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REVIEW ARTICLE

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Gastric polyps: an update of their pathology and biological significance

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Abstract Gastric polyps are clinically important lesions that are frequently encountered in routine pathology (2–3% of all gastroscopies). Polyps may occur sporadically or in polyposis syndromes, such as familial adenomatous polyposis coli (FAP), Peutz–Jeghers syndrome, juvenile polyposis, Cowden's disease and Cronkhite–Canada syndrome. In biopsy specimens taken during routine gastroscopic examinations, it is almost always possible to differentiate between neoplastic and non-neoplastic polyps and to type polyps. In this review, we focus on the morphological spectrum of gastric polyps in an attempt to assist the pathologist and the gastroenterologist in recognising the lesion and in treating patients with gastric polyps, respectively. Further, we propose that the World Health Organization (WHO) classification should be modified to include the following categories: non-neoplastic polyps (WHO: tumour-like lesion), hamartomatous polyps/polyps of polyposis syndromes (WHO: tumour-like lesion), heterotopic tissue polyps (WHO: tumour-like lesion), neoplastic polyps (WHO: epithelial, non-epithelial and endocrine tumours) and reactive polypoid lesions.

Keywords Gastric polyps · Adenoma · Carcinoma · Non-neoplastic polyps

Introduction

Gastrointestinal polyps are by definition lesions elevated above the surrounding mucosa. In the stomach, they are found in 2–3% of all gastroscopic examinations [11]. Usually, they are between 1 cm and 2 cm in diameter. In most cases, polyps are an incidental finding during routine endoscopy, because they only rarely produce symptoms, such as gastrointestinal bleeding with or without anaemia or delayed gastric emptying.

Polyps in the stomach are a heterogeneous group of tumours that comprise non-neoplastic polyps, such as fundic gland polyps, neoplastic polyps, such as adenomas or adenocarcinomas, "reactive" polypoid lesions, such as foveolar hyperplasia and polypoid intramural masses. In contrast to the situation in the colon, most gastric polyps are non-neoplastic. Although the endoscopic appearance of some polyps may already be diagnostic, the final diagnosis must be based on a histological examination. This review describes polyps on the basis of a new classification that should assist the pathologist and the gastroenterologist in recognising the lesions and in treating patients with gastric polyps, respectively.

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Fundic gland polyps

Histologically, fundic gland polyps are characterised by a focal increase in the glandular elements of the mucosa, which usually show dilated glands forming small cysts lined with parietal and chief cells or occasionally mucinous cells (Fig. 1). Older names for this entity are fundic gland hyperplasia, Elster's gland cysts and cystic hamartomatous gastric polyp.

The pathogenesis of the fundic gland polyp is unknown. Fundic gland polyps may develop after a shift of the proliferation zone into the gland area. They may also be potentially reversible glandular dilations caused by changes in the secretory activity of the glands. Finally, some authors regard them as hamartomatous lesions. However, their occurrence in older patients and their potential reversibility make a hamartomatous nature unlikely.

Fundic gland polyps comprise up to 47% of all gastric polyps [67] and are completely harmless in virtually all cases [18]. As a rule, multiple small polyps in the fundus are fundic gland polyps. They present as multiple

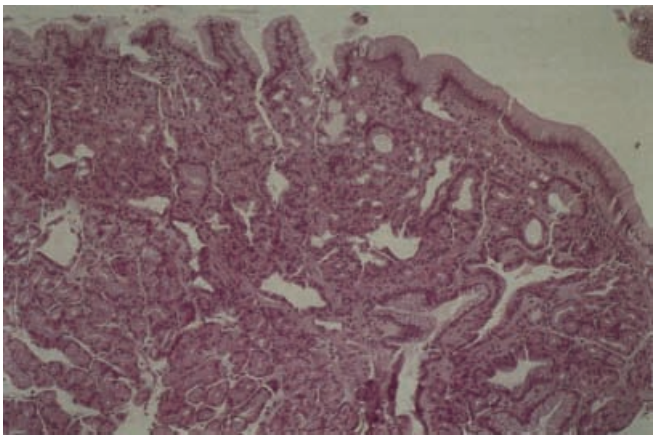

Fig. 1 Fundic gland polyp. The diagnostic histological finding is the occurrence of cysts within the fundic glands. In this case, most of them are lined by columnar epithelium. Haematoxylin and eosin; original magnification ×400

2–3 mm sessile lesions coating the body and fundus, which can be plucked like grapes with the biopsy forceps. A peculiarity of fundic gland polyps is that they almost always appear in healthy gastric mucosa or only in minimally chronic inactive gastritis in *Helicobacter pylori*-negative patients.

