

Verrucous Carcinoma of the Esophagus

Farooq P. Agha, M.D., Lee Weatherbee, M.D., and Jeffrey S. Sams, M.D.

Department of Radiology, Pathology, and Internal Medicine, University of Michigan Hospitals and Veterans Administration Medical Center, Ann Arbor, Michigan

INTRODUCTION

We report a case of verrucous carcinoma of the esophagus in a 66-year-old man who had sustained acid burns of the pharynx and esophagus 27 years before admission. Only seven cases of this rare variant of squamous cell carcinoma of the esophagus have previously been reported in the English literature.

CASE REPORT

A 66-year-old man with chronic dysphagia and chronic cough of 2 years duration was admitted to the Veterans Administration Medical Center, Ann Arbor, MI in October 1983, complaining of progression in dysphagia for both solids and liquids, and 20-lb weight loss during the 2 months before admission. Approximately 27 years before, he sustained extensive battery acid burns to his face, neck, upper part of the thorax, pharynx, and esophagus during a motor vehicle accident. He underwent multiple reconstructive and skin graft operations during the next 4 years. An esophageal stricture resulting from the caustic injury subsequently required frequent dilatations. He continued to be a heavy smoker and alcohol drinker until recently.

On physical examination he was a cachectic, dehydrated man in moderate discomfort. There were confluent scars across his face neck and upper chest. Chest examination revealed coarse rales in the right upper lobe and bilateral basilar rhonchi. The remainder of the physical examination was unremarkable.

The laboratory studies revealed Hb 13 g/dl, hematocrit 39.6%, white blood cell count 28,600/mm³, and normal serum electrolytes. A chest radiograph revealed cavitating infiltrates in the right upper lobe. A PPD was negative and no acid-fast bacilli were found in the sputum. The sputum cytology showed malignant cells. A barium swallow (Fig. 1) revealed a large polypoid mass in the proximal esophagus almost completely obstructing the lumen. The contrast medium extravasated through an esophageal perforation and filled a mediastinal abscess cavity on the right side. A large diverticulum of the proximal esophagus was also filled with the contrast medium. Computed tomography of the chest (Fig. 2) showed right upper lobe infiltrates

with cavity formation and a mediastinal abscess on the right side. Fine needle aspiration of the right upper lobe lesion yielded purulent exudate and budding yeast consistent with aspiration pneumonia. A laryngoscopic examination revealed a paralyzed right vocal cord. Bronchoscopy revealed no intrabronchial mass. Esophagoscopy showed a large cauliflower-like mass occluding the esophageal lumen at 17 cm from the incisors. Biopsy revealed verrucous squamous cell carcinoma of the esophagus (Fig. 3). Initial treatment consisted of antibiotics and nutritional support requiring a feeding gastrostomy tube. Due to combination of severe chronic obstructive pulmonary disease, mediastinal abscess, and marked debilitation, he was considered a poor surgical candidate. The patient refused chemotherapy. His general condition continued to deteriorate and on December 8, 1983 he died due to respiratory arrest. No autopsy was performed.

DISCUSSION

Although verrucous carcinoma of the oral cavity was initially described by Friedall and Rosenthal in 1941 (1), it was only recognized as a distinct morphological variant of epidermoid carcinoma by Ackerman in 1948 (2). This lesion has been reported to occur in the mouth, nasal cavity, larynx, glans penis, scrotum, vulva, vagina, endometrium, cervix, urinary bladder, and anorectal region (3-9). Minielly *et al.* in 1967 (10) described two patients with this lesion in the esophagus. On review they found only three other cases in the files of Mayo Clinic during the 61-year period from 1906-1967. To date, only eight cases of verrucous carcinoma of the esophagus including one from the present report have been published in the English literature (10-12). Pertinent data from previously reported cases involving the esophagus are summarized in Table 1.

Verrucous carcinoma is a distinct morphological entity by virtue of its gross, microscopic, and behavioral characteristics. It is a squamous cell carcinoma possessing several distinguishing features from a typical squamous cell carcinoma. On gross examination it is exophytic, warty, and cauliflower-like or papillary in appearance. It occurs with equal frequency in upper,

