
CASE REPORT

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METASTATIC HEAD AND NECK CARCINOMA TO A PERCUTANEOUS ENDOSCOPIC GASTROSTOMY SITE

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Abstract: *Background.* Percutaneous endoscopic gastrostomy (PEG) tube placement is a safe and widely accepted alternate route for enteral alimentation in the head and neck cancer patient population. Cancer metastatic to a PEG tube exit site is a rare but serious complication of this procedure. We sought to determine the route of spread responsible for PEG site metastases such that we may prevent further occurrences of this highly morbid condition. We also report a case of PEG site metastasis at our institution.

Methods. We performed a MEDLINE search for the years 1962 to 2002 and conducted a review of the literature. In the case at our institution, a 63-year-old man was referred to our institution with recurrent squamous cell carcinoma of the right base of tongue; he also had a 1.5-cm left apical lung nodule. He underwent PEG tube placement at the time of staging panendoscopy. Six months after the original tube placement, he had an ulcerated mass develop at the PEG site; biopsy of the mass revealed squamous cell carcinoma histologically identical to the base of tongue tumor. He also had recurrent lung cancer and four hepatic lesions develop.

Results. In our MEDLINE search, of the five patients diagnosed with PEG site disease >10 months after PEG placement, all five (100%) had synchronous distant metastatic disease. In the group of patients diagnosed with PEG site metastases ≤10 months after PEG placement, only four (24%) of 17 had synchronous distant metastatic disease. All patients underwent PEG placement by means of the “pull” technique.

Direct implantation with a variable-sized initial tumor burden can explain all cases of PEG site metastasis. The presence of distant metastases is representative of the natural history of advanced head and neck malignancies. Smaller initial tumor implants present later than would larger initial tumor burdens, when the patient is more likely to have distant metastatic disease. In the case at our institution, the patient did not respond to treatment for his hepatic and PEG site metastases and his lung cancer, and he died 4 months after detection of the PEG site metastasis.

Conclusions. PEG site metastases are iatrogenic complications of PEG tube placement in patients with squamous cell carcinoma of the upper aerodigestive tract. The use of laparoscopic, open, or the “push” technique of PEG tube placement in patients with head and neck cancer may prevent direct implantation of malignant cells into an enteral access site. © 2005 Wiley Periodicals, Inc. *Head Neck* 27: 339–343, 2005

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Head and neck carcinoma, and its treatment, often significantly alters the normal functioning of the upper aerodigestive tract, affecting both mastication and deglutition. When these alterations are likely to lead to malnutrition, one should consider one of the available options for enteral alimentation. The percutaneous endoscopic gastrostomy (PEG) tube is one of the most well tolerated and widely used modalities available to

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bypass the upper aerodigestive tract and allow for maintenance of the patient's nutritional status during treatment or for reversal of malnutrition.

The PEG technique, introduced in 1980 by Gauderer and Ponsky, had its safety and utility confirmed in the head and neck cancer patient population by Ruppin and Lux in 1986.¹ By 1989, Preyer and Thul² reported the first case of upper aerodigestive tract cancer metastatic to a PEG site, and in 1996 Schneider and Loggie³ performed the first successful resection of a PEG site metastasis. Efforts to codify the existing the described cases of PEG site metastases were provided by Potochny et al.⁴ It is to this body of knowledge that we add our experience with a PEG site metastasis, discuss critically the possible mechanisms of malignant spread to a PEG site, and make new recommendations for prevention of this potentially lethal complication of a common procedure performed in patients with head and neck cancer.

LITERATURE REVIEW

We performed a comprehensive MEDLINE search of the literature (1962–2002) to identify cases of metastatic involvement of a PEG site in patients with a primary squamous cell carcinoma of the upper aerodigestive tract. Data collected included TNM classification, time interval between PEG placement and diagnosis of PEG site metastasis, occurrence of synchronous distant metastatic disease, treatment for the primary tumor, and eventual patient outcome. A total of 21 cases in the literature are reviewed in addition to a new case of PEG site metastasis identified at our institution.

