Review paper

Benign and non-neoplastic tumours of the duodenum

Wojciech Latos[1], Aleksandra Kawczyk-Krupka[1], Natalia Strzelczyk[2], Aleksander Sieroń[3], Grzegorz Cieślar[1]

[1]Department of Internal Medicine, Angiology and Physical Medicine, Center for Laser Diagnostics and Therapy in Bytom, Medical University of Silesia in Katowice, Poland
[2]Department of Internal Medicine, District Hospital, Kłobuck, Poland
[3]Jan Długosz University, Częstochowa, Poland

Gastroenterology Rev 2019; 14 (4): 233–241
DOI: https://doi.org/10.5114/pg.2019.90250

Key words: benign duodenal tumours, ectopies, endoscopy.

Address for correspondence: Prof. Aleksandra Kawczyk-Krupka MD, PhD, Department of Internal Medicine, Angiology and Physical Medicine, Medical University of Silesia, 15 Batorego St, 41-902 Bytom, Poland, phone: +48 32 786 16 30, e-mail: akawczyk@gmail.com

Abstract

This review study describes the problem of duodenal tumours, which are rare but important in gastrological practice. The most common location of small intestinal tumours is the duodenum, and this observation is probably partly due to the greater diagnostic availability for most proximal segments of the small intestine. Among tumours the following should be mentioned – benign: adenomas, lipomas, haemangiomas, and leiomyomas; and malignant: malignant tumours of epithelial origin, primary gastrointestinal stromal tumours, neuroendocrine tumours and carcinoids, lymphomas, sarcomas, teratomas, and secondary metastases. Early duodenal tumour recognition, especially with histological assessment, plays a crucial diagnostic role with future therapeutic implications. In recent years the prevalence of benign duodenal tumours has been rising due to a higher level of clinicians' doubts and the convenience of gastrointestinal endoscopy; hence, knowledge of this problem is important in routine clinical practice. The method of duodenal tumour treatment should be selected on an individual basis.

Introduction

Duodenum is the shortest part of the small intestine. The name is derived from the fourth century BC, when Herofilus determined its length at 12 finger widths.

The term tumour is usually used as a working diagnostic term to describe any atypical structure constituting emphasis or palpable resistance until a detailed explanation of the aetiology, histogenesis, or malignancy of the observed lesion and its clinical-biological properties are described.

The duodenum is the most common location of small intestinal tumours, between the pyloric canal and Bauhin's valve [1].

Differential diagnosis of duodenal tumours should include inflammatory tumours, hypertrophic changes, congenital ectopic lesions and tumours, both benign and malignant, which can derive from all types of cells and intestinal wall layers.

Among benign tumours the following should be mentioned: adenomas, lipomas, haemangiomas, and leiomyomas, and malignant: cancers, i.e. malignant tumours of epithelial origin, primary gastrointestinal stromal tumours, neuroendocrine tumours and carcinoids, lymphomas, sarcomas, teratomas, and secondary metastases. The progression from duodenal adenoma to adenocarcinoma can take up to 15–20 years.

In fact, apart from the presence of primary malignant tumours, there are also cases of metastasis to the duodenum of gastric, pancreatic or ovarian cancers, and various forms of lymphoma [1, 2].

It has been assumed that tumours of Vater's ampulla, although located in the duodenum, are discussed together with other tumours of the biliary system [3].

Aetiopathogenesis

The aetiopathogenesis of primary duodenal tumours is unknown. Among other factors, the pathogenic importance of bile, the components of which have a proven mutagenic effect, which mainly encourages proliferation of epithelial cells, is taken into account. The other factor is the fact that the presence of bile encourages

Creative Commons licenses: This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International (CC BY -NC -SA 4.0). License (http://creativecommons.org/licenses/by-nc-sa/4.0/).

formation of DNA adducts, i.e. the combination of DNA with some substances contained within it, mainly bile acids. This phenomenon occurs extremely easily in the duodenum, which is favoured by a particularly low pH. DNA adducts have mutagenic potential, which has been demonstrated, inter alia, in patients with familial adenomatous polyposis (FAP) [4].

Symptomatology

The symptoms of duodenal tumours depend on their aetiology and location. Often, their presence in the duodenum may be asymptomatic for a very long time.

Early clinical manifestation in the form of colic pain, jaundice, or symptoms of inflammation of the bile system or pancreas may refer to duodenal tumours located nearby, or even including the Vater papilla.

Courvoisier's syndrome – characteristically palpable through the abdominal wall, a significantly enlarged and painless gallbladder, associated with the closure of the final biliary tract by infiltrating or compressive tumour – is sporadic and usually suggests advanced disease [3].

In cases with a different location of tumours in the duodenum late symptoms associated with acute or chronic bleeding from the gastrointestinal tract (haemorrhage, anaemia) may occur, as well as symptoms of (sub) obstruction, and finally perceptible pathological resistance in the epigastric region. Some of the duodenal tumours may have a secretory capacity, and in those cases the clinical spectrum may be dominated by symptoms associated with uncontrolled endocrine secretion.

