Neoplasia of the Stomach

- Gastric adenocarcinoma accounts for more than 90% of malignant lesions of the stomach.
- Besides this entity, numerous neoplastic lesions with malignant or benign characteristics as well as lesions with uncertain malignant potential occur.
- Other types of neoplasia of the stomach include gastric polyps, gastrointestinal stromal tumors, gastric lymphoma and neuroendocrine neoplasia.

Practical Implications

- Presenting with a broad spectrum of symptoms, ranging from unspecific abdominal discomfort to gastrointestinal bleeding or symptoms of gastric outlet obstruction, different rare neoplastic lesions of the stomach with demand of specific diagnostic and therapeutic work-up occur.

- Diligent endoscopic evaluation of the entire gastric mucosa, preferably by high-definition endoscopy techniques, is essential in addition to histopathological examination of lesional and surrounding tissue.

Gastric tumor entities

Epithelial tumors	**Non-epithelial tumors**
Adenoma with intraepithelial neoplasia	Leiomyoma
Carcinoma	Schwannoma
Adenocarcinoma	Granular cell tumor
Intestinal type	Glomus tumor
Diffuse type	Leiomyosarcoma
Papillary adenocarcinoma	**GIST**
Tubular adenocarcinoma	Kaposi sarcoma
Mucinous adenocarcinoma	**Malignant lymphomas**
Signet-ring cell carcinoma	Marginal zone B-cell lymphoma of MALT type
Adenosquamous carcinoma	Mantle cell lymphoma
Squamous cell carcinoma	Diffuse large B-cell lymphoma
Undifferentiated carcinoma	**Secondary tumors**
Neuroendocrine neoplasms	

Gastric Polyps

- In approximately 6% of asymptomatic patients undergoing esophagogastroduodenoscopy in the United States gastric polyps are detected.

- The majority of gastric polyps are fundic gland polyps (77%), followed by hyperplastic polyps (17%), adenomas (0.69%) and inflammatory fibroid polyps (0.1%). Only 2% of gastric polyps are diagnosed as malignant neoplasia.

- Hyperregenerative epithelium can result in the development of hyperplastic polyps.

- These conditions are observed in chronic inflammatory stimuli like *Helicobacter pylori* infection, adjacent mucosa to gastric ulcer or near gastroesophageal or gastrointestinal anastomoses.

- . Advanced endoscopy techniques allow the differentiation of hyperplastic polyps due to their typical surface.

- The risk of malignancy increases with the size of these polyps. Polyps >1 cm as well as pedunculated polyps carry a higher risk. The diagnostic assessment should include gastric biopsies from the surrounding mucosa. *H. pylori* should be eradicated.

- Hyperplastic polyps exceeding a size of 0.5 cm should be resected, preferably during endoscopy, allowing for histopathological examination of the resected tissue

- Fundic gland polyps are the most common polyps and frequently occur in association with long-term proton pump inhibitor therapy (four-fold increase) or gastrinoma.

- The majority of these neoplasias are sporadic, whereas a minority occurs in patients with familial adenomatous polyposis, with polyposis syndromes, with MUTYH-associated polyposis and with gastric adenocarcinoma and proximal polyposis of the stomach.

- While sporadic fundic gland polyps and fundic gland polyps in association with long-term proton pump inhibitor therapy are without risk, somatic APC mutations are detectable in >70% of fundic gland polyps associated with polyposis syndromes.

- Patients with >20 fundic gland polyps, young onset of the polyps (<40 years), additional duodenal adenomas and fundic gland polyps in other regions than the gastric corpus are under suspicion for familial adenomatous polyposis.

- A colonoscopy is recommended in these patients. Furthermore, few case reports of fundic gland polyposis with gastric adenocarcinoma have been published.