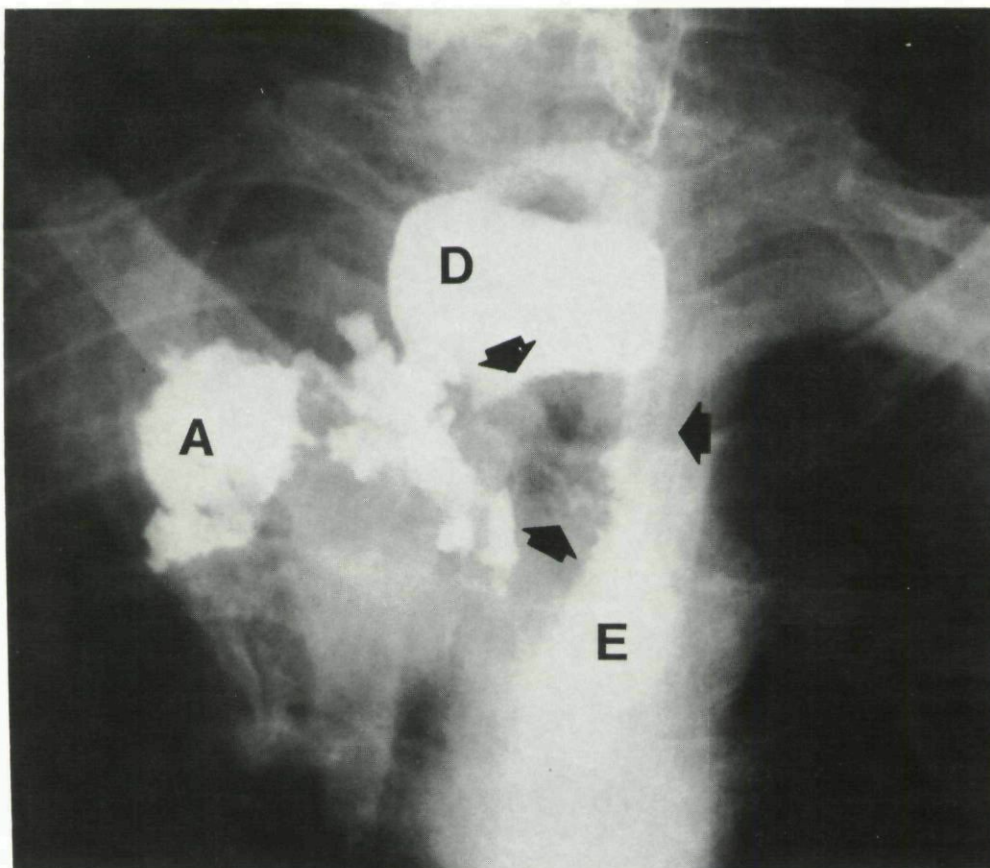


FIG. 1. An anterior posterior view from a barium swallow shows a large polypoid mass (arrows) in the proximal esophagus (E) partially obstructing the lumen with extravasation of barium into a mediastinal abscess (A). Note a large diverticulum (D) in the cervical esophagus.

middle, and lower thirds of the esophagus. It grows slowly with reported intervals between first symptoms and diagnosis of 18 months to 7 years, invades locally in a relentless fashion, and rarely metastasizes. Microscopically it is well to moderately well differentiated, shows hyperkeratosis, and marked acanthosis with swollen rete-pegs formed of well-differentiated squamous cells. Its mode of invasion shows a neoplastic lobule with a pushing margin rather than individual or small groups of invasive cells. Because of its well differentiated and often benign appearance the diagnosis of verrucous carcinoma may be missed on routine endoscopic biopsy, therefore, multiple biopsies, close clinical correlation, and a high index of suspicion are necessary for making an early diagnosis.

It is interesting to note that two of the eight cases reported had achalasia and two had esophageal diverticula. Among the eight reported cases of verrucous carcinoma this is the second case with a history of prior caustic ingestion with stricture formation. A number of etiological factors are implicated in squamous cell carcinoma of the esophagus including ethanol, smoking, achalasia, caustic stricture, Plummer-Vinson syndrome, tylosis, and radiation. Kiviranta (13) estimated that patients with caustic stricture have at least 1000-

fold higher prevalence of esophageal carcinoma than the general population. Appelqvist and Salmo (14) reviewed 63 patients with lye corrosion carcinoma and found a latency interval ranging from 13–71 years with an average of 41 years. He also found that patients with a history of caustic ingestion, although less operable (38 versus 45%), were more likely to be resectable (83 versus 65%) and to have greater 5-year survival (44 versus 33%) as contrasted with conventional squamous cell carcinoma.

Napalkov and Pozhariski (15) experimentally induced verrucous carcinoma in the esophagus after prolonged administration of an oil solution of N-methyl-N-nitrosoaniline in rats. The lesion progressed through stages of leukoplakia, epithelial proliferation and hypertrophy, and proliferation of connective tissue papillae. The smooth surface of the esophagus was transformed into a verrucous exophytic surface with several large pedicles in approximately 500 days.