Most cases are sporadic. In the setting of familial adenomatous polyposis (FAP) or Gardener's syndrome [75], however, they occur in up to 53% of patients. In both syndromes, they have been observed as early as 8 years of age. In some patients, there is a gradual increase in the number of polyps, while in others, a decrease is observed. The additional development of adenomatous changes and dysplasia in fundic gland polyps has been found in 1% [80] of sporadic cases and in 25–44% of patients with familial adenomatous polyposis [2, 17, 80]. In one case report, the development of an adenocarcinoma within a fundic gland polyp in FAP was demonstrated [81]. Fundic gland polyps have also been found in patients receiving long-term therapy with proton pump inhibitors (PPI) [68]. The association is, however, probably incidental. In our material, we have found no difference in the frequency of *H. pylori*-negative patients under long-term treatment with PPI (5%) or in patients who are not receiving such therapy (5.1%; M. Stolte, personal observation).

Although the polyps themselves are non-neoplastic, it appears that they signal an increased risk in a patient of harbouring a colorectal adenoma or carcinoma. Eidt and Stolte found colorectal adenomas in 35.5% of cases and, if only patients younger than 40 years were considered, colorectal neoplasms were found in 60.7% of patients with fundic gland polyps [16]. Wörmann and Seifert reported colorectal neoplasms, again mainly adenomas, in up to 50% of these patients [62, 79]. Clearly, prospective studies are needed to support these retrospective studies and to determine whether fundic gland polyps can be considered marker lesions for colorectal neoplasms.

Endoscopically, these polyps may be difficult to differentiate from carcinoid tumours which, in a certain subgroup of patients (see endocrine tumours), are also small, often multiple and exclusively located in the corpus fundus region. However, carcinoid tumours are usually yellowish and have a firm consistency. Endoscopically, atrophic (autoimmune) gastritis with multiple persistent islands of oxyntic glands in the corpus mucosa may mimic fundic gland polyps. Histologically, atrophic gastritis is observed in biopsy specimens taken from non-polypoid areas of the stomach. The polypoid areas present as fundus mucosa with hyperplasia and hypertrophy of parietal cells in the biopsy specimens [14]. Finally, focal foveolar hyperplasia may resemble fundic gland polyps.

Hyperplastic polyps

Histologically, hyperplastic polyps are characterised by an elongation, twisting, branching and cystic dilatation of the foveolae. The surface is often eroded, and the epithelium may show regeneration that could be misinterpreted as adenomatous or dysplastic changes. True neoplastic change is not associated with these features and is usually more extensive than regenerative changes (Fig. 2). Regenerative epithelium is cuboidal, shows enlarged nuclei with distinct nucleoli and is often associated with ulceration and granulation tissue.

A bewildering variety of names have been used in the literature for hyperplastic polyps, including hyperplasiogenic polyps, regenerative polyps, hyperplastic-adenomatous polyps, adenomatous polyps and benign polyps. Hyperplastic polyps are among the most frequently observed gastric polyps and comprise 28–75% of all gastric polyps [12, 22, 61, 67]. This is dependent upon the authors' definition of hyperplastic polyps, because hyperplastic polyp and focal foveolar hyperplasia are considered by some authors to be a single entity. Hyperplastic polyps are usually solitary, sessile lesions less than 1.5 cm in size. They tend to be softer and "shinier" than the other polyps, and their surface is almost always eroded or may show central umbilication.

It is still a matter of debate whether focal foveolar hyperplasia is a precursor of hyperplastic polyps. Because hyperplastic polyps may contain neoplastic foci, this is an important issue. Militating against a relationship between focal foveolar hyperplasia and hyperplastic polyp is the fact that the former is found mainly in the antrum following healing of ulcerative or erosive lesions, whereas the latter is more commonly located in the body. The difference in shape of the epithelium, which is significantly taller in hyperplastic polyps, allows a differentiation between those two lesions in forceps biopsy material [69]. Furthermore, focal foveolar hyperplasia exhibits a lengthening of the foveolae, whereas hyperplastic polyps display architectural changes, such as a cystic dilation of the glands, widening of the stroma and an increase and hyperplastic bundling of smooth muscle cells [69].