Ectopies

Ectopy (from the Greek: "displacement") stands for the term used in medicine if there is an organ (including tissue) located in a place other than physiological. Another term used for ectopia without the colon is heterotopia. In duodenum ectopies ectopic pancreas as well as gastric mucosa ectopies are found. Both of those pathologies localised in the duodenum take the form of a tumour that fills the luminal part of the intestine.

Ectopy of gastric mucosa

Heterotopia of stomach mucosa within the upper digestive tract, encountered both in the proximal part of the oesophagus as well as in the duodenum, is a congenital anomaly. Easier access to endoscopic examinations and their high standard explains the increasing frequency of new diagnoses [5]. As in the case of the location in the oesophagus (gastric heterotopia in the oesophagus takes the form of a flat "stain at the entrance") the most common form gastric heterotopia occurring in the duodenum is a flat-raised or exophytic tumour with inflamed mucous membrane changes [6].

Terada in his work distinguished two histological types of gastric heterotopia: the first with gastric glands, which is clearly congenital, and the second characterised by the absence of glands, but only by foveolar mucosa hyperplasia with lymphocyte infiltrates.

Terada postulates of ectopy the connection of the other type with the possibility of gastric metaplasia in the duodenum in the mechanism of colonisation of the duodenum in the course of *Helicobacter pylori* infection [7]. The same author calculated the total occurrence frequency of gastric duodenal heterotopia in the duodenum in up to 9% of the Japanese population studied [8].

The most common confirmed clinical form of gastric mucosa ectopy are polypoid lesions; less often they have the form of ulceration, submucosal tumour, or infiltrative, flat, inflammatory lesions.

The presence of two types of histopathological gastric heterotopy in the duodenum: foveolar proliferation with the presence of stomach glands or foveolar epithelium alone, without presence of stomach glands, confirms the study of Chinese authors who report the occurrence of heterotopic gastric mucosa (HGM) in the duodenum in the Chinese population at a level close to 0.5%, with a slightly higher occurrence in men.

The Chinese authors reported possible outbreaks of intestinal metaplasia within the heterotopic gastric area in the duodenum, as confirmed in several cases.

They did not find dysplasia from HGM lesions in any case. At the same time, they confirmed the possibility of colonisation of *H. pylori* observed in HGM, which concerned about 20% of the studied lesions, and the vast majority were accompanied by confirmed *H. pylori* infection in the stomach [9].

Pancreatic ectopias

Ectopic pancreas or pancreatic ectopia (also called heterotopic pancreas, pancreatic heterotopy, aberrant pancreas) is a developmental anomaly consisting of the presence of pancreatic tissues in various locations outside the pancreas, both inside the gastrointestinal tract as well as outside it. In the digestive tract, during endoscopy pancreatic ectopia is visible as a nodular, elevated, obtuse, and well-limited lesion covered with mucosa that does not differ from its surroundings, sometimes with a yellowish coloration, soft, and most often with a umbilical hollow at the top, with a diameter of up to 30 mm [10].

The mechanism of pathogenesis of ectopic pancreas formation remains unclear. Armstrong *et al.* suggest that its formation is a result of disturbances in the de-

velopment of the intra-pectoral pancreas, but Skandalakis *et al*. claim that this anomaly results from metaplasia cell pluripotent, and this could explain the location of changes in extraordinary places, such as the chest or skull cavity, which was described in a review study by Huang *et al*. [11].

However, the Heinrich classification is more commonly used, in which three types of histopathological images are distinguished: 1 – contains acini, endocrine islet cells, and ducts; 2 – contains acini and ducts but does not contain islet cells; and 3 – contains ducts but no acini and no islet cells (this type is most commonly found in the stomach) [10].

In the autopsy studies ectopic pancreas is found at a frequency of 0.6% to 13.7%, and this anomaly occurs in: stomach (38% of patients), duodenum (36% of patients), jejunum (16% of patients), and less often in Meckel's diverticulum, ileum, large intestine, oesophagus, bile duct, duodenal ampulla and papilla, liver, spleen, navel, mesentery, fallopian tube, mediastinum, lungs, and lymph nodes; the occurrence of ectopic pancreas was even described in the central nervous system [12, 13].

In the ectopic pancreatic tissue the same typical diseases occur as in the pancreas: acute and chronic inflammation with increased activity in lipase serum and amylase, abscesses, cysts that may be the result of efflux disorders of pancreatic enzymes, endocrine tumours: insulinoma - causing hypoglycaemia, gastrinoma causing Zollinger Ellison syndrome, and acromegaly caused by increased growth hormone secretion [14, 15]. So far, about 30 cases of malignancy in the ectopic pancreas have been described [16]. Moreover, cystic wall degeneration, which occurs in the ectopic pancreas, most often affects the location of pancreatic ectopia in the wall of the duodenum.

Benign duodenal tumours

Among neoplastic tumours of the small intestine, two-thirds of lesions are benign [9].

The most common location of benign small intestinal tumours is the duodenum, and this observation is probably partly due to the greater diagnostic availability for most proximal parts of the small intestine. In addition to hypertrophic lesions, the most common duodenal epithelial tumours are adenomas: serrated, tubular, tubulovillous, and villous, which occur sporadically either in polyposis syndromes or derived from the Brunner glands.