All these studies lend credence to the theory that chronic inflammation and retention of food particles including dietary carcinogens may contribute to the pathogenesis of squamous cell carcinoma including verrucous type.

The diagnosis of verrucous carcinoma may be missed

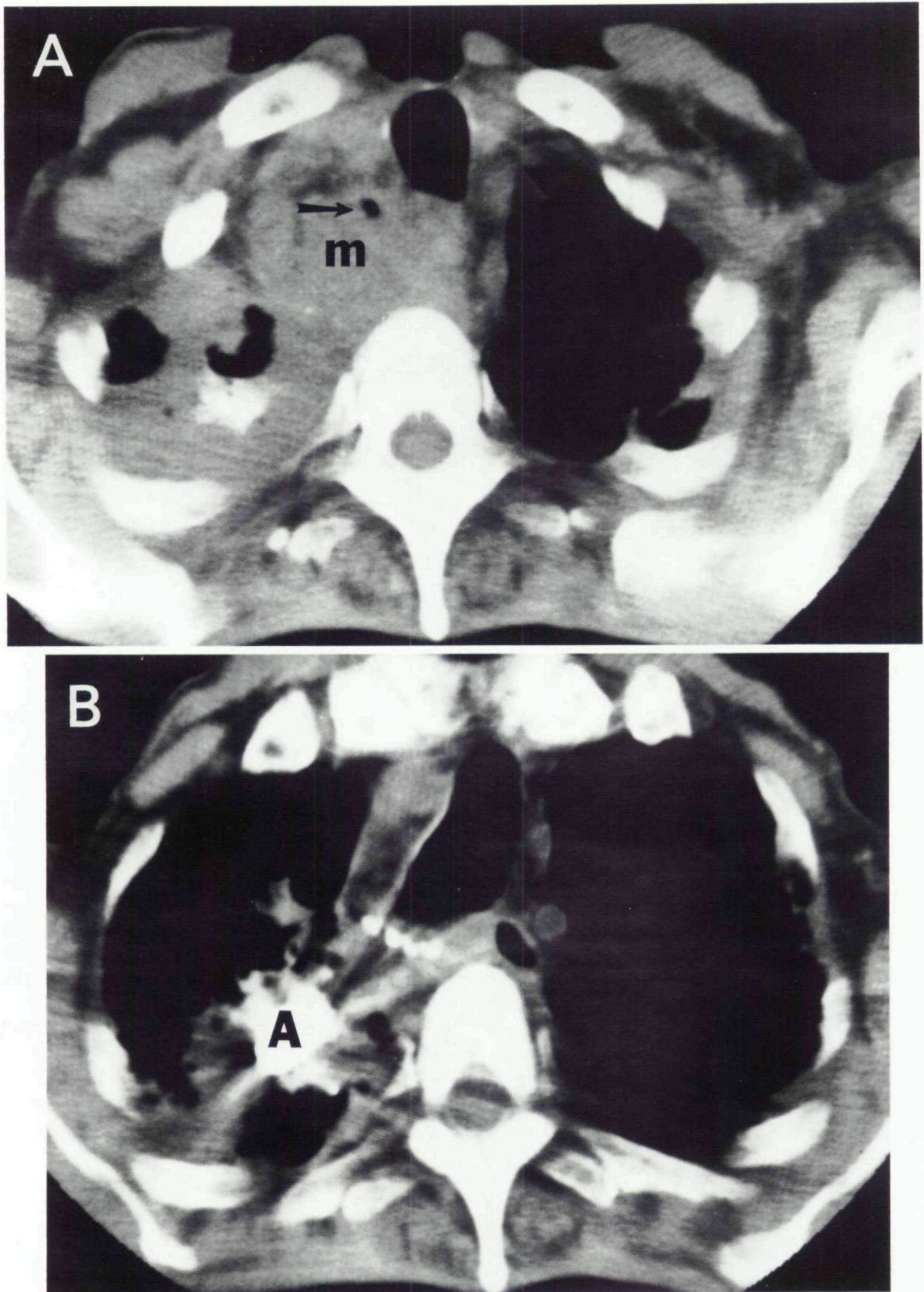


FIG. 2. CT scan of the cervical region and thorax. *A*, a section through the upper thoracic region shows a large solid mass (*M*) reducing the esophageal lumen to 2 mm (*arrow*). *B*, a section 4 cm below the level shown in *A* through the upper thorax shows contrast in the mediastinal abscess (*A*) on the right side and upper lobe pulmonary infiltrates.