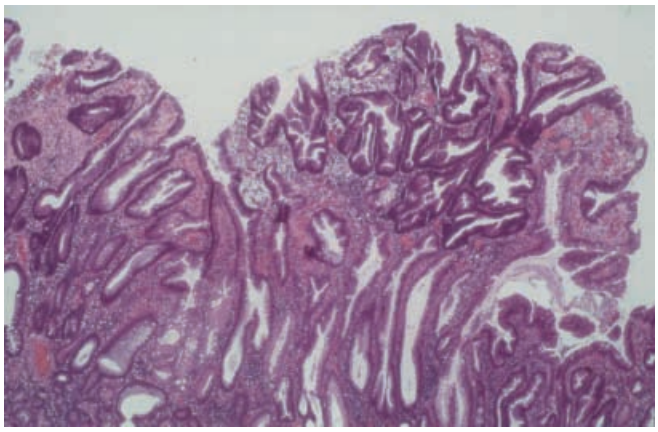

Fig. 2 Hyperplastic polyp. In the center of the polyp, bordering the luminal area, the epithelial cells show stratification of the nuclei. The glands are cribriform in appearance, suggesting the development of a highly differentiated adenocarcinoma. Haematoxylin and eosin; original magnification ×400

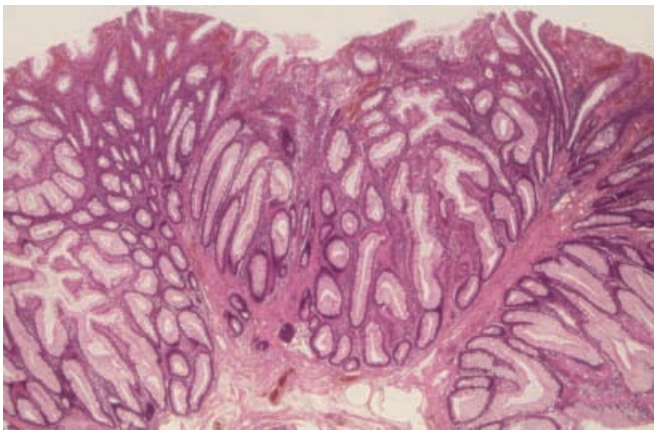

Fig. 3 A Peutz–Jeghers polyp with normal-appearing mucosa supported by tree-like branched muscularis mucosae. Haematoxylin and eosin; original magnification ×400

Although the hyperplastic polyp itself is non-neoplastic, dysplastic changes and/or gastric adenocarcinoma may develop within the lesion in rare cases [25]. The risk of developing an adenocarcinoma within a hyperplastic polyp ranges from 0–8% (mean 2.1%)[10, 67]. Therefore, hyperplastic polyps should be treated by means of polypectomy. Recently, it has been demonstrated that hyperplastic polyps may disappear after *H. pylori* eradication [51]. *H. pylori* eradication therapy may, therefore, be a therapeutic option for hyperplastic polyps occurring in association with *H. pylori* gastritis.

The risk of patients with multiple hyperplastic polyps of developing a gastric carcinoma appears to be increased and may be as high as 3.6% [69]. Reported percentages of up to 57% are probably too high [61]. Hyperplastic polyps develop in atrophic gastric mucosa in 40–75% of cases and may thus reflect the presence of atrophic gastritis [42]. It is possible that in many cases, the chronic atrophic gastritis, which is mostly the consequence of *H. pylori* infection, increases the risk of developing a gastric carcinoma.

Inflammatory fibroid polyp

Histologically, an inflammatory fibroid polyp is a mesenchymal tumour located in the deep mucosa and the adjacent submucosa. It is composed of loose connective tissue made up of reticular fibres that often show a characteristic onion-skin arrangement around vessels and an infiltration by eosinophilic granulocytes. The muscularis mucosae is often fragmented. On the surface, these polyps are frequently eroded. They account for 3% of gastric polyps [67] and are most likely a reactive lesion developing after focal damage to the mucosa and muscularis mucosae. Their content of $CD117^+$ ($c\text{-}kit^+$) and $CD34^+$ cells suggests that they may originate from interstitial cells of Cajal [36]. They neither undergo malignant change nor recur after removal [65]. The most common location of this polyp is the distal stomach, where it may obstruct the pylorus. Some patients suffer from bleeding from the eroded surface of the polyps.

