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Esophageal adenocarcinoma and squamous cell carcinoma in children and adolescents: Report of 3 cases and comprehensive literature review

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ABSTRACT

Malignant esophageal tumors are exceedingly rare in children and adolescents. We present 3 cases of esophageal adenocarcinoma (AC) and squamous cell carcinoma (SSC) in patients <21 years of age who were treated at our institution between 1950 and 2015. We also undertook an analysis of those cases, combined with cases from a review of the literature, to examine patient demographics, disease characteristics, and outcomes. We identified one patient with AC and two patients with SCC treated at our institution, as well as 19 cases of AC (median age 16) and 23 cases of SCC (median age 15) reported in the literature. Male predominance was noted at a ratio of 2.2 to 1. Dysphagia, weight loss, and anemia were the most common presenting symptoms for both entities. Approximately 84% of AC tumors were located in the distal esophagus and gastroesophageal junction whereas SCC tumors were distributed evenly throughout esophagus. Metastatic disease at presentation was found in 68.4% of patients with AC compared to 30.4% of those with SCC. Survival was not significantly different between SCC and AC (P =0.36), between genders (P = 0.13), and between patients treated with surgery vs. multimodality therapy (P = 0.15). Metastasis, however, predicted worse outcome (P = 0.0019). We found that adolescent AC and SCC show characteristics similar to such tumors when presenting in adults. Though extremely rare in the adolescent population, these malignant diseases should always be ruled out when young patients present with a short history of dysphagia with signs of clinical deterioration.

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Malignant esophageal tumors are the sixth leading cause of death from cancer worldwide [1], with a peak prevalence between 35 and 64 years of age [1]. The presentation of an esophageal tumor in children and adolescents is an exceedingly rare event. Between 1973 and 2008, the Surveillance, Epidemiology, and End Results (SEER) program identified only nine malignant esophageal tumors in patients under age 20 [2]. The largest series was presented by Kumar et al., in 1992 with four cases of squamous cell carcinoma (SCC) and three of adenocarcinoma (AC) with the oldest patient being 19 years of age [3]. With the report of three new cases of our own and an extensive literature review, we aim to contribute to the general understanding of these rare childhood tumors.

1. Patients and methods

The review was conducted under an Institutional Review Board waiver in accordance with the Health Insurance Portability and Accountability Act regulations. All patients 21 years and younger with AC and SCC treated in our institution between 1950 and 2015 were reviewed. Histopathology diagnosis was confirmed by the pathology service of our institution.

The international literature was reviewed for reports on malignant tumors of the esophagus in patients under the age of 21 years using the U.S. National Library of Medicine (www.pubmed.gov). Search terms used: cancer, adenocarcinoma, squamous cell carcinoma, esophagus, and children, childhood, child, pediatrics. Publications in languages other than English were professionally translated.

All cases of AC and SSC identified at our institution and in the literature were analyzed for age at presentation, gender, presenting

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Patients un	der the	age of 21 wit	h esopha£	zeal adenocarcii	noma and squamo	ous cell carcinoma treated at our institu	tution.			
Case no.	Year	Histology	Age/sex	Esophageal location	Histologic differentiation	Presenting symptoms (duration)	Metastasis	Therapy	Follow-up period (months)	Follow-up status
	1985	SCC	18/M	Middle third	Not noted	Dysphagia, weight loss, retrosternal pain (1 month)	Lung, visceral + parietal pleura, liver, diaphragm, lymph nodes (mediastinal, peripancreatic, peri- aortic, coeliac)	Palliative laser therapy, feeding gastrostomy ^a	11	DOD
7	1993	AC	21/M	Distal third	Poor	Dysphagia, regurgitation (1 month)	Liver, bone (vertebral body (12), 2nd rib), brain (frontal epi-dura), lymph nodes (mediastinal, peri- aortic, para caval, mesenteric, left renal hilum)	Chemotherapy, ^b later palliative radiotherapy to the brain and spine ^c	2.2	DOD
ε	2004	SCC	21/F	Middle third	Moderate	Dysphagia, weight loss, odynophagia, retrosternal pain (4 months)	None	Neo-adjuvant chemo- and radiotherapy, ^{d.e} Ivor Lewis esophagectomy (RO), esophagogastrostomy	64	NED
M = male.	F = fem	ale. DOD = di	ed of dise	sase. NED = no	evidence of diseas	se. R0 = margin of resection free of dis	sease.			