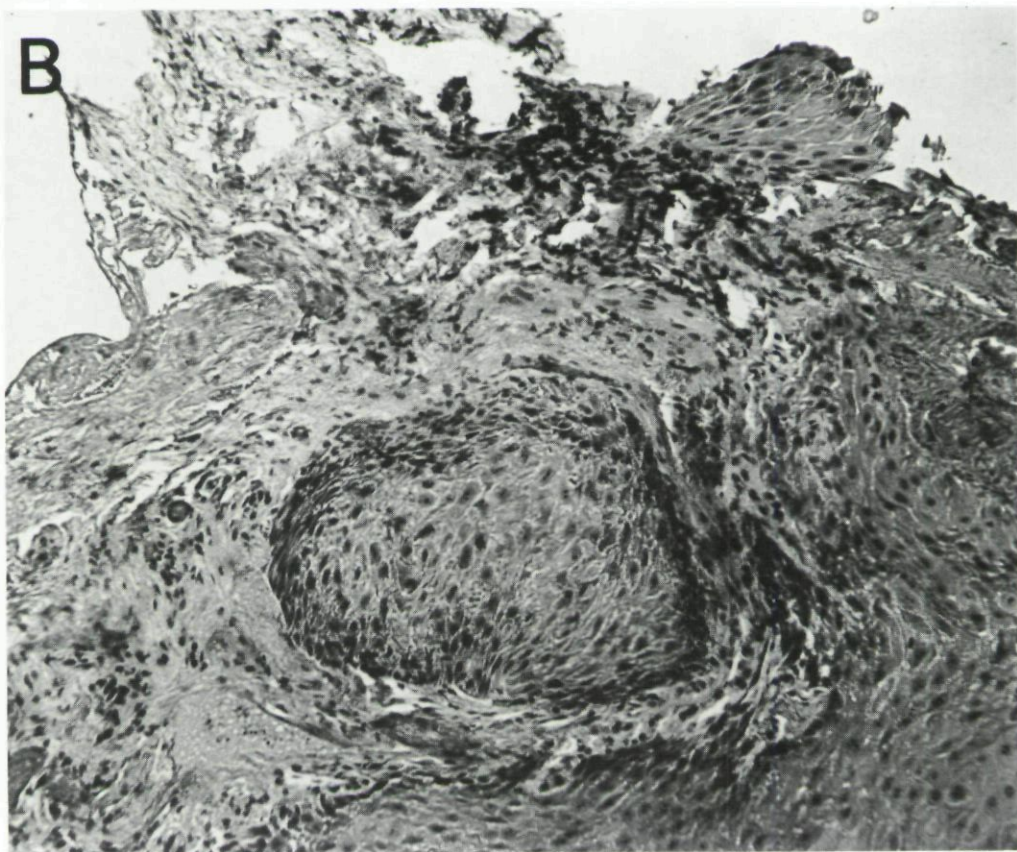
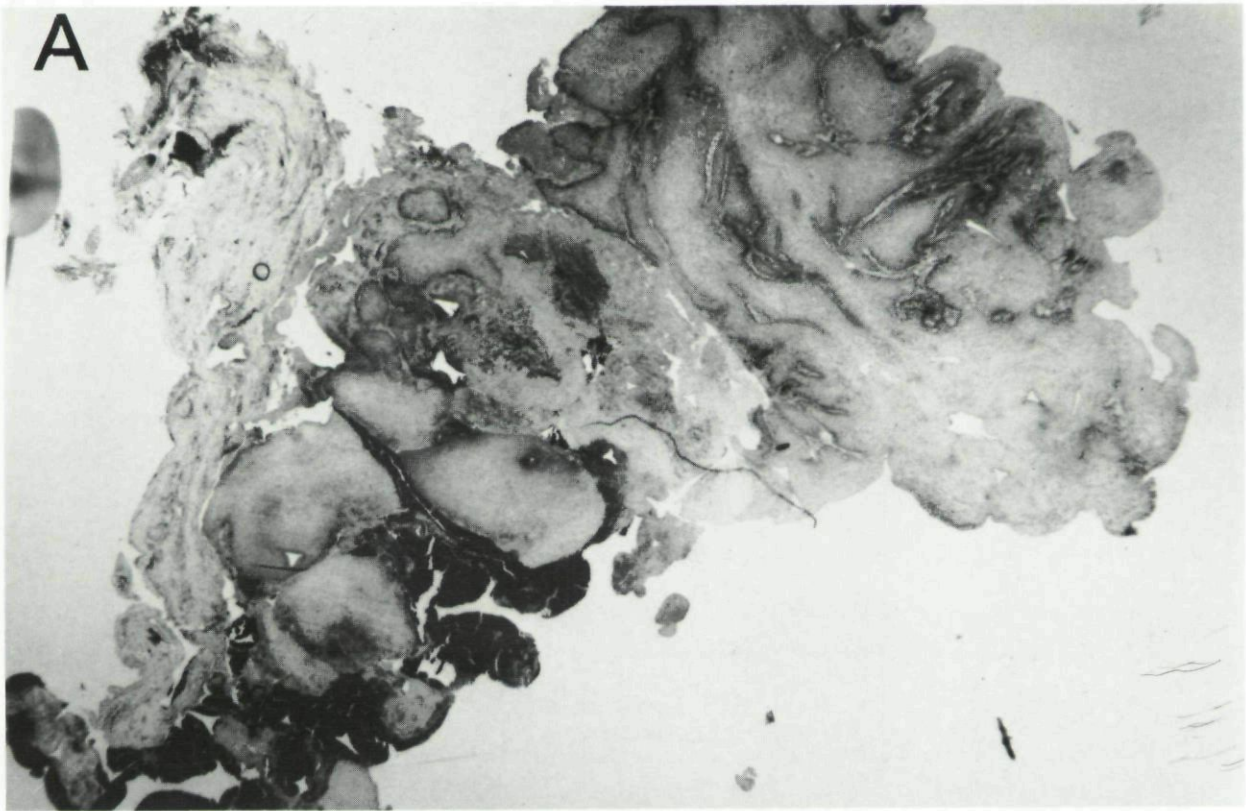