Less frequent are neoplasms of mesenchyme origin, including the following: lipomas, leiomyomas (including leiomyoblastoma), haemangiomas, fibroids and neurofibroma-like (neurofibroma), schwannomas, gangliomas, and lymphangiomas.

Mesenchymal tumours

Mesenchymal tumours are the most common submucosal tumours in the gastrointestinal tract, and these are cancers from the connective tissue, muscle, adipose tissue, lymphatic tissues, blood vessels, and nerves located below the submucosa. The most frequent location of mesenchymal tumours in the gastrointestinal tract is the stomach wall, followed by the small intestine.

Among benign tumours of mesodermal origin of the stomach, those derived from smooth muscle constitute over 90% [17].

Leiomyomas

Leiomyomas are most often found in the oesophagus, but they can also be present in the duodenum. A biopsy of lesions should be considered depending on their size and tumour anatomy because the correlation between leiomyoblastoma (LMB), leiomyoma (LM), and leiomyosarcoma (LMS) is unknown [18].

In the small intestine, leiomyomas are the most common form of benign tumours, while leiomyosarcoma accounts for about 19% of malignant tumours. The most common clinical symptom of leiomyomas are as follows: abdominal pain (37.5%), followed by bleeding (27.1%), presence of palpable mass, indigestion, and weight loss.

The fibroids are most common in men aged 50–70 years. Mostly, 10–20% of those lesions in the small intestine are found in the duodenum. They are usually asymptomatic, but anaemia occurs in 50% of all cases, due to ulceration of the mucous membrane [17].

Lipomas

Duodenal lipomas grow in the submucosa, and they take the third place, after colon and ileum, in the frequency of occurrence in the gastrointestinal tract [9].

Lipomas under 1 cm in size are usually asymptomatic. Larger, especially above 4 cm, can cause obstruction, bleeding, or intussusception.

Haemangiomas and neuromas

Haemangiomas and lymphangiomas are tumours built of well-defined submucosal masses of blood or lymph vessels. The most common complication of these tumours is severe bleeding. Tumours of the nerve tissue (schwannomas, neurofibromas, neuroblastoma-like) constitute from 3% to 6% of all small tumours of the small intestine. The most common of these are schwannomas and neurofibromas. Another duodenal tumour, gangliocytic paraganglioma (GP), usually arising in the second part of the duodenum, is often misdiagnosed as a grade 1 (G1) neuroendocrine tumour (NET) [19].

Duodenal adenomas

Occasional duodenal adenomas (in patients without FAP) constitute 7% of duodenum polyps. In the duodenum, adenomas are usually located in its descending part. Adenoma is a benign neoplasm originating from benign epithelial dysplasia, but it can be the starting point of cancer [20].

In terms of histopathological structure, we can distinguish the following adenomas: serrated, tubular, tubulovillous, and villous. An adenoma derived from the Brunner glands is separately qualified.

Among 40% of villous adenomas, high-grade dysplasia cells are detected, and those adenomas have the highest risk of becoming cancerous.

The size of adenomas is not directly related to the risk of malignant transformation.

Despite the total risk of developing duodenal cancer and, more broadly, small intestine cancer, there remains little relation between the incidence of colon adenomas coexisting with colorectal cancer.

For this reason, it is important to remember the necessity of performing urgent colonoscopy in patients of all ages, who have been diagnosed with polyps in the small intestine, including the duodenum.

In turn, patients with Crohn's disease, among which the incidence of adenomas and small intestine adenocarcinoma is up to 32 times greater, should always be subjected to control endoscopy with inspection as far as possible beyond the duodenal bulb [20].

All polypoid lesions found in the duodenum that are adenomas should be qualified for endoscopic polypectomy. In cases of difficult qualification for resection it is extremely helpful to perform endoscopic examinations of polyps using special imaging techniques (narrow-band imaging endoscopy – NBI, autofluorescence – AFE) or endosonography (EUS).

In comparison to lesions of similar size removed from other parts of the digestive tract, the risk of serious complications after endoscopic polypectomy performed in the duodenum is much greater.

To a large extent, the unique features of the duodenal anatomy are responsible for this, such as thin wall and narrow light [21]. For those reasons, endoscopic submucosal dissection (ESD), developed in Japan as a method of endoscopic excision of superficial tumours limited to the mucosa, has little application in the treatment of duodenal tumours [22, 23].

Brunner's glands polyps

Brunner gland (BG) adenoma is a rare benign tumour of the duodenum, which accounts for 10% of all benign tumours in this location. Generally, BG adenomas are very rarely observed benign tumours in the duodenum – reported by 0.008% in a series of 21,500 autopsies. Hyperplasia of the Brunner glands most often occurs in the fifth and sixth decade of life, and it is therefore quite rare in children and adolescents [24]. The Brunner glands located in the mucosa and submucosa are most numerously located in the proximal part of the duodenum, and they secrete a basic mucus containing a number of glycoproteins and antimicrobial peptides, which plays an important barrier function [25].