Hamartomatous polyps and polyps associated with polyposis syndromes

Peutz–Jeghers polyps

Peutz–Jeghers polyps (PJPs) are histologically characterised by normal mucosa supported by tree-like branched muscularis mucosae (Fig. 3; Table 1). PJPs may be as small as 1–2 mm and are therefore easily overlooked in forceps biopsy material. PJPs are rare (0.3% of gastric polyps). Usually, they are a manifestation of the Peutz–Jeghers syndrome (PJS), but they may also occur sporadically. In exceptional cases, dysplasia or invasive adenocarcinoma develop in these polyps.

PJS is a dominantly inherited genetic trait characterised by gastrointestinal polyposis and mucocutaneous pigmentations involving mainly the perioral skin, gums and buccal mucosa. Gastric polyps occur in approximately 49% of these patients [73]. Recently, it was found that most patients with PJS have a mutation in the serine/threonine kinase gene, which is located at 19q13.3 [26, 52] and encodes LBK1/STK11. The clinical presentation of PJS includes colicky abdominal pain due to intestinal obstruction and anaemia caused by gastrointestinal bleeding. Patients suffering from PJS have an increased risk of developing intestinal and extraintestinal carcinomas at a relatively young age. The extraintestinal carcinomas comprise some unusual forms, including ovarian sex-cord tumour with annular tubules, minimal deviation adenocarcinoma (adenoma malignum) of the cervix, Sertoli cell tumour of the ovary and feminising Sertoli cell tumour of the testes.

Table 1 Differential diagnosis of non-neoplastic gastric polyps. *FFH* focal foveolar hyperplasia, *PRM* polypous regenerative mucosa, *HP* hyperplastic polyp, *JP* juvenile polyp, *PJP* Peutz–Jeghers polyp, *CCP* Cronkhite–Canada polyp

	FFH	PRM	HP	JP	PJP	CCP
Size	~0.5 cm	~0.5 cm	~1 cm	~1 cm	2–3cm	0.5–2cm
Polyposis	–	–	Rarely	Frequently	Frequently	Frequently
Foveolar epithelium	Normal	Regenerative	Taller than normal	Normal	Normal	Normal
Foveolar architecture	Elongated, winding	Elongated, winding, cystic	Irregular, branching	Elongated, multiple cysts	Often only elongated, rarely cysts	Cystic
Lamina propria	Normal or edematous/ fibrotic	Normal or edematous/ fibrotic	Moderately broadened, capillaris, focal fibrosis	Abundant loose stroma	Normal	Broadened through strong edema
Smooth muscles	Normal or slightly increased	Normal or slightly increased	Moderately increased, irregular	Normal	Tree-like branching	Normal or slightly increased
Colonoscopy	–	–	Often adenomas	JP	PJP	CCP

Juvenile polyps

Juvenile polyps are histologically characterised by abundant loose stroma and by elongated, rarely cystic mucinous glands (Table 1). Juvenile polyps can occur sporadically and in the juvenile polyposis syndrome (JPS). In JPS, an autosomal dominant trait is recognised in 20–50% of patients [13]. JPS [28] usually affects the colon (i.e. juvenile polyposis coli) and infrequently the stomach and small intestine, the latter termed "generalised juvenile gastrointestinal polyposis" [28]. Juvenile polyposis may also be limited to the stomach (i.e. juvenile polyposis of the stomach [76]). The gastric polyps are usually multiple.

The risk for patients with JPS of developing a gastrointestinal malignancy ranges between 9% [33] and 17% [29] and may be as high as 55% [30]. Juvenile polyposis is therefore considered a precancerous condition. There is evidence of genetic heterogeneity in JPS. Some families have mutations in PTEN (phosphatase and tensin homologue deleted on chromosome 10) located at 10q23.3 [43], others in DPC4 (deleted in pancreatic carcinoma locus 4)/SMAD4 (small mothers against decapentaplegic deleted in pancreatic carcinoma, locus 4) located at 18q21 [31, 78]. Interestingly, the molecular changes causing JPS may involve the subepithelial mesenchymal stroma cells and not the epithelium [37].

In patients with JPS, the most striking clinical feature is anaemia (89%), probably resulting from disturbed iron uptake and blood loss and hypoproteinaemia (67%). Affected individuals may present in childhood with rectal bleeding, anaemia and anal prolapse of a polyp. In affected family members, sphincter-sparing proctocolectomy has been advocated to remove much of the organ at risk [59], with the exception of patients with only a few polyps. Regular endoscopic polypectomy (upper and lower endoscopy), with surgery reserved for patients with abundant polyps, dysplastic changes in juvenile polyps or those with gastrointestinal bleeding, has also been proposed [30].