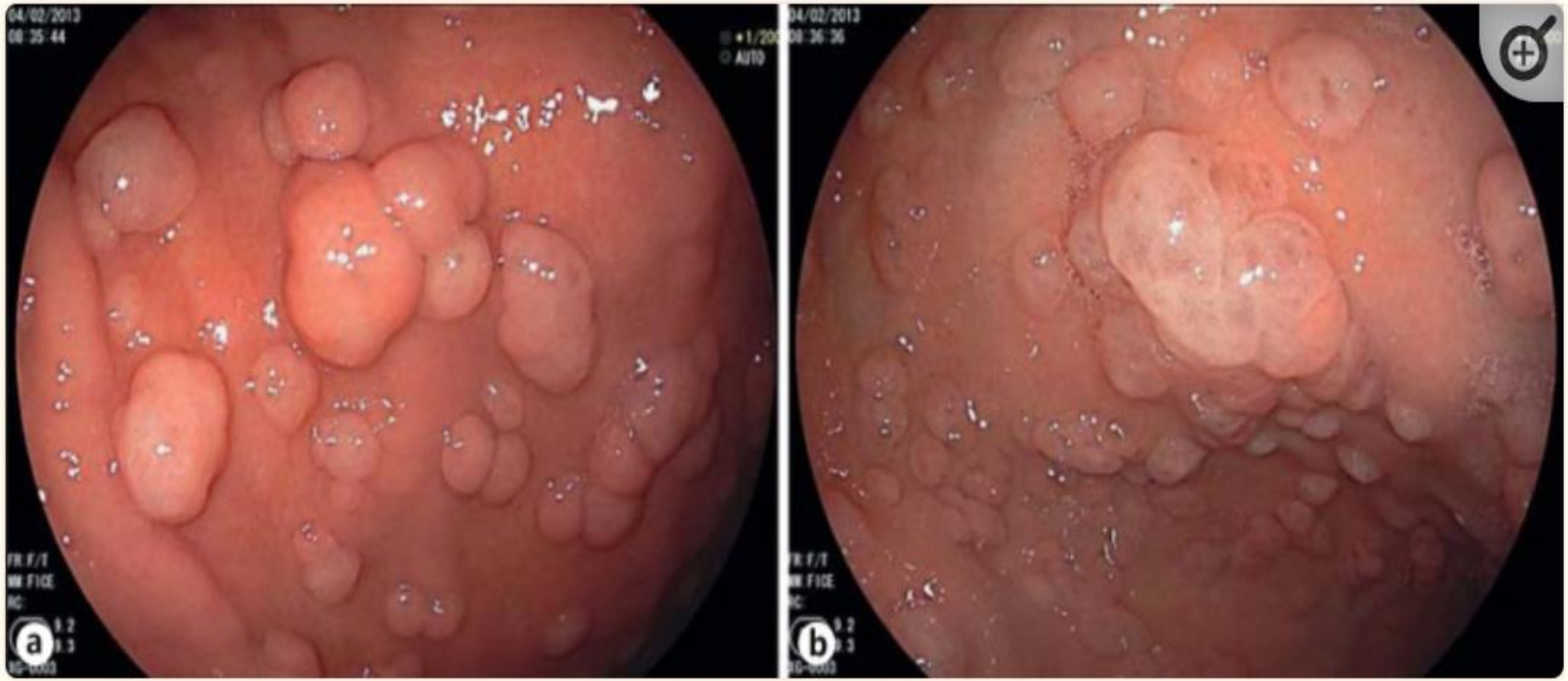


Fig. 1

a Fundic gland polyps. **b** Fundic gland polyps and adenoma.

- Gastric adenoma is the most frequent neoplastic lesion of the stomach.

- These neoplasias occur mostly isolated and located in the distal stomach and are less frequently associated with familial adenomatous polyposis than fundic gland polyps.

- 8-59% of gastric adenomas are associated with gastric cancer, therefore the entire stomach has to be examined diligently.

- Due to their malignant potential, all gastric adenomas should undergo endoscopic resection and follow-up

Endoscopic features of gastric polyps

	Hyperplastic polyps	Adenomas	Fundic gland polyps
Macroscopy	most frequently in the antrum, often multiple, usually smooth, dome-shaped, 0.5 – 1.5 cm in diameter; large hyperplastic polyps often become lobulated and pedunculated, and the surface epithelium is typically eroded	Velvety lobulated appearance, usually solitary; located more often in the antrum	multiple, small (<1 cm), appear smooth, glassy, and sessile