Table 1

= male, F = female, DOD = died of disease, NED = no evidence of disease, R0 = margin of resection free of disease.

Chemo- and radiotherapy at outside hospital (unknown agents and dosage).

VP-16, cisplatin.

3000 cGy to lumbar spine (10 fractions), 1500 cGy to whole brain (5 fractions). Irinotecan, platinum (over 3 weeks), changed to taxol, 5-fluorouracil (over 5 weeks)

5040 cGy (28 fractions)

symptoms, preexisting conditions, tumor histology, tumor location, tumor differentiation, metastatic disease, treatment, and outcome. Only reports with complete information on the histopathology subtype of the tumor were included in later analysis. Survival was analyzed using the Kaplan-Meier method, and the log-rank test was used.

2. Results

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We identified one patient with AC and two patients with SCC of the esophagus treated at our institution. One 21-year-old male presented with a poorly differentiated AC of the distal esophagus. No Barrett's esophagus was reported in the endoscopy histologic report sections of the endoscopy or in the previous history. He died 2.2 months after chemotherapy with liver, vertebral, brain and lymph node metastasis (Table 1). An 18-year-old male was treated with palliative therapy for late stage SCC of the mid-esophagus with metastasis to lung, liver, diaphragm and lymph nodes. He died 11 months after first presentation. The other patient with a

Table 2

Patient characteristics of esophageal adenocarcinoma and squamous cell carcinoma in patients 21 years and younger