FIG. 3. *A*, lower power photomicrograph from the biopsy shows a lobular mass of well-differentiated carcinoma that extends into surrounding connective tissue in a pushing fashion (hematoxylin and eosin, $\times 40$). *B*, high power photomicrograph shows the relatively benign appearance of the neoplasm and illustrates the mode of extension into the adjacent connective tissue (hematoxylin and eosin, $\times 140$ of original magnification).

TABLE 1
Review of Eight Reported Cases of Verrucous Carcinoma of the Esophagus

Case	Author and Reference	Age	Sex	Location	Clinical Features	Esophagogram	Esophagoscopy	Pathology	Treatment and Follow-up
1	Minielly <i>et al.</i> (10)	58	M	Upper third	Achalasia for 43 yr; dysphagia worsened for 9 mo; 30 lb wt loss	Large, polypoid mass in achalasic esophagus	Large Friable mass	Biopsied 4 times in 9 mo read as benign; 5th biopsy; grade 1; verrucous carcinoma	Esophagectomy colonic interposition; postoperative tracheocolonic fistula; died of aspiration pneumonia
2	Minielly <i>et al.</i> (10)	70	F	Upper third	Dysphagia 8 yr; pharyngoesophageal diverticulum	Large mass	Reddish, tan mass at esophageal introitus	Biopsy; grade 1; verrucous carcinoma	Treated with radiation therapy
3	Minielly <i>et al.</i> (10)	70	F	Middle third	Achalasia 20 yr; dysphagia worsened for 2 mo	Large polypoid tumor	Extensive bulky tumor at 14 cm from incisor	Biopsy; grade 1; verrucous carcinoma	Bronchoscopy showed TEF; died of bronchopneumonia
4	Minielly <i>et al.</i> (10)	36	M	Lower third	Dysphagia for 10 yr; worse for 3 mo	Perforating carcinoma with periesophageal abscess; epiphrenic esophageal diverticulum	Esophagitis; mass in distal esophagus	Grade 1; verrucous carcinoma	Esophagectomy and proximal gastrectomy; postoperative esophagopleural fistula repaired; recurrence of gastropleural fistula; died of pulmonary complications
5	Minielly <i>et al.</i> (10)	57	M	Lower third	Dysphagia 4 yr; worse for 2 wk; anorexia; 20-lb wt loss	Large obstructing mass	Obstructing cauliflower-like mass at 35 cm from incisors	Several biopsies; verrucous carcinoma	Died 1 mo after diagnosis
6	Parkinson <i>et al.</i> (11)	76	M	Middle third	Lye ingestion 31 yr ago at age 45 yr with completely obstructing stricture of esophagus; had permanent feeding gastrostomy; hematemesis 18 mo ago; endoscopy showed esophageal ulceration; presented with loss of wt and generalized weakness	Dilated esophagus with obstructing stricture in the middle third	Cauliflower-like mass	Cytological examination diagnostic of verrucous carcinoma	Died of pneumonia 6 days after admission
7	Meyerowitz and Shea (12)	45	M	Lower third	Hematemesis feeling of fullness after meals but no dysphagia	Large polypoid mass; barium swallow 7 yr ago showed a smaller mass present in the distal esophagus	Endoscope could not be passed beyond 33 cm from incisor safely because of large mass	Esophagogastrectomy 8.0 × 5.5 cm mass; verrucous carcinoma	3 mo later died of bronchopneumonia
8	Agha <i>et al.</i> (present report)	66	M	Upper third	Dysphagia 2 yr worse for the past 2 mo with productive cough; acid burns to face, pharynx, and esophagus 27 yr ago required several esophageal dilatations	Large mass with mediastinal abscess	Large cauliflower-like mass; right vocal cord paralysis	Biopsy; verrucous carcinoma	Died of aspiration pneumonia 2 mo after diagnosis