Gastrointestinal Stromal Tumors

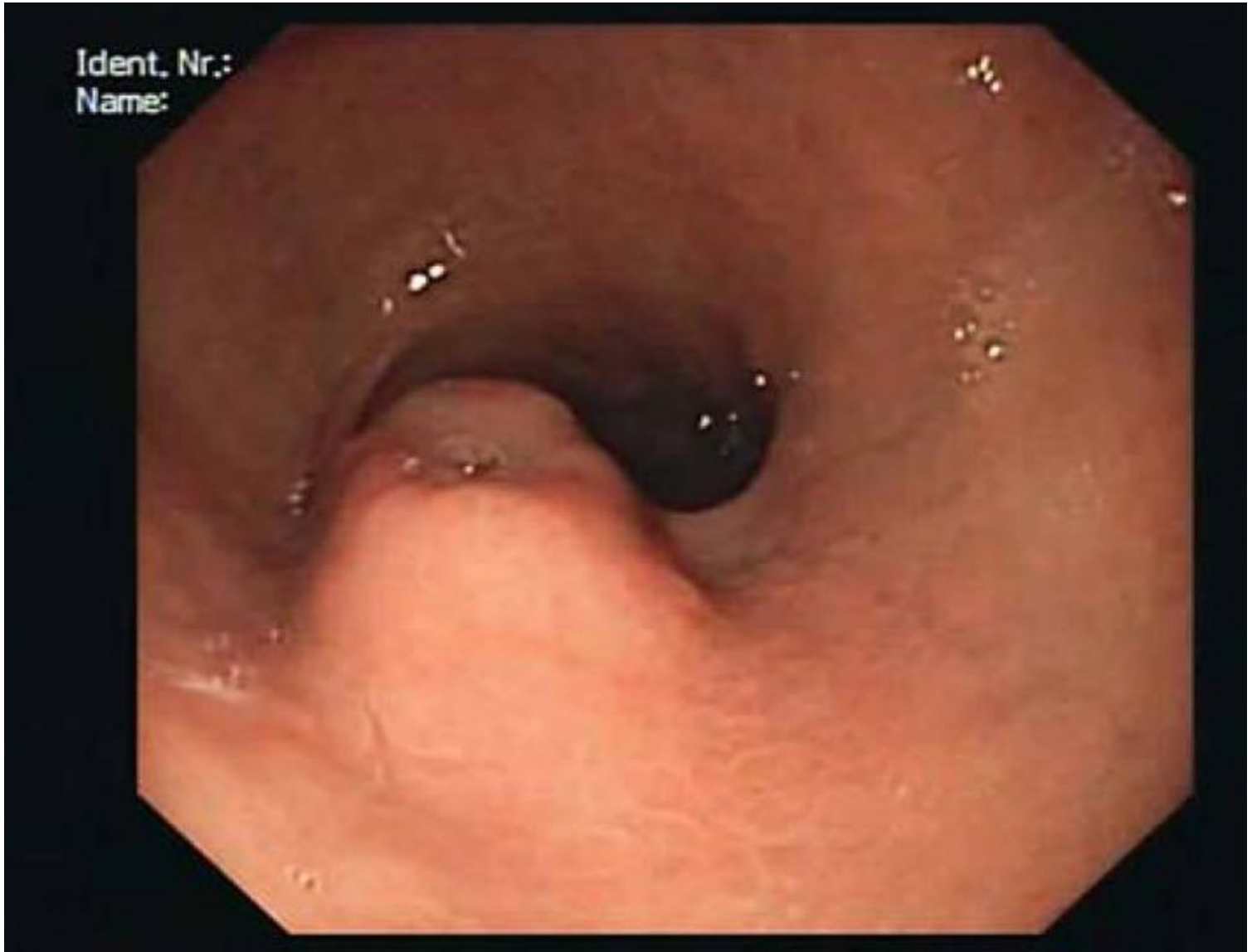
- Mesenchymal tumors typically present as subepithelial neoplasms.
- GISTs are the most prevalent entity.
- Other significantly less frequent gastric mesenchymal tumors are leiomyoma, leiomyosarcoma and schwannoma.
- Histologically, GISTs are characterized by spindle cell, epithelioid or rarely pleomorphic tumors arising from the interstitial cells of Cajal or their precursors.
- In the majority of these cases they are driven by mutations in KIT and/or PDGFRA receptor tyrosine kinases. Less common oncogenic driver mutations include NF1, BRAF and succinate dehydrogenase mutations [10]. The classification of GISTs evolved significantly during the past decades.