ACSSCOverallNumber of cases Absolute (percent)19 (45.2%)23 (54.8%)42 (100%)Median age Years (range)16 (8–21)15 (8–21)15 (8–21)Sex distribution Male: Female5.3: 11.3: 12.2: 1Presenting symptoms 0 20 (87.0%)35 (83.3%)Dysphagia15 (78.9%)20 (87.0%)35 (83.3%)Weight loss9 (47.4%)14 (60.9%)23 (54.8%)Anemia6 (31.6%)8 (34.8%)14 (33.3%)Dehydration4 (21.1%)5 (21.7%)9 (21.4%)Nausea3 (15.8%)5 (21.7%)8 (19.0%)Epigastric or retrosternal2 (10.5%)4 (17.4%)6 (14.3%)pain/burning $-$ 5 (11.9%)VomitingGastroesophageal reflux5 (26.3%) $-$ 5 (11.9%)Vomiting3 (15.8%)2 (8.7%)5 (11.9%)Hematemesis2 (10.5%) $-$ 1 (2.4%)Odynophagia $-$ 1 (4.3%)1 (2.4%)Other conditions $-$ 1 (4.3%)1 (2.4%)Barrett's esophagus6 (31.6%) $-$ 6 (14.3%)Gigarette smoking3 (10.5%) ⁴ 2 (8.7%) ^c 5 (11.9%)Spinal palsy3 (15.8%) ⁴ $-$ 3 (7.1%)Caustic injury $-$ 3 (13.0%) ^d 2 (4.8%)Previous cancer treatment $-$ 1 (4.3%) ¹ 2 (4.8%)HP positive gastritis1 (5.3%) $-$ 1 (2.4%)Hiatal hernia1 (5.3%) ^a $-$ 1 (2.4%)Horev	1 , , , , , , , , , , , , , , , , , , ,			
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Epigastric or retrosternal pain/burning $2 (10.5\%)$ $4 (17.4\%)$ $6 (14.3\%)$ pain/burningGastroesophageal reflux $5 (26.3\%)$ $ 5 (11.9\%)$ Vomiting $3 (15.8\%)$ $2 (8.7\%)$ $5 (11.9\%)$ Hematemesis $2 (10.5\%)$ $ 2 (4.8\%)$ Recurrent pneumonia $ 1 (4.3\%)$ $1 (2.4\%)$ Hematochezia $1 (5.3\%)$ $ 1 (2.4\%)$ Constipation $1 (5.3\%)$ $ 1 (2.4\%)$ Odynophagia $ 1 (4.3\%)$ $1 (2.4\%)$ Other conditions $ 1 (4.3\%)$ $1 (2.4\%)$ Barrett's esophagus $6 (31.6\%)$ $ 6 (14.3\%)$ Cigarette smoking $3 (10.5\%)^a$ $2 (8.7\%)^c$ $5 (11.9\%)$ Spinal palsy $3 (15.8\%)^a$ $ 3 (7.1\%)$ Caustic injury $ 3 (13.0\%)^d$ $3 (7.1\%)$ Previous cancer treatment $ 1 (4.3\%)^c$ $2 (4.8\%)$ Hiatal hernia $1 (5.3\%)$ $ 1 (2.4\%)$ Positive gastritis $1 (5.3\%)^a$ $ 1 (2.4\%)$ Foreign body ingestion $1 (5.3\%)^a$ $ 1 (2.4\%)$ Foreign body ingestion $1 (5.3\%)^a$ $ 1 (2.4\%)$ Foreign body ingestion $1 (5.3\%)^a$ $ 1 (2.4\%)$ Polycystic kidney disease and $ 1 (4.3\%)^{1b}$ $1 (2.4\%)$ Polycystic kidney disease and $ 1 (4.3\%)^{1b}$ $1 (2.4\%)$ Polycystic kidney disease and $ 1 (4.3\%)^{1b}$ $1 (2.4\%)$ Polycystic kidney dise	Nausea	3 (15.8%)	5 (21.7%)	8 (19.0%)
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Epigastric or retrosternal	2 (10.5%)	4 (17.4%)	6 (14.3%)
$\begin{array}{ccccccc} Gastroesophageal reflux & 5 (26.3\%) & - & 5 (11.9\%) \\ Vomiting & 3 (15.8\%) & 2 (8.7\%) & 5 (11.9\%) \\ Hematemesis & 2 (10.5\%) & - & 2 (4.8\%) \\ Recurrent pneumonia & - & 1 (4.3\%) & 1 (2.4\%) \\ Hematochezia & 1 (5.3\%) & - & 1 (2.4\%) \\ Constipation & 1 (5.3\%) & - & 1 (2.4\%) \\ Odynophagia & - & 1 (4.3\%) & 1 (2.4\%) \\ Other conditions & & & & & \\ Barrett's esophagus & 6 (31.6\%) & - & 6 (14.3\%) \\ Cigarette smoking & 3 (10.5\%)^{4} & 2 (8.7\%)^{c} & 5 (11.9\%) \\ Spinal palsy & 3 (15.8\%)^{a} & - & 3 (7.1\%) \\ Gaustic injury & - & 3 (13.0\%)^{cl} & 3 (7.1\%) \\ Previous surgery & 1 (5.3\%) & 1 (4.3\%)^{f} & 2 (4.8\%) \\ Previous cancer treatment & - & 1 (4.3\%)^{g} & 1 (2.4\%) \\ Hiatal hernia & 1 (5.3\%) & - & 1 (2.4\%) \\ Overweight & 1 (5.3\%)^{a} & - & 