Cowden's disease polyps

Cowden's disease polyps are composed of distorted non-neoplastic mucosa, which is often inflamed or fibrotic or contains excessive smooth muscle in the centre. The histology of gastric polyps has not been described in detail [27, 77]. Cowden's disease (CD) [54] is also known as multiple hamartoma syndrome. It is a rare genodermatosis with an autosomal dominant inheritance pattern, but 60% of the patients diagnosed are female [19]. CD is considered to arise in patients with a mutation of the tumour suppressor gene PTEN [50] at 10q23. It is characterised by cutaneous trichilemmomas, oral mucosal papillomas and gastrointestinal polyps. The patients have an increased risk of breast and thyroid carcinoma. The incidence of gastrointestinal polyps is estimated to be close to 75% of patients.

Cronkhite–Canada polyps

Gastric Cronkhite–Canada polyps (Fig. 4) are sessile and composed of focally dilated irregular foveolar glands within a lamina propria expanded by oedema and often an inflammatory infiltrate. The majority of polyps contain smooth-muscle fibres in the lamina propria. A minority has surface erosions [3]. In the stomach, there is no reliable feature for distinguishing Cronkhite–Canada polyps from juvenile polyposis or hyperplastic polyps [3]. In contrast to Cronkhite–Canada polyps, hyperplas-

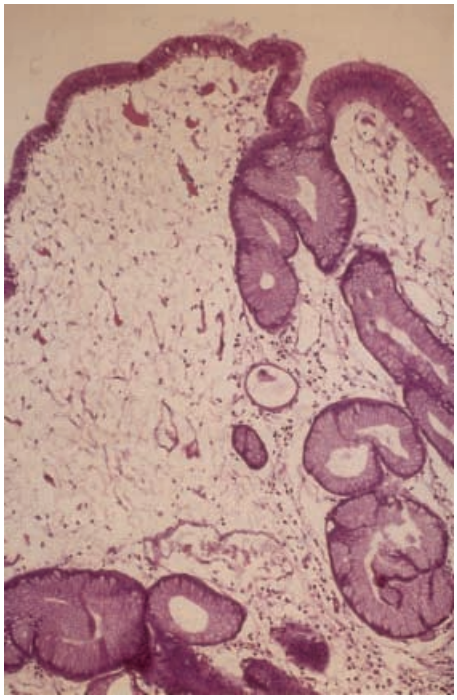

Fig. 4 A Cronkhite–Canada polyp with normal-appearing surface epithelium and a lamina propria expanded by oedema. Haematoxylin and eosin; original magnification ×400

tic polyps show a greater tendency toward surface erosion and pedunculation (Table 1).

In 1955, Cronkhite and Canada described the syndrome of multiple gastrointestinal polyps, onycholysis, alopecia and skin hyperpigmentation [7]. The onset of symptoms occurs at the mean age 59 years. The disorder is apparently not hereditary. Cronkhite–Canada polyps are rare (0.1% of gastric polyps), developing anywhere in the gastrointestinal tract. Patients have multiple polyps ranging from five to innumerable [3]. So far, they have not been observed to undergo malignant degeneration. Cronkhite–Canada polyposis has, in rare cases, been associated with adenocarcinoma of the colon [55].

Heterotopic tissue polyps

Pancreatic heterotopia

Pancreatic heterotopia is defined by the presence of islands of pancreatic tissue in the mucosa, submucosa and muscularis. Adenomyoma resembles pancreatic heterotopia without pancreatic acini, i.e. it consists of ducts surrounded by muscles of the muscularis. Both conditions are benign. Occasionally, pancreatic heterotopia and its probable relative, adenomyosis of the stomach, can present as polypoid lesions. They are found in the antrum and may lead to pyloric outlet obstruction.