- The diagnosis is based on conventional pathology together with immunohistochemical staining of characteristic marker proteins. c-KIT (CD117) is constitutionally expressed in 95% of all GISTs. DOG1 is useful in the diagnosis of KIT-negative GISTs .

- Due to the changes in the diagnostic pathways, the prevalence of GISTs decreased by exclusion of many neoplasias formerly considered to be GISTs. In the Surveillance, Epidemiology, and End Results database of the National Cancer Institute of the United States, GISTs are responsible for 2.2% of malignant gastric tumors without any gender preference (male:female 1.1:1).

- The predilected age groups are in the 6th to 8th decade. 60-70% of GISTs are located in the stomach, followed by the midgut (20-30%) and the esophagus and lower gastrointestinal tract (10%)

Gastric GIST

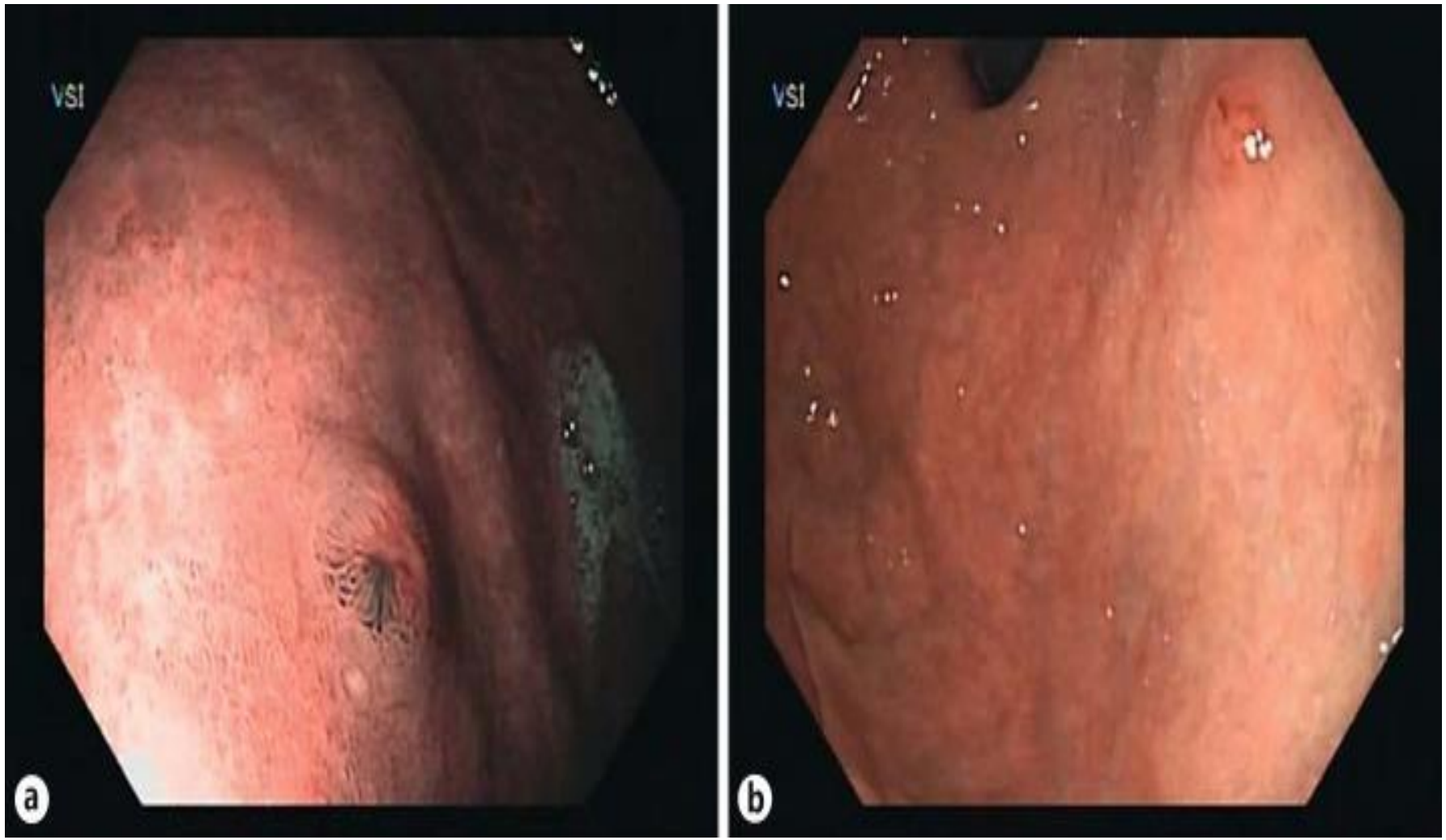


Neuroendocrine Tumors of the Stomach

- The incidence of neuroendocrine tumors (NETs) is constantly rising .
- Gastric NETs show an additional increase in proportional incidence compared to all NETs of the gastroenteropancreatic system, accounting now for about 6-23% of gastrointestinal NETs .
- It is not clear whether this is a consequence of rising numbers esophagogastroduodenoscopies performed with increasing awareness of these lesions or a true incidence effect.
- Although the majority of gastric NETs have a benign course and asymptomatic behavior, a subgroup has the potential to become aggressive and mimic the clinical course of gastric adenocarcinoma .