1 (2.4\%) \\ Foreign body ingestion & 1 (5.3\%)^{a} & - & 1 (2.4\%) \\ Foreign body ingestion & 1 (5.3\%)^{a} & - & 1 (2.4\%) \\ Foreign body ingestion & 1 (5.3\%)^{a} & - & 1 (2.4\%) \\ Polycystic kidney disease and & - & 1 (4.3\%)^{bb} & 1 (2.4\%) \\ Polycystic kidney disease and & - & 1 (4.3\%)^{bb} & 1 (2.4\%) \\ Polycystic kidney disease and & - & 1 (4.3\%)^{bb} & 1 (2.4\%) \\ Polycystic kidney disease and & - & 1 (4.3\%)^{bb} & 1 (2.4\%) \\ None & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \end{array}$	pain/burning			
Vomiting $3 (15.8\%)$ $2 (8.7\%)$ $5 (11.9\%)$ Hematemesis $2 (10.5\%)$ $ 2 (4.8\%)$ Recurrent pneumonia $ 1 (4.3\%)$ $1 (2.4\%)$ Hematochezia $1 (5.3\%)$ $ 1 (2.4\%)$ Constipation $1 (5.3\%)$ $ 1 (2.4\%)$ Odynophagia $ 1 (4.3\%)$ $1 (2.4\%)$ Other conditions $ 1 (4.3\%)$ $1 (2.4\%)$ Other conditions $ 6 (31.6\%)$ $ 6 (14.3\%)$ Gigarette smoking $3 (10.5\%)^{a1}$ $2 (8.7\%)^{c2}$ $5 (11.9\%)$ Spinal palsy $3 (15.8\%)^{a1}$ $ 3 (7.1\%)$ Caustic injury $ 3 (13.0\%)^{c1}$ $2 (4.8\%)$ Previous surgery $1 (5.3\%)^{a1}$ $ 1 (2.4\%)$ Hiatal hernia $1 (5.3\%)$ $1 (4.3\%)^{b1}$ $2 (4.8\%)$ HP positive gastritis $1 (5.3\%)^{a1}$ $ 1 (2.4\%)$ Foreign body ingestion $1 (5.3\%)^{a1}$ $ 1 (2.4\%)$ Factor VIII deficiency $1 (5.3\%)^{a1}$ $ 1 (2.4\%)$ Factor VIII deficiency $1 (5.3\%)^{a1}$ $ 1 (2.4\%)$ Polycystic kidney disease and $ 1 (4.3\%)^{1b}$ $1 (2.4\%)$ Polycystic kidney disease and $ 1 (4.3\%)^{1b}$ $1 (2.4\%)$ None $7 (36.8\%)$ $14 (60.9\%)$ $21 (50.0\%)$	Gastroesophageal reflux	5 (26.3%)	-	5 (11.9%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Vomiting	3 (15.8%)	2 (8.7%)	5 (11.9%)
$\begin{array}{ccccc} \mbox{Recurrent pneumonia} & - & 1 (4.3\%) & 1 (2.4\%) \\ \mbox{Hematochezia} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Constipation} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Odynophagia} & - & 1 (4.3\%) & 1 (2.4\%) \\ \mbox{Other conditions} \\ \mbox{Barrett's esophagus} & 6 (31.6\%) & - & 6 (14.3\%) \\ \mbox{Cigarette smoking} & 3 (10.5\%)^a & 2 (8.7\%)^c & 5 (11.9\%) \\ \mbox{Spinal palsy} & 3 (15.8\%)^a & - & 3 (7.1\%) \\ \mbox{Caustic injury} & - & 3 (13.0\%)^d & 3 (7.1\%) \\ \mbox{Previous surgery} & 1 (5.3\%)^e & 1 (4.3\%)^f & 2 (4.8\%) \\ \mbox{Previous cancer treatment} & - & 1 (4.3\%)^g & 1 (2.4\%) \\ \mbox{Hiata hernia} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Poreight} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Poreign body ingestion} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Foreign body ingestion} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Factor VIII deficiency} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Factor VIII deficiency} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Foreign with hyperthyroidism} & - & 1 (4.3\%)^{i,b} & 1 (2.4\%) \\ \mbox{Polycystic kidney disease and} & - & 1 (4.3\%)^{i,b} & 1 (2.4\%) \\ \mbox{Foreign with hyperthyroidism} & - & 1 (4.3\%)^b & 1 (2.4\%) \\ \mbox{None} & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \\ \end{array}$	Hematemesis	2 (10.5%)	-	2 (4.8%)