The main physiological function of the Brunner glands is the protection of the proximal part of the small intestine from the strongly acidic food content leaving the stomach. Hyperplasia of the Brunner glands is rare, and the pathogenesis of their hypertrophy remains unclear.

In many studies, more frequent occurrence of Brunner gland hypertrophy associated with excessive secretion of gastric acid in the stomach, chronic pancreatitis, uraemia, and *H. pylori* infection was observed. Hyperplasia of the Brunner glands is usually asymptomatic, although it may occasionally occur with abdominal pain and/or bleeding from the upper part of the gastrointestinal tract. The growth of the bile duct and consequent inflammation of the pancreas is particularly rare in the unrestrained growth of the Brunner glands; 68% of Brunner adenomas appear in the duodenum, 27% in the descending part, and only 5% in the horizontal part of the duodenum, which corresponds to the anatomical distribution of the glands [26].

In 1835, Curveilher described the growth of the Brunner glands in a patient with duodenal intussusception. Hyperplasia of the Brunner glands can be observed as diffuse glandular proliferation that gives the duodenum a coarse-grained nature or visible nodularity of the surface, and less frequently as exogenous lesions. The endoscopic picture is not characteristic, and it may resemble GIST, lymphoma, carcinoid, polyp in the course of the Peutz-Jeghers syndrome, prolapse of the pyloric mucosa, or pancreatic ectopia [26].

Without histopathological examination, the correct diagnosis is not possible. Endoscopic ultrasound (EUS) together with fine needle aspiration biopsy (FNA) may be helpful in obtaining a proper diagnosis [27]. The American Institute for Radiologic Pathology arbitrarily adopts the term "overgrowth of the Brunner gland" for lesions (whether alone or not) less than 5 mm, and the term "hamartoma of the Brunner glands" for polyps with a diameter of more than 5 mm [28].

In 1934, Feyrter divided the histopathologically hypertrophic changes of the Brunner glands into three types: type 1 – diffuse nodular hyperplasia within the

entire duodenum, type 2 – limited tubular hyperplasia of the duodenal gland, and type 3 – polypoid tumour with tumour-like dimensions [29]. Typically, hamartomas of the Brunner glands are composed of normal Brunner glands occurring in various proportions with adipose tissue, smooth muscle, and lymphatic tissue, and, in some cases, with areas containing sclerotic Brunner glands [28]. A study conducted by Sakurai *et al.* shows that the probability of Brunner glandular hypertrophy being switched to dysplastic lesions is about 2.1%, whereas the conversion into the invasive cancer is 0.3% [30].

The traditional way of dealing with patients with hypertrophy of the Brunner glands consists of endoscopic observation of the patient or possible qualification for surgical resection.

The question of whether small hypertrophic lesions require any treatment is still controversial.

With the development of devices and endoscopic techniques, endoscopic resection (ESD) is considered an alternative treatment option. Studies by Zhong *et al.* provide evidence of the efficacy of endoscopic resection in the local treatment of adenoma of the Brunner glands, with a relatively low number of complications and a low mortality rate [31].

When the tumour is small or pedunculated, endoscopic polypectomy is the treatment of choice. Open surgical excision is reserved for cases in which endoscopic therapy has failed or cases when the dimensions of the adenoma are too large [32].

Familial adenomatous polyposis (FAP)

Adenomas of the major duodenal papilla, also known as ampullary adenomas, occur rarely, especially in the context of genetic syndromes such as FAP.

FAP is an inherited disease, occurring at a frequency of approximately 1 : 10,000 newborns, and its basis is the formation of multiple adenomatous polyps, which leads in untreated patients to development of colorectal cancer [33]. Numerous polyps outside the large intestine are located mainly in the duodenum. In this genetically determined disease, in addition to polyps of the gastrointestinal tract, there is also a tendency to develop desmoid tumours, locally aggressive, not giving distant metastases, and tumours of the fibrous tissue [34]. Due to the emergence of the possibility of identifying genes responsible for FAP by means of DNA analysis (increasingly used) and the availability of endoscopic examinations, the prognosis of patients after early colectomy is generally good. However, they require surveillance and control endoscopy throughout their life [35]. In patients with FAP, duodenal adenomas are particularly localised in the distal part of this organ.

An alternative to classical endoscopy and single or double balloon enteroscopy in these patients is capsule endoscopy, which is a safe and convenient method for assessing the small intestine. Enteroclysis, is a radiographic examination of the small intestine by using a tube placed near the duodenum passage into the small intestine, through which a suspension contrasting intestinal lumen (usually consisting of barite and methylcellulose) is applied. However, CT- or MR-enterography without tube placement is a more convenient for the patient and more accurate.

It has less diagnostic efficacy in cases of adenomas in FAP [36]. The basic weakness of both methods (capsule endoscopy and enteroclysis) is the inability to take specimens from the observed lesions.

However, it is becoming increasingly evident that mild onset of disease causes a less aggressive variant of FAP. This is called attenuated FAP (AFAP).