CASE REPORT

A 63-year-old white man with a complicated history of multiple squamous cell carcinomas of the upper aerodigestive tract was referred for management of a newly diagnosed recurrence at the base of tongue (BOT). The patient had been treated 10 years previously with a full course of external beam radiation therapy (XRT) and a right neck dissection for a right BOT squamous cell carcinoma. He subsequently (5 years ago) had a new squamous cell carcinoma of the epiglottis develop, for which he underwent a total laryngectomy with pectoralis major myocutaneous flap reconstruction. His postoperative rehabilitation with regard to speech and swallowing function was above average, because the patient was quite

adept at using an electrolarynx and was maintaining his weight by eating a regular diet by mouth. The patient was initially seen with a 3-month history of progressive odynophagia and dysphagia, with confirmation of squamous cell carcinoma of the right BOT on biopsy.

He subsequently underwent complete restaging to include panendoscopy and imaging of the head, neck, abdomen, and pelvis, and he was noted to have a single 1.5-cm left apical lung nodule considered to be a synchronous primary tumor, staged as T4N0M0. Our tumor board recommended resection and reconstruction of the BOT lesion followed by left thoracotomy and lobectomy for a suspected primary lung cancer as determined by the thoracic surgery service. The patient underwent PEG tube placement at the time of his panendoscopy. Within a couple of weeks, he underwent resection of the right BOT lesion by way of a mandibulotomy approach, reconstruction with an anterior push back tongue flap, and left modified radical neck dissection. All surgical margins and lymph nodes were negative for malignancy. The patient had an unremarkable postoperative course, tolerating a liquid diet within a few weeks of surgery and advancing to a soft mechanical diet for the entirety of his caloric needs by the time of his thoracic procedure 1 month later. The PEG tube was removed at this time, and the patient continued to tolerate a soft diet. Monthly follow-up examinations were unremarkable until 6 months after his original PEG placement. The patient was found to have an ulcerated mass at the PEG site, which was biopsied and found to be squamous cell carcinoma identical in histologic findings to that of the BOT tumor. Further workup for metastatic disease was discouraging, because CT scans demonstrated recurrence of his lung cancer at the thoracotomy site, the interval development of four low-attenuation hepatic lesions of concern for metastatic disease, and a 6-cm left upper quadrant mass extending from the greater curvature of the stomach, through the left rectus abdominis muscle, and out through the skin at the site of the patient's former PEG tube. Physical examination, fiberoptic nasopharyngoscopy, and CT remained without evidence of recurrent disease within the head and neck region.

Metastatic disease involving the liver and the PEG site in addition to recurrence of the primary lung tumor were treated with two cycles of ifosfamide, paclitaxel, and carboplatin without response. The abdominal wall mass was treated with XRT without significant therapeutic effect.

The patient continued to experience complications of his metastatic disease, including hypercalcemia, wound infection, and anemia resulting from gastrointestinal hemorrhage; he was entered into hospice care and died 4 months after detection of the PEG site metastasis.

DISCUSSION

Deciphering the route of malignant spread is the key step in preventing this rare, but frequently lethal, complication of PEG tube placement. Most authors agree that one or more of three different mechanisms may play a role in the development of PEG site metastases. Direct translocation of malignant cells from a primary tumor of the upper aerodigestive tract to the PEG tube exit site implicates surgical instruments used in the procedure as the mechanism of iatrogenic spread.⁵⁻¹⁰ A second theory involves desquamation of malignant cells into the gastrointestinal tract with resultant distal implantation at the surgically disturbed PEG tube site.⁵⁻⁸ The third mechanism, hematogenous spread, is the well-established route by which malignant cells penetrate the circulatory system and travel to a site distant from the primary disease.^{5,6,11}