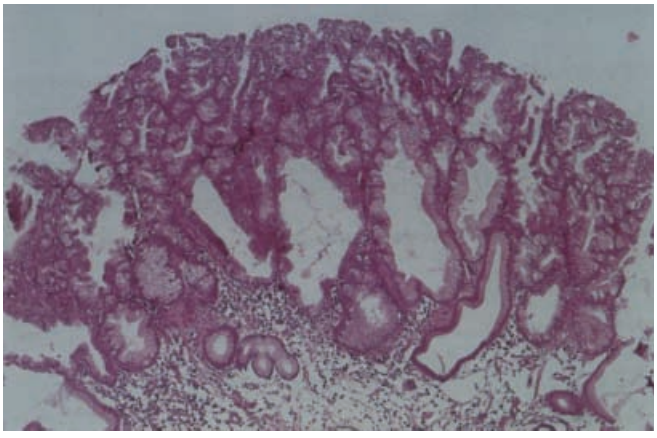

Fig. 5 A pyloric gland adenoma composed of small tubules lined by gastric-type epithelium. Haematoxylin and eosin; original magnification ×400

Brunner's gland heterotopia

Brunner's gland heterotopia is found mainly (in 81%) in the prepyloric antrum [67]. Usually, it is less than 1 cm in diameter and is not associated with any risk of malignancy.

Neoplastic polyps

Adenomas

Histologically, adenomas are characterised by columnar epithelium that is pseudostratified and shows elongated atypical nuclei and increased mitotic activity. Adenomas represent approximately 10% of gastric polyps [67]. In 60%, they are antral, sessile, solitary and eroded. The distribution of adenomas reveals no gender preference. Adenomas appear in tubular, tubulovillous and villous forms or as pyloric gland adenoma (Fig. 5). In the "Western" literature, flat tubular adenomas are frequently called dysplasia, a term we do not encourage, because all types of adenomas present endoscopically as a circumscript lesion that can be clearly identified as an adenoma. In biopsy specimens, adenoma/dysplasia is often graded as low-grade or high-grade. This should not, however, influence the clinical decision to remove the lesion, because carcinomas may develop focally and may not be detected by biopsy.

The presumptive endoscopic diagnosis of gastric tubular adenoma is relatively certain, since this lesion is mainly found in the form of a flat, only slightly elevated polyp. This type can also present as tiny elevations or flat and depressed areas [49]. The tubulovillous-type of adenoma is a rare lesion and presents as a large polyp. Villous adenomas are sessile and tend to cover large areas of the gastric luminal surface. Pyloric gland adenomas are rare, with an incidence of 2.7% among gastric polyps (M. Stolte, personal observation). They originate

preferentially in the corpus/fundus mucosa. Histologically, they are composed of small tubules lined by gastric-type epithelium. Immunohistologically, they express foveolar mucin M1 and deep gastric mucin M2 [41]. It appears that most of them cover large areas of the gastric lumen [58] and have a mean diameter of 16.5 cm. Gastric adenocarcinoma may be found in up to 21% of cases (M. Stolte, personal observation).

Adenomas are precancerous lesions, comparable to colonic adenomas. Therefore, high-grade dysplasia and frank carcinoma may develop in adenomas. The incidence of carcinomas within adenomas varies greatly, ranging from 3.4% [46] to 11% [35] or up to 75% [48]. The risk of developing adenocarcinoma in an adenoma correlates with its size and structure. Polyps more than 2 cm in diameter may harbour a focal adenocarcinoma in 40% of cases. In a study by Nakamura and Nakano, focal adenocarcinomas were found in 5.9% of flat tubular adenomas and in 33.3% of villous and tubulovillous adenomas [48], further supporting the concept that the type of adenoma indicates its risk. Also, gastric adenomas are a marker for an increased risk of the remainder of the stomach to develop a gastric carcinoma. According to the literature, coincident gastric carcinomas occur at a rate of 8–59% [35, 57]. Gastric adenomas are found in familial adenomatous polyposis (FAP) and Gardener's syndrome or the hereditary flat adenoma syndrome [44].

Gastric polyps and FAP

FAP is inherited as an autosomal dominant trait characterised by the development of multiple adenomatous polyps of the colon. The syndrome is caused by mutations of the APC (adenomatous polyposis coli) gene, a tumour suppressor gene found on the large arm of chromosome 5 [24]. Depending on the class of APC mutations, specific phenotypes are observed, such as the attenuated form, Gardener's syndrome (i.e. adenomatous polyposis coli in combination with osteomas of the skull, epidermal cysts, soft tissue tumours and extracolonic tumours) and a subgroup of patients with Turcot syndrome (combination of brain tumours and adenomatous polyps).

Fundic gland polyps are found in 13% [71] to 53% [34] of patients with FAP; adenomas, which are more common in the antrum, are found in 6–12% [15, 34]. Gastric carcinoma seems to develop from adenomas. In one series of patients, it occurred in 0.6% [32]. It occured in 2.1% in another series of patients [72].