In its course, fewer polyps (10–100) are formed, the polyps develop at a later age, and they may be more frequent in the upper gastrointestinal tract than in the colon [37]. In AFAP the risk of cancer transformation is smaller and does not exceed 70% [38].

Gardner syndrome is one of the variants of FAP characterised by the presence of multiple adenomatous polyps with simultaneous occurrence of benign tumours such as desmoid tumours, osteomas, and fibromas. Gardner syndrome is caused by germline APC mutations inherited in affected families in an autosomal dominant manner [39]. Mutation refers to a small area of DNA located on the long arm of chromosome 5 (5q21-22), which occurs at a geographically variable frequency in the range between 1/4000 and 1/12,000 [40]. In about 30% of cases, the disease appears spontaneously, due to the *de novo* mutation. Sometimes there is no damage to the APC gene and the disease is caused by damage to the RAS gene on chromosome 12, P53 gene on chromosome 17, or loss of DNA methylation. This genetic disease is characterised by the co-occurrence of intestinal symptoms caused by the presence of numerous intestinal polyps and parenteral symptoms in the form of accompanying lesions. Parenteral lesions include the possibility of multiple osteomas, connective tissue tumours and thyroid cancer. Desmoid tumours in this syndrome do not have the ability to produce distant metastases, although they tend to aggressively invade neighbouring tissues [41]. Desmoid tumours can appear in any location [42]. Depending on the location, course, and epidemiology, the extra-abdominal, abdominal, and intra-abdominal forms are distinguished [43–45]. In a large group of patients (60–90%), the diagnostic symptom enabling suspicion of

the disease is congenital hypertrophy of the retinal pigmented epithelium (CHRPE). This defect may be found in an ophthalmological study using a slit lamp or in the evaluation of optical coherence tomography (OCT) [45]. Osteomas are benign tumours of bone tissue with slow continuous growth, which usually occur in the bones of the skull (mainly the jaws and the walls of the sinuses) and long bones, often constituting the main symptom of Gardner syndrome [39]. Numerous gastrointestinal adenomas may be the starting point for malignant tumours. There is also an increased risk of developing duodenal cancer, particularly in the ampulla of Vater. Facial and mouth anomalies are commonly observed in these patients, so it is important to draw the doctors' attention, including dentists, to the early diagnosis of this syndrome, which can ultimately prevent the patient from developing malignancy [40]. Early recognition of Gardner syndrome is important because in the case of this genetic anomaly, adenomas usually transform into cancer in the fourth decade of life [46]. Turina *et al*. conducted research on 37 families in which Gardner syndrome occurred, and showed that the use of appropriate screening allows good long-term control of colorectal cancer [47]. To complement the review of various FAP variants, Turcot syndrome should be mentioned, in which the coexistence of brain tumours and colon polyps occurs.

Peutz-Jeghers syndrome

The genetic conditioning of Peutz-Jeghers syndrome (PJS) is characterised by the coexistence of characteristic pigmentation of the skin and mucous membranes: lentigo lesions, located mainly on the lips and fingers and on the mucous membrane of cheeks (lentiginosis syndrome) with the presence of hamartomatous polyps in the gastrointestinal tract. PJS is associated with predisposition to the occurrence of malignant tumours of various organs and systems. The teratocarcinoma polyps may be present in any part of the gastrointestinal tract, but they most often affect the small intestine. It is believed that hamartomatous polyps do not pose a high risk of neoplastic transformation, but they usually appear in young adults, where they are the cause of obstruction or intussusception, and usually having a long stalk and a tendency for autoamputation, and are sometimes the source of acute haemorrhage or chronic bleeding into the gastrointestinal tract and subsequent anaemia [48]. PJS polyps are found primarily in the small intestine (64%, in the order of occurrence: jejunum > ileum > duodenum), as well as in the colon (53%), stomach (49%), and rectum (32%) [49].

Treatment

The treatment options for benign duodenal tumours are varied, but usually are done through endoscopic removal (only small polypoidal lesions) or, in cases of large tumours (> 2 cm), through surgical resection by laparotomy or laparoscopy. In the past, ampullary adenomas have been treated only surgically, by pancreaticoduodenectomy (the Whipple procedure) or by transduodenal ampullectomy, but these methods are associated with high morbidity, dehiscence, and fistulae.

Traditional procedures with local resections also can be performed, but the development of new surgical options (minimally invasive surgery (MIS), like laparoscopic or combined laparoscopic-endoscopic) has provided a breakthrough in minimally invasive duodenal tumour treatment [19]. The MIS method of treatment offers the following advantages: less pain, shorter time of recovery, earlier discharge, and more comfortable course of treatment.

Modern endoscopic techniques, like endoscopic mucosal resection (EMR), are developing rapidly and represent a helpful and alternative tool to surgical therapy in certain indications. Techniques of endoscopic removal of ampullary tumours are still inconsistent, but the term ampullectomy refers mostly to the surgical removal of the ampulla of Vater, which requires surgical connection of the bile and pancreatic ducts with the duodenal wall. In turn, the term papillectomy is reserved for the endoscopic resection of lesions at the major papilla. In some cases, endoscopic papillectomy is preceded by submucosal injection (epinephrine, fibrin glue injection, and viscous materials, to avoid bleeding), or the new technique of "underwater" EMR is used for the resection of ampullary adenomas without necessity of the submucosal injection.