despite several biopsies because the neoplasm is so well differentiated and often appears benign histologically. Careful clinical, endoscopic, and pathological correlation with adequate sized biopsy material and high index of suspicion are necessary. Cytological examination

may be useful in supporting the diagnosis, as it was in this patient and as has been reported by Parkinson *et al.* (11). In our patient by the time the diagnosis of verrucous carcinoma of the esophagus was made, he had developed esophageal perforation with a medias-

tinal abscess, right vocal cord paralysis due to recurrent laryngeal nerve involvement, and right upper lobe aspiration pneumonia.

Reprint requests: Dr. Farooq P. Agha, Department of Radiology, Box 13, University Hospital, Ann Arbor, MI 48109.

REFERENCES

1. Friedell HL, Rosenthal LM. The etiologic role of chewing tobacco in cancer of the mouth: report of eight cases treated with radiation. *JAMA* 1941;116:2130-5.
2. Ackerman LV. Verrucous carcinoma of the oral cavity. *Surgery* 1948;23:670-8.
3. Goethals PL, Harrison EG, Devine KD. Verrucous squamous carcinoma of the oral cavity. *Am J Surg* 1963;106:845-51.
4. Kraus FT, Perez-Mesa C. Verrucous carcinoma, clinical and pathologic study of 105 cases involving oval cavity, larynx and genitalia. *Cancer* 1966;19:26-38.
5. Gilbert EF, Palladino A. Squamous papillomas of the uterine cervix: review of the literature and report of a giant papillary carcinoma. *Am J Clin Pathol* 1966;46:115-21.
6. Sebai I, Sherif M, Bolkainy MM, et al. Verrucose squamous carcinoma of bladder. *Urology* 1974;4:407-10.
7. Gingrass PJ, Bubrick MP, Hitchcock CR, et al. Anorectal Verrucose squamous carcinomas: report of two cases. *Dis Colon Rectum* 1978;21:120-2.
8. Ryder DE. Verrucous carcinoma of the endometrium a unique neoplasm with long survival. *Obstet Gynecol* 1982;59(6 suppl):789-805.
9. Anscombe AM, Isaacson P. An unusual variant of squamous cell carcinoma (inverted verrucous carcinoma) arising in a pilonidal sinus. *Histopathology* 1983;7:123-7.
10. Minielly JS, Harrison EG Jr, Fontana RS, et al. Verrucous squamous cell carcinoma of esophagus. *Cancer* 1967;20:2078-87.
11. Parkinson AT, Haidak GL, McInerney RP. Verrucous squamous cell carcinoma of the esophagus following lye stricture. *Chest* 1970;57:489-92.
12. Meyerowitz BR, Shea LT. The natural history of squamous verrucose carcinoma of the esophagus. *J Thorac Cardiovasc Surg* 1971;61:646-9.
13. Kiviranta UK. Corrosion carcinoma of the esophagus: 381 cases of corrosion and nine cases of corrosion carcinoma. *Acta Otolaryngol (Stockh)* 1952;42:89-95.
14. Appelqvist P, Salmo M. Lye corrosion carcinoma of the esophagus: a review of 83 cases. *Cancer* 1980;45:2655-8.
15. Napalkov NP, Pozhariski KM. Morphogenesis of experimental tumors of the esophagus. *J Natl Cancer Inst* 1969;42:927-40.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.