Gastric polyps and hereditary flat adenoma syndrome

Hereditary flat adenoma syndrome [1, 47] is a colorectal cancer-prone disorder that is inherited as an autosomal dominant trait. It is characterised by a predisposition to multiple colonic adenomas (usually less than 100), with proximal predominance and a flat rather than polypoid growth pattern. In the stomach, most patients show fundic gland polyps and adenomas. Periampullary epithelial neoplasias develop in a few patients only [45].

Polypoid gastric carcinoma

Gastric adenocarcinomas may develop as polypoid lesions (Bormann type A) and are differentiated into type I (protruded, polypous type) and type IIa (flat elevated type). Probably many of these polypoid carcinomas originate from adenomas (see above).

Polypoid endocrine tumours

Polypoid endocrine tumours (Table 2) are neoplastic lesions and comprise 1.7% of gastric polyps [67], with up to 90% found in the gastric body. The prognosis of polypoid endocrine tumours is based on pathogenesis, size and histology. Endocrine tumours may develop in atrophic autoimmune gastritis and in Zollinger-Ellison syndrome (ZES) induced by elevated gastrin levels [56] or as sporadic tumours. It has been proposed to draw the line between well-differentiated neuroendocrine microtumours and their precursors (hyperplasia and dysplasia) at a size of 0.5 mm [63]. The risk of developing metastasis is influenced by the underlying cause of neuroendocrine tumour formation. In autoimmune gastritis (AIG), neuroendocrine tumours are considered harmless in essentially all cases and may therefore be treated by follow-up or polypectomy. The prognosis for patients with ZES/MEN1, who have a genetic defect (MEN1) [9], is good, but there is an increased risk for developing metastases in lesions larger than 1 cm. Sporadic neuroendocrine tumours are considered malignant if they are larger than 1 cm. Therefore, if endocrine tumours are found in a gastric biopsy specimen, the remainder of the gastric mucosa must be investigated histologically in order to properly classify the risk associated with the lesion. All in all, non-functioning and well-differentiated neuroendocrine tumours that measure up to 1 cm in size and are confined

Table 2 Clinicopathological classification of endocrine tumours of the stomach [38, 40]

Well-differentiated endocrine tumour (carcinoid)
Benign behaviour: non-functioning, confined to mucosa–submucosa, non-angioinvasive, ≤1 cm in size; association (body/fundus region only) with hypergastrinemia (autoimmune gastritis, MEN1)
Uncertain behaviour: like well-differentialted endocrine tumour with benign behaviour but >1 cm in size or angioinvasive enterochromaffin-like (ECL)-cell tumours, sporadic carcinoid
Well-differentiated endocrine carcinoma (malignant carcinoid): Extending beyond submucosa, angioinvasive or metastasis
Poorly differentiated endocrine carcinoma (small cell carcinoma, high-grade malignant)

to the mucosa or have invaded only the muscularis mucosa and lack frank cytological atypia have been shown to behave benignly [4, 38, 39, 40].

Mesenchymal tumours

Mesenchymal polypoid tumours are characterised by a spindle cell or epitheloid appearance. Most of them are classified as gastrointestinal stroma tumours (GIST) on the basis of their immunohistological positivity for c-kit$^+$ (=CD117) and/or CD34$^+$. The c-kit expression suggests an origin from the interstitial cells of Cajal, which are the gastrointestinal pacemaker cells. GISTs may also show areas with smooth muscle cell (expression of smooth muscle actin and, rarely, desmin) or neurogenic (S-100$^+$ and NSE$^+$) differentiation. Their malignant potential is difficult to assess. Generally, tumours with a diameter less than 5 cm, fewer than two mitoses/10 HPF and a lack of necrosis are held to have no or only a low malignant potential [21, 70]. The remainder is considered high risk GIST. Local excision with a margin of approximately 2 cm is regarded as sufficient therapy.

Leiomyomas can be observed in 0.9% of gastric resection specimens [5]. They are asymptomatic and are found incidentally at endoscopy, surgery or autopsy. When they are symptomatic, bleeding is the most common problem. Rarely, leiomyosarcomas may develop in lesions greater than 2–3 cm in diameter. When ten mitotic figures are found per 50 HPF, the lesion is considered to be a leiomyosarcoma [8].