Klein *et al.* performed a study with endoscopic resection of 106 adenomas higher than 10 mm with complete endoscopic excision in 96%, and intraprocedural bleeding in 43% of cases, connected with large lesion size. The authors emphasise that endoscopic resection of duodenal adenomas is a safe and effective alternative to surgery [50].

Other endoscopists report that small adenomas (smaller than 10 mm) may be removed by cold snare polypectomy (CSP), using a stiff thin-wire snare, and application of electrocautery should be used in case of polyps greater than 10 mm in size, while ablative methods such as argon plasma coagulation (APC) and 'hot-snare' polypectomy (HSP) technique should be limited due to the risk of delayed bleeding [51]. Another endoscopic technique is an endoscopic submucosal dissection (ESD) in the duodenum, which is not recommended by many endoscopists, due to higher (about 30%) risk of perforation [52].

Conventional tumour resection by surgical pancreaticoduodenectomy or ampullectomy is reserved for patients suspected of malignancy in duodenal tumour cases when the size is greater than 10 mm, and in another states such as the lack of endoscopic procedure modalities or experts [53].

Rare tumours, like gangliocytic paraganglioma, similarly to other periampullary neoplasms, usually have malignant potential, and endoscopic resection is the treatment of choice for tumours without evidence of metastasis, whereas pancreaticoduodenectomy is suggested for those with large tumour size, submucosal extent, or pancreatic GP [54].

Some authors suggest that endoscopic papillectomy, a feasible option for duodenal tumour resection, should be considered only in selected patients, because of the relatively high rate of procedure-related complications (haemorrhage, pancreatitis) [55].

The new modalities of the treatment, like ablative therapies (argon plasma coagulation, laser therapy, photodynamic therapy, monopolar or bipolar electrocoagulation), ultrasonic shears, staplers, and intracorporeal sutures are also increasingly used. In regard to submucosal benign tumours, endoscopic submucosal dissection (ESD) and full-thickness resection (FTR) excise these lesions, and endoscopic suturing is used to close large defects and perforations [56].

Generally, all researchers emphasise that all kinds of per oral endoscopic tumour resection (POET) are limited by the size, histopathological type, and location of the tumour [57].

To summarise, the treatment method for duodenal tumours should be selected individually, based on each patient's state, to prevent delayed complications, but with the reservation that ablative therapies should be used in cases of duodenal tumours, which were not attempted during previous snare resection [58, 59].

Conclusions

Benign duodenal tumours are infrequent and less common than malignant tumours, but they cover an extensive variation of pathologies. The diagnostic correctness rate of endoscopic biopsy is 62–85%, with a quite high false-negative rate. The most common symptoms of those tumours are abdominal pain and upper gastrointestinal bleeding. Regardless of the fact that they are rare, it is necessary to know about them for early recognition, especially with histological assessment, which plays a crucial diagnostic role with future therapeutic implications, and it is possible by classical endoscopy, single- or double-balloon enteroscopy and capsule endoscopy, which is a safe and convenient method for assessing the small intestine in these patients. Also, endoscopic ultrasound is a useful tool for finding submucosal involvement of these tumours. The treatment of benign duodenal tumours is done through endoscopic removal or, in cases of large tumours (> 2 cm), through surgical resection by laparotomy or laparoscopy, although the treatment method should be selected individually, based on each patient's state, to prevent delayed complications.

Conflict of interest

The authors declare no conflict of interest.

References

1. Terada T. Malignant tumors of the small intestine: a histopathologic study of 41 cases among 1,312 consecutive specimens of small intestine. Int J Clin Exp Pathol 2012; 5: 203-9.
2. Zheng W, Zihaid D, Shijie H, et al. Experience in clinical diagnosis and treatment of duodenal tumors. Mol Clin Oncol 2016; 5: 731-9.
3. Raymond P, Kerremans D, Lerut J, et al. Primary malignant duodenal tumors. Ann Surg 1979; 190: 179-82.
4. Ginsberg GG, Kochman ML, Norton I, et al. Kliniczna endoskopia przewodu pokarmowego. Vol. II. Nowak A, Nowakowska-Duława E. (eds. of Polish edition). Medipage, Warsaw 2009; 561-6.
5. Genta RM, Kinsey RS, Singhal A, et al. Gastric foveolar metaplasia and gastric heterotopia in the duodenum: no evidence of an etiologic role for Helicobacter pylori. Hum Pathol 2010; 41: 1593-600.
6. Latos W, Sieroń-Stołtny K, Kawczyk-Krupka A, et al. Clinical evaluation of twenty cases of heterotopic gastric mucosa of upper esophagus during five-year observation, using gastroscopy in combination with histopathological and microbiological analysis of biopsies. Contemp Oncol 2013; 17: 171-5.
7. Terada T. Heterotopic gastric mucosa of the gastrointestinal tract: a histopathologic study of 158 cases. Pathol Res Pract 2011; 207: 148-55.
8. Terada T. Pathologic observation of the duodenum in 615 consecutive duodenal specimens in a single Japanese hospital: II. malignant lesions. Int J Clin Exp Pathol 2012; 5: 52-7.
9. Yu L, Yang Y, Cui L, et al. Heterotopic gastric mucosa of the gastrointestinal tract: prevalence, histological features, and clinical characteristics. Scand J Gastroenterol 2014; 49: 138-44.
10. Chen HL, Chang WH, Shih SC, et al. Changing pat tern of ectopic pancreas: 22 years of experience in a medical center. J Formos Med Assoc 2008; 107: 932-6.
11. Huang YC, Chen HM, Jan YY, et al. Ectopic pancreas with gastric outlet obstruction: report of two cases and literature review. Chang Gung Med J 2002; 25: 485-90.
12. Fikatas P, Sauer IM, Mogl M, et al. Heterotopic ileal pancreas with lipoma and coexisting fibromatosis associated with a rare case of gastrointestinal bleeding. A case report and review of the literature. JOP 2008; 9: 640-3.
13. Mortelé KJ, Rocha TC, Streeter JL, et al. Multimodality imaging of pancreatic and biliary congenital anomalies. Radiographics 2006; 26: 715-31.