Our case represents only the 22nd patient reported with head and neck cancer metastatic to a PEG tube site. Douglas et al⁸ examined tumor growth kinetics and made several intriguing conclusions regarding the six cases he identified in his literature review. He suggested that hematogenous spread is possible in patients who have PEG site metastases develop more than 1 year after surgery, because the long interval could be explained by a tiny initial tumor burden small enough to traverse the pulmonary circulation.⁸ Rapidly developing PEG site disease is more plausibly a result of a large direct deposition of tumor cells at the time of PEG placement.⁸ The unpredictable size of an initial tumor inoculum, as well as the cancer's inherent biologic growth features and properties of host resistance, can explain the variable time from PEG placement to the initial presentation of metastatic disease.⁸

In reviewing all 22 cases, we note for the first time that all five patients with a PEG site metastasis occurring more than 10 months after placement had distant metastases synchronous with PEG site disease.⁴ Of the 17 patients who had PEG site metastases develop ≤ 10 months after placement, only four patients (24%) had synchronous distant metastases (see Table 1).^{2,4}

Table 1. Reported cases of head and neck cancer metastatic to a PEG site.

Time until diagnosis of PEG site metastases	Distant metastases at the time of PEG site metastasis	Upper aerodigestive tract site	Stage at diagnosis of primary tumor	Histology	PEG technique	Reference
18 mo	Lung	Supraglottic	T4N3bM0	SCC	Pull	7
16 mo	Lung	Tongue	T2N0M0	SCC	Pull	6
13 mo	Intraabdominal (peritoneal)	Tongue	T4N2bM0	SCC	Pull	9
12 mo	Lung	Larynx	T3N2bM0	SCC	Pull	6
11 mo	Liver	Hypopharynx	T1N0M0	SCC	Pull	13
10 mo	None	Mouth, tongue, epiglottis	T4N0M0	SCC	Pull	3
9 mo	None	Hypopharynx	T2N2M0	SCC	Pull	4
9 mo	Bone, colon	Tongue	T4N2bM0	SCC	Pull	11
6 mo	None	Floor of mouth	T4N3M0	SCC	Pull	5
6 mo	None	Supraglottic	T4N3M0	SCC	Pull	14
6 mo	NA	Hypopharynx	T4N2aM0	SCC	Pull	10
6 mo	Liver	Tongue	T4N0M0	SCC	Pull	Present report
5 mo	NA	Esophagus	T3N1M0	SCC	Pull	11
5 mo	None	Esophagus	NA	SCC	Pull	16
4 mo	NA	Hypopharynx	NA	SCC	Pull	15
4 mo	NA	Esophagus	Stage III	SCC	Pull	11
4 mo	None	Tongue	T2N0M0	SCC	Pull	4
3 mo	Lung	Hypopharynx	T4N3M0	SCC	Pull	11
3 mo	Lung	Hypopharynx	NA	SCC	Pull	2
3 mo	None	Oropharynx	T4N3M0	SCC	Pull	8
2 mo	None	Hypopharynx	T4N0M0	SCC	Pull	17
2 wk	NA	Esophagus	T4NxM0	AdenoCa	Pull	11

Abbreviations: PEG, percutaneous endoscopic gastrostomy; NA, not available; SCC, squamous cell carcinoma; AdenoCa, adenocarcinoma.

The longer patients with advanced head and neck squamous cell carcinoma survive after treatment, the greater the likelihood of distant metastatic disease developing. These data support the hematogenous spread theory of Douglas et al,⁸ in that intravascular dissemination of tiny initial burdens could, over time, arrive and develop into clinically relevant lesions at the surgically disturbed PEG site just as they do in other, more typical locations within the body. The higher incidence of synchronous distant metastases in patients >10 months after PEG placement may be more reflective of the natural history of biologically aggressive, advanced head and neck squamous cell carcinoma than it is proof of hematogenous spread of cancer to the PEG site; however, in those patients initially seen with widely metastatic squamous cell carcinoma, one cannot exclude the possibility of hematogenous spread to the PEG site as simply another distant metastasis.