Lipomas, haemangiomas, lymphangiomas, glomangiomas, osteomas, osteochondromas, granular cell tumours and neurogenic tumours are very rare. The latter are differentiated into tumours of Schwann cells [neurinoma (also called neurilemmoma and Schwannoma) and neurosarcoma], tumours of the autonomic nerve plexus (gastrointestinal autonomic nerve cell tumour, GANT) and neurofibromas. A case of gastric polyposis caused by multifocal histiocytosis X has also been reported [74].

Mucosa-associated lymphoid tissue lymphomas

Very rarely, gastric mucosa-associated lymphoid tissue (MALT) lymphomas may present as a polypoid lesion [64]. In the majority of cases, however, MALT lymphomas spread over a large area and present with a variegated appearance with erosions, ulcers, thickened folds, scars and regenerating mucosa [66].

Reactive polypoid lesions

Focal foveolar hyperplasia

Histologically, focal foveolar hyperplasia reveals lengthening of the foveolae with a normal content in mononuclear leukocytes in the lamina propria and a normal architecture. Endoscopically, focal foveolar hyperplasia usually presents as multiple small-sized polyps with an intact surface. This is a regenerative residual change subsequent to the healing of an erosion. The lesion is harmless (see “Hyperplastic polyps”).

Lymphoid follicles

Histologically, lymphoid follicles are found in the deep mucosa. Endoscopically, they may present as polypoid lesions. In most cases, lymphoid follicles are small in size and are found in patients infested with *H. pylori*, where they give the mucosa a so-called goose pimple appearance.

Gastritis varioliformis (gastritis en nappe)

Chronic erosions of the gastric mucosa may present as multiple polyps, mostly with a central erosion lining gastric folds. They occur in the gastric body and fundus. The underlying disease is lymphocytic gastritis, which is in most cases induced by *H. pylori*. After eradication therapy, the polyps may vanish (M. Stolte, personal observation).

Gastritis cystica profunda

Histologically, gastritis cystica profunda is readily recognised, because it is composed of mucosa with cystically dilated glands. Grossly, this polypoid lesion is the result of mucosa displaced into the submucosa. The lesion is harmless.

Conclusions

We propose classifying gastric polyps according to the categories listed in Table 3. Recommendations for diagnosis and treatment of gastric epithelial polyps are controversial, mostly because there is no consensus with respect to their malignant potential and the reliability of endoscopic forceps biopsy [6, 53, 60].

Forceps biopsy sampling may provide inadequate tissue for correct histologic diagnosis even in polyps smaller than 2 cm in diameter. In hyperplastic polyps, biopsy sampling may be misleading because areas of focal carcinoma are missed [20, 23, 60]. The incidence of local recurrence of gastric polyps after snare biopsy is low (0–7.5%) and is most often attributed to incomplete primary polyp removal [12, 22].

In a recent study (Muehldorfer S et al., unpublished), there was complete agreement between the histologic diagnosis of forceps biopsy and the final diagnosis of the polypectomy specimen in 55.8% (124 polyps). In an additional 34.7%, the clinically important distinction between neoplastic and non-neoplastic polyps was made

Table 3 Modified World Health Organization classification of gastric polypoid. *GIST* gastrointestinal stroma tumour, *MALT* mucosa-associated lymphoid tissue

Gastric polyploid classification
Non-neoplastic polyps
Fundic gland polyp
Hyperplastic polyp
Inflammatory fibroid polyp
Hamartomatous polyps/polyps of polyposis syndromes
Peutz–Jeghers polyp
Juvenile polyp
Cowden's disease polyp
Cronkhite–Canada polyp
Heterotopic tissue polyps
Heterotopic pancreas and adenomyomatous hamartomas
Brunner's gland heterotopia
Neoplastic polyps
Epithelial benign
Tubular adenoma
Tubulopapillary adenoma
Papillary adenoma
Pyloric gland adenoma
Epithelial malignant
Adenocarcinoma
Endocrine
Neuroendocrine tumours
Mesenchymal benign
GIST, leiomyoma, neurinoma, neurofibroma, granular cell tumour, lipoma
Mesenchymal malignant
Malignant GIST, neurosarcoma, fibrosarcoma, leiomyosarcoma
Lymphoid
Polypoid MALT lymphoma
Reactive polypoid lesions
Foveolar hyperplasia
Lymphoid follicles
Gastritis varioliformis
Gastritis cystica profunda

correctly. In 9.5%, a significant discrepancy was seen. However, when an experienced reference pathologist reviewed the cases, relevant differences remained in only 2.7%. Therefore, forceps biopsy was considered sufficient for a diagnosis in the majority of patients.

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