Tumors of the Esophagus and the Stomach

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Dietrich von Schweinitz

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31.1 Tumors of the Esophagus

In contrast to adults, neoplastic tumors of the esophagus are exceedingly rare during childhood and adolescence (Pappo and Furman 2006). As primary tumors of other parts of the gastrointestinal tract, also those of the esophagus almost never affect infants and toddlers but rather school-age children and adolescents (Ladd and Grosfeld 2006). In the SEER registry of 1992–2007, a rate of < .02 per 1 million children was documented. But also in this age group, carcinomas are the most frequent neoplasms and both adenocarcinomas and squamous cell carcinomas can occur (Pappo and Furman 2006). Esophageal carcinomas may be more frequent in Asia than in Europe or North America proposedly both on the basis of environmental and on genetic factors (Khushed et al. 2007). Adenocarcinomas of the esophagus in adults are usually associated with Barret's esophagus because of chronic gastroesophageal reflux, and there have been reports on this association also in children. Esophageal carcinomas can occur during childhood in the context of cancer predisposing syndromes and are more frequent in boys than in girls. According to reports on single patients, other malignant neoplasms as leiomyosarcomas and undifferentiated mesenchymal tumors and also benign tumors as leiomyomas, hamartomas, lipomas and fibromatosis can be found in children (Heij 2008).

Patients with an esophageal tumor usually present with dysphagia and weight loss. Other typical symptoms are vomiting, cough, regurgitation and hematemesis and retrosternal pain. In patients with these symptoms, other more-frequent causes as foreign body impactation, inflammatory diseases of the esophagus and malformations as bronchogenic cysts and esophageal duplications have to be ruled out. The

D. von Schweinitz
Kinderchirurgische Klinik und Poliklinik,
Dr. von Haunersches Kinderspital,
Lindwurmstraße 4, 80337 München, Germany
e-mail: dietrich.schweinitz@med.uni-muenchen.de

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SEER data 1992–2007															
Males and females				00–14 years		00–19 years		00–04 years		05–09 years		10–14 years		15–19 years	
ICCC code	ICCC	SRCode	Site recode	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count
42	IX(d.1) Ewing tumor and Askin tumor of soft tissue	10	Esophagus	0	0	0.01	1	0	0	0	0	0	0	0.02	1
89	XI(f.10) Carcinomas of other specified sites	10	Esophagus	0.02	3	0.02	4	0	0	0.02	1	0.04	2	0.02	1
			Sum	**0.02**	**3**	**0.03**	**5**	**0**	**0**	**0.02**	**1**	**0.04**	**2**	**0.04**	**2**
38	IX(b.1) Fibroblastic and myofibroblastic tumors	11	Stomach	0.01	1	0.01	1	0	0	0	0	0.02	1	0	0
39	IX(b.2) Nerve sheath tumors	11	Stomach	0	0	0.01	1	0	0	0	0	0	0	0.02	1
47	IX(d.6) Leiomyosarcomas	11	Stomach	0.02	3	0.03	5	0	0	0.07	3	0	0	0.05	2
53	IX(e) Unspecified soft tissue sarcomas	11	Stomach	0.01	1	0.01	1	0	0	0	0	0.02	1	0	0
61	X(b.2) Malignant teratomas: extracranial/ extragonadal	11	Stomach	0.01	1	0.01	1	0.02	1	0	0	0	0	0	0
89	XI(f.10) Carcinomas of other specified sites	11	Stomach	0.01	2	0.1	19	0	0	0	0	0.04	2	0.4	17
91	XII(a.1) Gastrointestinal stromal tumor	11	Stomach	0.02	3	0.03	5	0	0	0.02	1	0.04	2	0.05	2
97	XII(b) Other unspecified malignant tumors	11	Stomach	0.01	1	0.01	2	0.02	1	0	0	0	0	0.02	1
			Sum	**0.09**	**12**	**0.21**	**35**	**0.04**	**2**	**0.09**	**4**	**0.12**	**6**	**0.54**	**23**

Table 31.1 TNM clinical classification of esophageal cancer

T – Primary tumor		
TX	Primary tumor cannot be assessed	
T0	No evidence of primary tumor	
Tis	Carcinoma in situ/high-grade dysplasia	
T1	Tumor invades lamina propria, muscularis mucosae or submucosa	
	T1a	Tumor invades lamina propria or muscularis mucosae
	T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria	
T3	Tumor invades adventitia	
T4	Tumor invades adjacent structures	
	T4a	Tumor invades pleura, pericardium or diaphragm
	T4b	Tumor invades other adjacent structures such as aorta, vertebral body or trachea
N – Regional lymph nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in 1–2 regional lymph nodes	
N2	Metastasis in 3–6 regional lymph nodes	
N3	Metastasis in 7 or more regional lymph nodes	
M – Distant metastasis		
M0	No distant metastasis	
M1	Distant metastasis	

diagnostic procedure should include conventional radiology with contrast medium, a CT or MRI scan and an esophagoscopy with biopsies. Early stage tumors are asymptomatic and may be found incidentally during endoscopy for other reasons. A histological confirmation of the diagnosis is mandatory. In case of malignancy, other diagnostic procedures as thoracic CT, bone scan, FDG-PET scan and cerebral MRI become necessary for identification of metastases and staging. Esophageal carcinomas are staged according to the TNM system (Table 31.1; Sobin et al. 2009).