$\begin{array}{cccccc} \mbox{Hematochezia} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Constipation} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Odynophagia} & - & 1 (4.3\%) & 1 (2.4\%) \\ \mbox{Other conditions} \\ \mbox{Barrett's esophagus} & 6 (31.6\%) & - & 6 (14.3\%) \\ \mbox{Cigarette smoking} & 3 (10.5\%)^3 & 2 (8.7\%)^c & 5 (11.9\%) \\ \mbox{Spinal palsy} & 3 (15.8\%)^3 & - & 3 (7.1\%) \\ \mbox{Caustic injury} & - & 3 (13.0\%)^d & 3 (7.1\%) \\ \mbox{Previous surgery} & 1 (5.3\%)^c & 1 (4.3\%)^f & 2 (4.8\%) \\ \mbox{Previous cancer treatment} & - & 1 (4.3\%)^g & 1 (2.4\%) \\ \mbox{Hiatal hernia} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Postive gastritis} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Poreight} & 1 (5.3\%)^h & - & 1 (2.4\%) \\ \mbox{Foreign body ingestion} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Foreign body ingestion} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Factor VIII deficiency} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Factor VIII deficiency} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Polycystic kidney disease and} & - & 1 (4.3\%)^{i,b} & 1 (2.4\%) \\ \mbox{Polycystic kidney disease and} & - & 1 (4.3\%)^{i,b} & 1 (2.4\%) \\ \mbox{Polycereign with hyperthyroidism} & - & 1 (4.3\%)^b & 1 (2.4\%) \\ \mbox{None} & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \\ \end{array}$	Recurrent pneumonia		1 (4.3%)	1 (2.4%)
$\begin{array}{c cccc} Constipation & 1 (5.3\%) & - & 1 (2.4\%) \\ Odynophagia & - & 1 (4.3\%) & 1 (2.4\%) \\ Other conditions \\ \\ Barrett's esophagus & 6 (31.6\%) & - & 6 (14.3\%) \\ Cigarette smoking & 3 (10.5\%)^{3} & 2 (8.7\%)^{c} & 5 (11.9\%) \\ Spinal palsy & 3 (15.8\%)^{3} & - & 3 (7.1\%) \\ Caustic injury & - & 3 (13.0\%)^{cl} & 3 (7.1\%) \\ Previous surgery & 1 (5.3\%)^{c} & 1 (4.3\%)^{l} & 2 (4.8\%) \\ Previous cancer treatment & - & 1 (4.3\%)^{g} & 1 (2.4\%) \\ Hiatal hernia & 1 (5.3\%) & - & 1 (2.4\%) \\ HO positive gastritis & 1 (5.3\%) & - & 1 (2.4\%) \\ Overweight & 1 (5.3\%)^{h} & - & 1 (2.4\%) \\ Foreign body ingestion & 1 (5.3\%)^{a} & - & 1 (2.4\%) \\ Esophageal HPV-16 infection & - & 1 (4.3\%)^{lb} & 1 (2.4\%) \\ Factor VIII deficiency & 1 (5.3\%)^{a} & - & 1 (2.4\%) \\ Polycystic kidney disease and & - & 1 (4.3\%)^{lab} & 1 (2.4\%) \\ Polycystic kidney disease and & - & 1 (4.3\%)^{lab} & 1 (2.4\%) \\ Mone & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \\ \end{array}$	Hematochezia	1 (5.3%)	_	1 (2.4%)
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Constipation	1 (5.3%)	-	1 (2.4%)
$\begin{array}{l lllllllllllllllllllllllllllllllllll$	Odynophagia	-	1 (4.3%)	1 (2.4%)
$\begin{array}{cccccccc} & & & & & & & & & & & & & & & $	Other conditions			