14. Christodoulidis G, Zacharoulis D, Barbanis S, et al. Heterotopic pancreas in the stomach: a case report and literature review. World J Gastroenterol 2007; 13: 6098-100.
15. Mulholland KC, Wallace WD, Epanomeritakis E, et al. Pseudocyst formation in gastric ectopic pancreas. JOP 2004; 5: 498-501.
16. Kim JH, Lim JS, Lee YC, et al. Endosonographic features of gastric ectopic pancreases distinguishable from mesenchymal tumors. J Gastroenterol Hepatol 2008; 23: e301-7.
17. Shin KN, Park YK, Suh HH, et al. Mesenchymal cell tumors of the gastrointestinal tract. J Korean Surg Soc 1998; 55: 84-91.
18. Lee EJ, Kim TD, Oh HA, et al. Is the invasive approach for all the upper gastrointestinal mesenchymal tumors necessary? Korean J Gastroenterol 2005; 45: 387-93.
19. Goh PMY, Lenzi JE. Benign tumors of the duodenum and stomach. In: Surgical treatment: evidence-based and problem-oriented. Holzheimer RG, Mannick JA (eds.). Zuckschwerdt, Munich 2001.
20. Genta RM, Feagins LA. Advanced precancerous lesions in the small bowel mucosa. Best Pract Res Clin Gastroenterol 2013; 27: 225-33.
21. Bourke MJ. Endoscopic resection in the duodenum: current limitations and future directions. Endoscopy 2013; 45: 127-32.
22. Jung JH, Choi KD, Ahn JY, et al. Endoscopic submucosal dissection for sessile, nonampullary duodenal adenomas. Endoscopy 2013; 45: 133-5.
23. Honda T, Yamamoto H, Osawa H, et al. Endoscopic submucosal dissection for superficial duodenal neoplasms. Dig Endosc 2009; 21: 270-4.
24. Kirmemış Ö, Çaltepe G, Süllü Y, et al. Diffuse circumferential hyperplasia of Brunner's glands causing obstruction in the duodenum in a 12-year-old child. Turk J Gastroenterol 2012; 23: 414-5.
25. Collaco AM, Jakab RL, Hoekstra NE, et al. Regulated traffic of anion transporters in mammalian Brunner's glands: a role for water and fluid transport. Am J Physiol Gastrointest Liver Physiol 2013; 305: 258-75.
26. Ramachandra S, Kuruvila S. Brunner's gland hamartoma. Indian J Pathol Microbiol 2012; 55: 113-4.
27. Arena M, Rossi S, Morandi E, et al. Brunner's glands hyperplasia: diagnosis with EUS-FNA for suspected pancreatic tumor involving the duodenum. JOP 2012; 13: 684-6.
28. Houwers JB, de Bie SH, Hofstee N. AIRP best cases in radiologic-pathologic correlation. Brunner gland hamartoma. Radiographics 2012; 32: 213-8.
29. Bastlein C, Decking R, Voeth C, et al. Giant Brunneroma of the duodenum. Endoscopy 1988; 20: 154-5.
30. Sakurai T, Sakashita H, Honjo G, et al. Gastric foveolar metaplasia with dysplastic changes in Brunner gland hyperplasia: possible precursor lesions for Brunner gland adenocarcinoma. Am J Surg Pathol 2005; 29: 1442-8.
31. Zhong YS, Shi Q, Wu HF, et al. Endoscopic resection for the treatment of duodenal Brunner's adenomas. J Laparoendosc Adv Surg Tech A 2012; 22: 904-9.
32. Kini JR, Kini H, Pai M, et al. Brunner's gland hamartoma and hyperplasia. Trop Gastroenterol 2010; 31: 121-3.
33. Ruys AT, Alderlieste YA, Gouma DJ, et al. Jejunal cancer in patients with familial adenomatous polyposis. Clin Gastroenterol Hepatol 2010; 8: 731-3.
34. Spigelman AD, Williams CB, Talbot IC, et al. Upper gastrointestinal cancer in patients with familial adenomatous polyposis. Lancet 1989; 2: 783-5.
35. Bülow S. Familial adenomatous polyposis. Ugeskr Laeger 2013; 175: 1335-9.
36. Plum N, May A, Manner H, et al. Small-bowel diagnosis in patients with familial adenomatous polyposis: comparison of push enteroscopy, capsule endoscopy, ileoscopy, and enteroclysis. Z Gastroenterol 2009; 47: 339-46.