The mainstay of treatment of esophageal tumors is a complete surgical resection. Depending on tumor extension, this can be accomplished by a local excision or by a removal of the esophagus with a replacement by either a gastric or a colonic interposition. In case of a malignant tumor, especially a carcinoma, it is important to perform a thorough lymph node dissection. Adjuvant chemotherapy and/or radiation may be administered for malignant neoplasms. In carcinomas these are of very little to no effect, while in sarcomas they can be cytotoxic in a regime according to the existing different national and international soft tissue sarcoma trials (Pappo and Furman 2006).

The prognosis of children with a benign tumor is good; however, depending of the extension of the tumor, long-term functional problems may be a result of surgical treatment. In case of mesenchymal neoplasms, the patients' chance for survival will be similar to that of the same entities (i.e. leiomyosarcoma, undifferentiated mesenchymal tumor) at other locations and the tumor extension. Other factors for survival are possible radicality of surgery and response of the tumor to chemotherapy and radiation. The prognosis of children with esophagus carcinoma has been dismal in the very few reported cases. This may be due to an advanced stage of disease at diagnosis, but possibly also of an increased aggressiveness of carcinomas in young patients in comparison to adults (Heij 2008).

31.2 Tumors of the Stomach

Although not as exceedingly rare in childhood and adolescence as esophageal neoplasms, primary tumors of the stomach occur only sporadically in the pediatric age group; thus only 0.05% of all gastric cancers are

found in children (Pappo and Furman 2006), and the SEER registry for 1992–2007 documented a rate of.21 per 1 million population <20 years of age. In contrast to adults, carcinomas do not comprise the vast majority of all gastric neoplasms of the young age. As primary benign tumors of the stomach, teratomas, hamartomas, lipomas, inflammatory myoblastic tumors, as well as leiomyomas and leiomyomatosis, have been described in children. Soft tissue sarcomas, mostly leiomyosarcomas, and lymphomas are the most common malignant tumors of the stomach in children; also GastroIntestinal Stroma Tumors (GIST) are found (Heij 2008; Curtis et al. 2008). Adenocarcinomas comprise only 5% of all gastric tumors in this age group (Pappo and Furman 2006). While as in adults the carcinomas seem to be associated with *Helicobacter pylori* infection, this was also proposed for lymphomas in childhood (Imrie et al. 2001). Gastric neoplasms may also be associated with tumor predisposing syndromes in children. A combination of GIST with extra-adrenal paraganglioma and pulmonary chondroma in children has been called Carney's triad.

Over 100 cases of gastric teratomas have been described in the literature (Heij 2008). These usually occur in early childhood and behave like teratomas of other localizations. Thus they usually are benign but with increasing age become malignant. Therefore, a complete excision is important at an early stage. Inflammatory myoblastic tumors occur rarely in the gastrointestinal tract. Here they are found mostly in the stomach. They are benign, grow slowly and do not metastasize, but often demonstrate local infiltration and a relatively high rate of local recurrences after surgery. Leiomyomas can grow in the stomach mainly in young children. As they are essentially benign tumors, surgical resection usually leads to cure.

Also malignant leiomyosarcomas are mostly found in children of young age; a number of these occur during the newborn period (Ladd and Grosfeld 2006). Other cases have been described in patients with a depression of the immune system, e.g. after organ transplantation or HIV infection. These tumors are highly malignant with a frequent development of metastases (Heij 2008). Some lymphomas are thought to develop from atopically arising mucosa associated lymphatic tissue (MALT) after a *Helicobacter pylori* infection, which then can develop into a low malignant lymphoma. These MALT lymphomas are usually locally spreading and seldomly disseminate. In a longer course of disease however, they can transform into highly malignant lymphomas, which takes place in 20% of the cases (Imrie et al. 2001). However, also typical Burkitt lymphomas of the stomach have been found in some pediatric cases.

GIST is a malignant mesenchymal tumor arising from primitive precursor cells which are related to the interstitial cells of Cajal. The majority (88%) of GISTs occurring in children are located in the stomach and are diagnosed in school-age girls (Miettinen et al. 2005). The biological and histological characteristics of GISTs are described in detail in a separate chapter of this book. Some GISTs of the stomach metastasize at local lymph nodes and the liver. The response rate of GISTs in children to imatinib mesylate is estimated to be approximately 50%.

The very rare carcinomas of the stomach in school-age children and adolescents do not seem to differ very much from those in adults concerning histopathology and biological behavior. Thus, they grow locally aggressive and spread via lymphatic and blood vessels as well as by peritoneal seeding. Therefore, they can involve adjacent organs such as esophagus, duodenum, pancreas, colon and liver. Distant metastases can affect the liver, lungs, bones and skin (Pappo and Furman 2006). The tumor status and the extension of disease can best be classified with the TNM system (Table 31.2; Sobin et al. 2009).