- In general, all NETs have malignant potential. In the stomach, three distinct types of neuroendocrine neoplasms are distinguished from each other.

Features of gastric NETs according to [20]

Feature	Type 1	Type 2	Type 3
Proportion among gastric neuroendocrine neoplasms	70 – 80%	5 – 6%	14 – 25%
Macroscopic aspect	often small (<1 – 2 cm), 78% polypoid, 65% multiple	often small (<1 – 2 cm), polypoid and multiple	unique, large (>2 cm), polypoid, ulcerated
Pathological differentiation	often NET G1	NET G1 –G2	NEC G3
Proportion of metastases	2 – 5%	10 – 30%	50 – 100%
Associated conditions	chronic atrophic gastritis	gastrinoma/MEN – 1	none


VSI
a
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Lymphoma of the Stomach

- Primary lymphoma of the stomach is defined to either originate from the gastric wall or from the adjacent lymph nodes.
- More than 40% of non-Hodgkin lymphomas arise from extranodal locations, and the gastrointestinal tract is one of the most common extranodal sites.
- The prevalence of primary lymphoma of the gastrointestinal tract ranges from 4 to 18% in the Western world and is about 25% in the Middle East .
- While the stomach is the most frequent site of origin in the Western world, the midgut is predominantly involved in the Middle East.
- The average age of onset is in the 5th decade without any gender differences.

