
14. Emamian SA, Shalaby-Rana E, Majd M. The spectrum of heterotopic gastric mucosa in children detected by Tc-99m pertechnetate scintigraphy. Clin Nucl Med 2001; 26(6): 529-35.
15. Ehara S, Shiraishi H, Abe M, et al. Reactive heterotopic ossification. Its patterns on MRI. Clin Imaging 1998 Jul-Aug; 22(4): 292-6.
16. Chan R, Common AA, Sugar L. Sonographic appearance of renal transplant osseous metaplasia: case report. Can Assoc Radiol J 1999 Dec; 50(6): 390-2.
17. Kijima H, Watanabe H, Iwafushi M, et al. Histogenesis of gallbladder carcinoma from investigation of early carcinoma and microcarcinoma. Acta Pathol Jpn 1989; 39: 235-44.

18. Xeropotamos N, Skopelitou AS, Batsis Ch, et al. Heterotopic gastric mucosa together with intestinal metaplasia and moderate dysplasia in the gallbladder: report of two clinically unusual cases with literature review. Gut 2001; 48 (5): 719-24.
19. Makhlouf HR, Almeida JL, Sobin LH. Carcinoma in jejunal pancreatic heterotopia. Arch Pathol Lab Med 1999; 123: 707-11.
20. Noguchi T, Takeno S, Takahashi Y, et al. Primary adenocarcinoma of the cervical esophagus arising from heterotopic gastric mucosa. J Gastroenterol 2001; 36: 704-9.
21. Emerson L, Layfield LJ, Rohr LR, et al. Adenocarcinoma arising in association with gastric heterotopic pancreas: a case report and review of the literature. J Surg Oncol 2004; 87: 53-7.