$\begin{array}{ccccccc} {\rm Cigarette smoking} & 3 (10.5\%)^{\rm a} & 2 (8.7\%)^{\rm c} & 5 (11.9\%) \\ {\rm Spinal palsy} & 3 (15.8\%)^{\rm a} & - & 3 (7.1\%) \\ {\rm Caustic injury} & - & 3 (13.0\%)^{\rm d} & 3 (7.1\%) \\ {\rm Previous surgery} & 1 (5.3\%)^{\rm e} & 1 (4.3\%)^{\rm f} & 2 (4.8\%) \\ {\rm Previous cancer treatment} & - & 1 (4.3\%)^{\rm g} & 1 (2.4\%) \\ {\rm Hiatal hernia} & 1 (5.3\%) & - & 1 (2.4\%) \\ {\rm Hiatal hernia} & 1 (5.3\%) & - & 1 (2.4\%) \\ {\rm Overweight} & 1 (5.3\%)^{\rm h} & - & 1 (2.4\%) \\ {\rm Foreign body ingestion} & 1 (5.3\%)^{\rm a} & 1 (2.4\%) \\ {\rm Foreign body ingestion} & 1 (5.3\%)^{\rm a} & - 1 (2.4\%) \\ {\rm Factor VIII deficiency} & 1 (5.3\%)^{\rm a} & - 1 (2.4\%) \\ {\rm Factor VIII deficiency} & 1 (5.3\%)^{\rm a} & - 1 (2.4\%) \\ {\rm vesicoureteral reflux IV^{\circ}} \\ {\rm Goiter with hyperthyroidism} & - & 1 (4.3\%)^{\rm b} & 1 (2.4\%) \\ {\rm None} & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \\ \end{array}$	Barrett's esophagus	6 (31.6%)	_	6 (14.3%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Cigarette smoking	3 (10.5%) ^a	2 (8.7%) ^c	5 (11.9%)
$\begin{array}{c cccc} \text{Caustic injury} & - & 3 & (13.0\%)^{\text{cl}} & 3 & (7.1\%) \\ \text{Previous surgery} & 1 & (5.3\%)^{\text{cl}} & 1 & (4.3\%)^{\text{cl}} & 2 & (4.8\%) \\ \text{Previous cancer treatment} & - & 1 & (4.3\%)^{\text{cl}} & 1 & (2.4\%) \\ \text{Hiatal hernia} & 1 & (5.3\%) & - & 1 & (2.4\%) \\ \text{Hy positive gastritis} & 1 & (5.3\%) & - & 1 & (2.4\%) \\ \text{Overweight} & 1 & (5.3\%)^{\text{bl}} & - & 1 & (2.4\%) \\ \text{Foreign body ingestion} & 1 & (5.3\%)^{\text{al}} & - & 1 & (2.4\%) \\ \text{Esophageal HPV-16 infection} & - & 1 & (4.3\%) & 1 & (2.4\%) \\ \text{Factor VIII deficiency} & 1 & (5.3\%)^{\text{al}} & - & 1 & (2.4\%) \\ \text{Polycystic kidney disease and} & - & 1 & (4.3\%)^{\text{lib}} & 1 & (2.4\%) \\ \text{Poiter with hyperthyroidism} & - & 1 & (4.3\%)^{\text{bb}} & 1 & (2.4\%) \\ \text{None} & 7 & (36.8\%) & 14 & (60.9\%) & 21 & (50.0\%) \\ \end{array}$	Spinal palsy	3 (15.8%) ^a	_	3 (7.1%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Caustic injury	_	3 (13.0%) ^d	3 (7.1%)
$\begin{array}{ccccc} \mbox{Previous cancer treatment} & - & 1 (4.3\%)^g & 1 (2.4\%) \\ \mbox{Hiatal hernia} & 1 (5.3\%) & 1 (4.3\%)^b & 2 (4.8\%) \\ \mbox{HP positive gastritis} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Overweight} & 1 (5.3\%)^h & - & 1 (2.4\%) \\ \mbox{Foreign body ingestion} & 1 (5.3\%)^h & - & 1 (2.4\%) \\ \mbox{Esophageal HPV-16 infection} & - & 1 (4.3\%) & 1 (2.4\%) \\ \mbox{Factor VIII deficiency} & 1 (5.3\%)^a & - & 1 (2.4\%) \\ \mbox{Polycystic kidney disease and} & - & 1 (4.3\%)^{i,b} & 1 (2.4\%) \\ \mbox{vesicoureteral reflux IV}^\circ & & & & \\ \mbox{Goiter with hyperthyroidism} & - & 1 (4.3\%)^b & 1 (2.4\%) \\ \mbox{None} & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \\ \end{array}$	Previous surgery	1 (5.3%) ^e	1 (4.3%) ^f	2 (4.8%)
$\begin{array}{cccccc} \mbox{Hiatal hernia} & 1 (5.3\%) & 1 (4.3\%)^{\rm b} & 2 (4.8\%) \\ \mbox{HP positive gastritis} & 1 (5.3\%) & - & 1 (2.4\%) \\ \mbox{Overweight} & 1 (5.3\%)^{\rm b} & - & 1 (2.4\%) \\ \mbox{Foreign body ingestion} & 1 (5.3\%)^{\rm a} & & 1 (2.4\%) \\ \mbox{Esophageal HPV-16 infection} & - & 1 (4.3\%) & 1 (2.4\%) \\ \mbox{Factor VIII deficiency} & 1 (5.3\%)^{\rm a} & - & 1 (2.4\%) \\ \mbox{Polycystic kidney disease and} & - & 1 (4.3\%)^{\rm i,b} & 1 (2.4\%) \\ \mbox{vesicoureteral reflux IV}^{\circ} & & & \\ \mbox{Goiter with hyperthyroidism} & - & 1 (4.3\%)^{\rm b} & 1 (2.4\%) \\ \mbox{None} & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \\ \end{array}$	Previous cancer treatment	-	1 (4.3%) ^g	1 (2.4%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Hiatal hernia	1 (5.3%)	1 (4.3%) ^b	2 (4.8%)