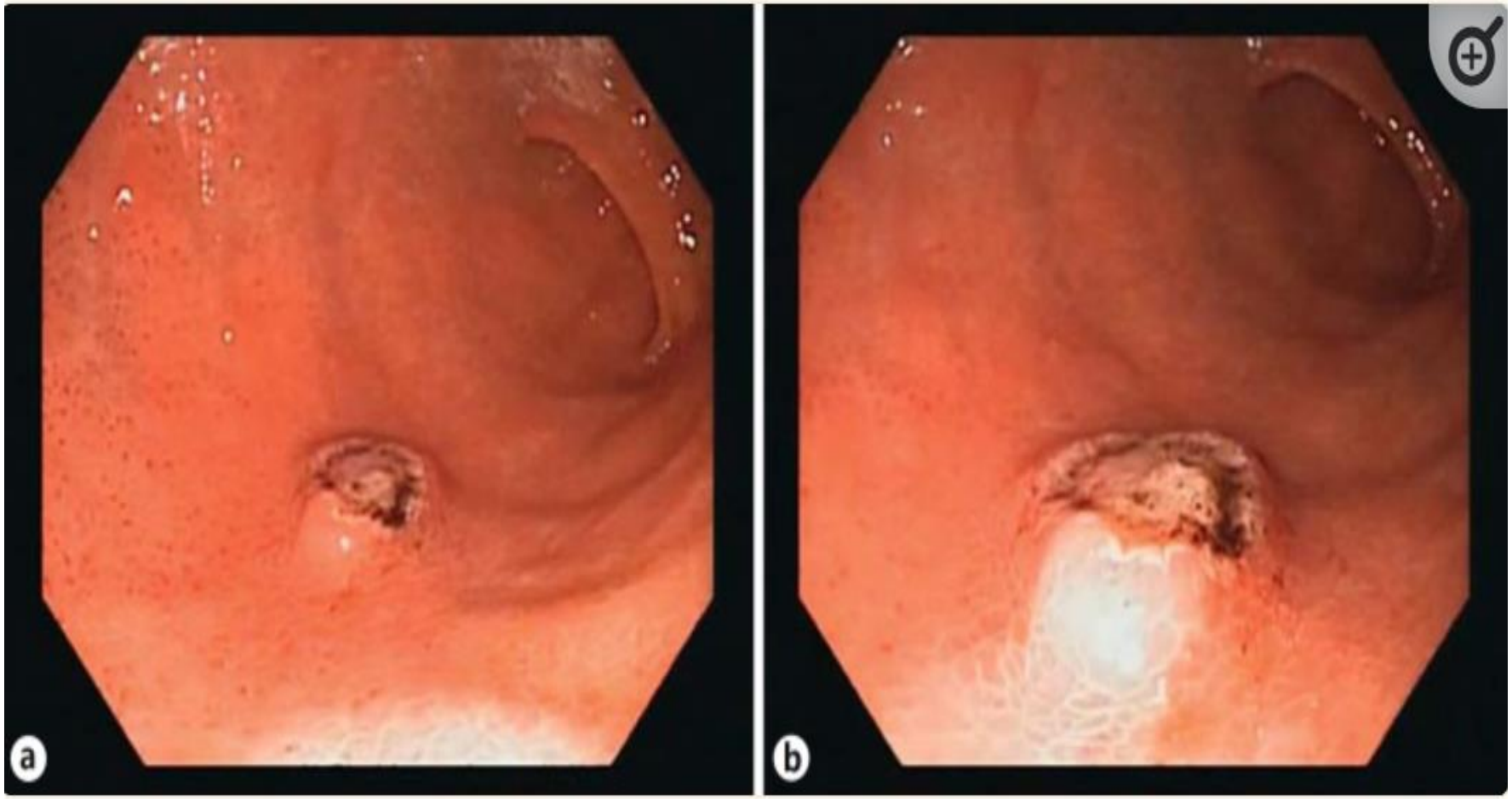
- *H. pylori* infection is the leading cause of gastric mucosa-associated lymphoid tissue (MALT) lymphoma, accounting for about 90% of cases.

- B-cell-associated antigens such as CD19, CD20, CD22 and sIg are frequently positive in immunohistochemical staining, whereas CD5, CD10, CD38 and IgD are negative [31].

- Acquired or congenital immunosuppressive conditions are risk factors for lymphoma as well. Up to 23% of lymphomas arising from the gastrointestinal tract are described in HIV-positive patients.

- B-cell MALT lymphomas are the only low-grade lymphomas of the stomach, whereas the majority of gastric lymphomas belong to the high-grade B-cell lymphomas.

MALT lymphoma



- Symptoms are frequently unspecific, with abdominal discomfort and nausea, vomiting or signs of bleeding. Large lesions may be palpable in the epigastrium in advanced situations.

- The therapeutic approach depends on histopathological classification and staging according to the Ann Arbor classification.

- Early-stage MALT lymphoma regresses in most cases after H. pylori eradication therapy. Lymphomas with genetic alterations [t(11:18)(q21:q21)] are at risk for eradication failure and the development of diffuse large B-cell lymphoma [33].

- Advanced MALT lymphoma should be treated by radiotherapy with curative intention, and mantle cell lymphoma, diffuse large B-cell lymphoma or rare Burkitt lymphoma are treated by systemic chemotherapy in accordance with the stage of disease.

- Surgical therapy is indicated in case of complications such as bleeding or perforation.

Secondary Neoplasia of the Stomach

- Metastases in the stomach from tumors of other origin are rare. Autopsy studies in cancer patients revealed a prevalence of gastric metastases in a range of 1.28-1.7%.

- Most frequently gastric metastases originate from breast cancer, followed by melanoma and lung cancer.