37. Half E, Bercovich D, Rozen P. Familial adenomatous polyposis. Orphanet J Rare Dis 2009; 4: 22.
38. Leoz ML, Carballal S, Moreira L, et al. The genetic basis of familial adenomatous polyposis and its implications for clinical practice and risk management. Appl Clin Genet 2015; 8: 95-107.
39. Brucoli M, Giarda M, Benech A. Gardner syndrome: presurgical planning and surgical management of craniomaxillofacial osteomas. J Craniofac Surg 2011; 22: 946-8.
40. Cankaya AB, Erdem MA, Isler SC, et al. Oral and maxillofacial considerations in Gardner's syndrome. Int J Med Sci 2012; 9: 137-41.
41. Goldblum JR, Weiss SW, Folpe AL. Enzinger and Weiss's soft tissue tumors. 6th edn. Elsevier, Milton 2013: 289.
42. Brennan MF, Antonescu CR, Maki RG. Management of soft tissue sarcoma. Springer, New York 2013: 161.
43. Rutkowski P. Biblioteka chirurga onkologa. Mięsaki tkanek miękkich. Via Medica, Gdańsk 2015: 257.
44. Kawecki S, Nyk Ł, Szostek P, et al. Zwężenie moczowodu w następstwie guza włókniakowatego przestrzeni zaotrzewnowej. Post N Med 2016; 29: 831-5.
45. Fung AT, Pellegrini M, Shields CL. Congenital hypertrophy of the retinal pigment epithelium: enhanced-depth imaging optical coherence tomography in 18 cases. Ophthalmology 2014; 121: 251-6.
46. Silva CA, Moraes Pde C, Furuse C, et al. Gardner syndrome with no clinical family history. J Craniofac Surg 2009; 20: 1186-9.
47. Turina M, Pavlik CM, Heinimann K, et al. Recurrent desmoids determine outcome in patients with Gardner syndrome: a cohort study of three generations of an APC mutation-positive family across 30 years. Int J Colorectal Dis. 2013; 28: 865-72.
48. McGarrity TJ, Amos C. Peutz-Jeghers syndrome: clinicopathology and molecular alterations. Cell Mol Life Sci 2006; 63: 2135-44.
49. Utsunomiya J, Gocho H, Miyanaga T, et al. Peutz-Jeghers syndrome: its natural course and management. Johns Hopkins Med J 1975; 136: 71-82.
50. Klein A, Nayyar D, Bahin FF, et al. Endoscopic mucosal resection of large and giant lateral spreading lesions of the duodenum: success, adverse events, and long-term outcomes. Gastrointest Endosc 2016; 84: 688-96.
51. Ma MX, Bourke MJ. Management of duodenal polyps. Best Pract Res Clin Gastroenterol 2017; 31: 389-99.
52. Musumba C, Sonson R, Tutticci N, et al. Endoscopic submucosal dissection of a duodenal neuroendocrine tumor Gastrointest Endosc 2014; 79: 716.
53. Klein A, Ahlenstiel G, Tate DJ, et al. Endoscopic resection of large duodenal and papillary lateral spreading lesions is clinically and economically advantageous compared to surgery Endoscopy 2017; 49: 659-67.

54. Chiang CS, Shyr BU, Chen SC, et al. Periampullary gangliocytic paraganglioma. J Gastrointest Surg 2018 Dec 18. doi: 10.1007/s11605-018-4019-z. [Epub ahead of print]
55. Li S, Wang Z, Cai F, et al. New experience of endoscopic papillectomy for ampullary neoplasms. Surg Endosc 2019; 33: 612-9.
56. Chang KJ. Endoscopic foregut surgery and interventions: the future is now. The state-of-the-art and my personal journey. World J Gastroenterol 2019; 25: 1-41.
57. Chiu PWY, Yip HC, Teoh AYB, et al. Per oral endoscopic tumor (POET) resection for treatment of upper gastrointestinal subepithelial tumors. Surg Endosc 2019; 33: 1326-33.
58. Ochiai Y, Kato M, Kiguchi Y, et al. Current status and challenges of endoscopic treatments for duodenal tumors. Digestion 2019; 99: 21-6.
59. Chathadi KV, Khashab MA, Acosta RD, et al. The role of endoscopy in ampullary and duodenal adenomas. ASGE Standards of Practice Committee, Gastrointest Endosc 2015; 82: 773-81.

Received: 18.11.2018
Accepted: 3.03.2019