$\begin{array}{ccccc} \text{Overweight} & 1 \ (5.3\%)^{\text{h}} & - & 1 \ (2.4\%) \\ \text{Foreign body ingestion} & 1 \ (5.3\%)^3 & & 1 \ (2.4\%) \\ \text{Esophageal HPV-16 infection} & - & 1 \ (4.3\%) & 1 \ (2.4\%) \\ \text{Factor VIII deficiency} & 1 \ (5.3\%)^3 & - & 1 \ (2.4\%) \\ \text{Polycystic kidney disease and} & - & 1 \ (4.3\%)^{\text{i,b}} & 1 \ (2.4\%) \\ \text{Polycystic kidney disease and} & - & 1 \ (4.3\%)^{\text{i,b}} & 1 \ (2.4\%) \\ \text{vesicoureteral reflux IV}^\circ & & \\ \text{Goiter with hyperthyroidism} & - & 1 \ (4.3\%)^{\text{b}} & 1 \ (2.4\%) \\ \text{None} & & 7 \ (36.8\%) & 14 \ (60.9\%) & 21 \ (50.0\%) \end{array}$	HP positive gastritis	1 (5.3%)	-	1 (2.4%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Overweight	1 (5.3%) ^h	-	1 (2.4%)
$\begin{array}{ccccc} \text{Esophageal HPV-16 infection} & - & 1 (4.3\%) & 1 (2.4\%) \\ \text{Factor VIII deficiency} & 1 (5.3\%)^{a} & - & 1 (2.4\%) \\ \text{Polycystic kidney disease and} & - & 1 (4.3\%)^{i,b} & 1 (2.4\%) \\ \text{vesicoureteral reflux IV}^{\circ} & & \\ \text{Goiter with hyperthyroidism} & - & 1 (4.3\%)^{b} & 1 (2.4\%) \\ \text{None} & 7 (36.8\%) & 14 (60.9\%) & 21 (50.0\%) \end{array}$	Foreign body ingestion	1 (5.3%) ^a		1 (2.4%)
$\begin{array}{cccc} \mbox{Factor VIII deficiency} & 1 \ (5.3\%)^a & - & 1 \ (2.4\%) \\ \mbox{Polycystic kidney disease and} & - & 1 \ (4.3\%)^{i,b} & 1 \ (2.4\%) \\ \mbox{vesicoureteral reflux IV}^\circ & & & \\ \mbox{Goiter with hyperthyroidism} & - & 1 \ (4.3\%)^b & 1 \ (2.4\%) \\ \mbox{None} & 7 \ (36.8\%) & 14 \ (60.9\%) & 21 \ (50.0\%) \end{array}$	Esophageal HPV-16 infection	-	1 (4.3%)	1 (2.4%)
$\begin{array}{c c} \mbox{Polycystic kidney disease and} & - & 1 \ (4.3\%)^{i,b} & 1 \ (2.4\%) \\ \mbox{vesicoureteral reflux IV}^\circ & & & \\ \mbox{Goiter with hyperthyroidism} & - & 1 \ (4.3\%)^b & 1 \ (2.4\%) \\ \mbox{None} & & 7 \ (36.8\%) & 14 \ (60.9\%) & 21 \ (50.0\%) \end{array}$	Factor VIII deficiency	1 (5.3%) ^a	-	1 (2.4%)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Polycystic kidney disease and	-	1 (4.3%) ^{i,b}	1 (2.4%)
Goiter with hyperthyroidism - 1 (4.3%) ^b 1 (2.4%) None 7 (36.8%) 14 (60.9%) 21 (50.0%)	vesicoureteral reflux IV°			
None 7 (36.8%) 14 (60.9%) 21 (50.0%)	Goiter with hyperthyroidism	-	1 (4.3%) ^b	1 (2.4%)
	None	7 (36.8%)	14 (60.9%)	21 (50.0%)

AC = Adenocarcinoma, SCC = Squamous cell carcinoma, HP = Helicobacter pylori, HPV-16 = Human papillomavirus 16.

Patients with Barrett's esophagus within this group.

h Same patient.

^c 3- and 5-year history of cigarette smoking.

^d One case of lye ingestion and two cases of ingestion of an unknown agent.

Esophageal atresia repair in infancy.

Gastrostomy for trichobezoar removal.

g Surgery and chemotherapy for osteosarcoma.

^h BMI = 26.7 kg/m².

ⁱ Chronic renal failure.

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