The clinical symptoms of gastric tumors are quite uniform. The patients have epigastric discomfort or pain, nausea and vomiting, sometimes anorexia and weight loss. Also hematemesis and anemia as well as occult blood in the stool may appear. Often the tumor is palpable in the upper abdomen at the time of diagnosis. For differential diagnosis, mainly space-occupying malformations of the stomach, especially a gastric duplication, have to be taken into account, but also extragastric tumors such as tumors of the pancreas, the liver and the retroperitoneum. Therefore besides a laboratory work-up, the diagnostic procedures should include abdominal ultrasound, radiology with an upper gastrointestinal contrast medium passage, a CT and/or MRI scan and a gastroscopy. During this procedure the essential biopsies can be taken. In case of malignancy, investigations for staging with thoracic CT, bone scan and eventually a FDG-PET scan should follow. In patients with a suspected gastric lymphoma, it is important to gain tumor material through a biopsy or

Table 31.2 TNM clinical classification of gastric cancer

T – Primary tumor		
TX	Primary tumor cannot be assessed	
T0	No evidence of primary tumor	
Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria, high-grade dysplasia	
T1	Tumor invades lamina propria, muscularis mucosae, or submucosa	
	T1a	Tumor invades lamina propria or muscularis mucosae
	T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria	
T3	Tumor invades subserosa	
T4	Tumor perforates serosa or invades adjacent structures[a–c]	
	T4a	Tumor perforates serosa
	T4b	Tumor invades other adjacent structures[a–c]
N – Regional lymph nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in 1–2 regional lymph nodes	
N2	Metastasis in 3–6 regional lymph nodes	
N3	Metastasis in 7 or more regional lymph nodes	
	N3a	Metastasis in 7–15 regional lymph nodes
	N3b	Metastasis in 16 or more regional lymph nodes
M – Distant metastasis		
M0	No distant metastasis	
M1	Distant metastasis	

[a]The adjacent structures of the stomach are the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum

[b]Intramural extension of the duodenum or esophagus is classified by the depth of greatest invasion in any of these sites, including stomach

[c]Tumor that extends into gastrocolic or gastrohepatic ligaments or into greater or lesser omentum, without perforation of visceral peritoneum, is T3

from other material as ascites, pleural effusion or bone marrow before planning of treatment.

The best therapy for most gastric tumors is a primary complete resection (Heij 2008). Obviously this has to be more extensive in malignant than in benign tumors. Therefore if the diagnosis is not established by a biopsy beforehand, intraoperative frozen sections should be performed by the pathologist. In benign tumors a local excision usually with preservation of some parts of the stomach is sufficient. In contrast to malignant tumors, a resection with wide margins and excision of regional lymph nodes is the procedure of choice. For pediatric GIST and sarcomas but also for gastric carcinomas, it is not clear whether a limited lymph node dissection with a low rate of surgical complication or an extended dissection with a high risk of complications is the better procedure. In relatively extended tumors, complete gastrectomies can be performed also in children without taking a risk for acute complications and long-term sequelae which would be higher than in adults.

Only for gastric lymphomas as for non-Hodgkin's lymphomas of other sites, the treatment of choice is primary chemotherapy according to the schemes of non-Hodgkin's lymphoma trials. In most cases this is very effective and the tumors show an extensive decrease of size. In some patients in whom this diagnosis has been established before start of treatment, surgery is not necessary any more after a complete regression of the tumor (Pappo and Furman 2006).

Adjuvant therapy is indicated in many cases with another malignant tumor. In sarcomas, chemotherapy

according to the different soft tissue sarcoma protocols often has at least some effect, and in cases of GIST, adjuvant therapy should mainly contain imatinib mesylate. Although gastric carcinomas mostly show a very poor response to chemotherapy, different cytotoxic agents such as 5-FU, doxorubicin, cisplatin, etoposide, mitomycin and irinotecan have been administered adjuvantly. Sarcomas and some carcinomas are responsive to radiation which may preferably be administered in addition to chemotherapy, especially after marginal resections. Patients with unresectable or metastasized malignant tumors should receive neoadjuvant treatment. For sarcomas the chemotherapy regimens shown to be effective in soft tissue sarcomas of other localizations should be applied. For GIST, imatinib mesylate should be administered while the effect of conventional chemotherapy is not clear especially in children. In extended unresectable and/or metastasized carcinomas, pre- or intraoperative radiation but also chemotherapy can be tried (Pappo and Furman 2006).

The prognosis of gastric tumors depends on the dignity, the histological diagnosis, the extension of disease, surgical resectability and the response to chemotherapy and radiation. Benign tumors usually have a very good prognosis. This also accounts for gastric lymphomas, while the prognosis for sarcomas is dependent on resectability and sensitivity to chemotherapy and radiation. For GIST it seems that children have a slightly poorer outcome than adults; approximately two thirds of the pediatric patients could be cured in the recent years (Cypriano et al. 2004). The prognosis of gastric carcinoma in childhood is very poor; only very few survivors have been reported (Pappo and Furman 2006; Heij 2008).

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