One argument against the theory of hematogenous spread of squamous cell carcinoma to PEG sites is the consistency with which a single endoscopic technique, directly contacting the tumor and the gastrostomy site, was used to perform all PEG placements in the reviewed cases. Every reported case of PEG site metastases, including our own, used the "pull" method of PEG tube placement in which the PEG tube and dome are pulled through the mouth, pharynx, esophagus, stomach, and abdominal wall until the retaining dome of the feeding tube is secured against the gastric mucosa.^{1,3,4,10,11} Other surgical procedures are routinely performed in patients with head and neck cancer, often at the same setting as an extirpative procedure, tracheotomy, or panendoscopy; however, the literature fails to produce any evidence of hematogenous spread to distant surgical sites. Harvest sites of flaps for microvascular free tissue transfer exemplify the type of surgical site to which one might expect to be involved by the hematogenous spread of malignant cells; fortunately, the literature reports no cases of tumor dissemination to these seemingly fertile, vascular, operative fields. To the best of our knowledge, the literature contains no reports of head and neck cancer metastatic to a PEG tube site when placed by the "push" technique at a laparoscopic gastrostomy tube site, MediPort site, or any other distant surgical location accessible only by the hematogenous route. A single case of squamous cell carcinoma metastasis from an oral cavity primary tumor to an open gastrostomy site has been reported; however, the

author himself concedes that "unwittingly...a contaminated scalpel" was likely used to perform the gastrostomy at the end of a long head and neck cancer operation.¹²

The possibility of malignant cells from an upper aerodigestive tract tumor desquamating and seeding of a more remote site is an accepted theory in the oncology literature.^{7,11} The malignant seeding of a PEG site by exfoliated tumor cells is similar to the favored mechanism of direct implantation. The theory requires that malignant cells at the periphery of an upper aerodigestive tract tumor become dislodged, swallowed, and remain viable within the gastric environment until they happen on the disturbed gastric mucosa or granulation tissue at the PEG site. A single case in the literature seems to support this mechanism until it is critically examined.

Bushnell et al⁷ report a patient with T4N3bM0 squamous cell carcinoma of the supraglottic larynx who had a PEG placed 6 weeks after total laryngectomy who then, 18 months later, had squamous cell carcinoma develop limited to the PEG site skin scar as well as in an adjacent area of abdominal skin not related to the PEG procedure. Complete workup identified multiple synchronous pulmonary masses consistent with metastatic carcinoma, without evidence of recurrent or new upper aerodigestive tract cancer.⁷ This case represents the longest interval ever reported between PEG placement and discovery of PEG site disease, as well as the only case with malignant cells limited to the skin without involvement of the stomach or abdominal wall. In the absence of an upper aerodigestive tract squamous cell carcinoma to seed the PEG site, the desquamation and seeding theory becomes increasingly difficult to support. On reviewing their case, we believe it represents not a case of PEG site metastases, but rather the development of dermal and pulmonary metastases in a patient 2 years after treatment for a stage IVb supraglottic squamous cell carcinoma.

Given our finding that PEG site metastases are possible iatrogenic complications of PEG tube placement, several recommendations for prevention can be offered. Many authors have recommended the oncologically sound avoidance of contact with malignant cells for fear of implanting disease in naive remote regions.^{7,9-11,13-15} Some authors suggest achieving local control of the upper aerodigestive tract malignancy before undertaking PEG placement,^{4,8} whereas others advocate abandoning the "pull" technique in any

patient with an upper aerodigestive tract malignancy in favor of alternative procedures for establishing enteral access.^{11,13,14} We believe that by performing laparoscopic or open gastrostomy tube placement, with meticulous care to keep the surgical sites and equipment separate, malignant disease involving the enteral access site may be prevented.

CONCLUSION

This article documents our experience with a case of head and neck squamous cell carcinoma metastatic to a PEG tube site. A critical review of the literature supports direct surgical implantation of malignant cells over the theories of hematogenous spread or direct tumor cell exfoliation as mechanisms responsible for PEG site metastases. Importantly, PEG site metastases resulting from direct implantation of tumor is the one possible mechanism that physicians can eliminate through changes in their practice.

We believe that PEG site metastases represent an iatrogenic complication of the “pull” technique of PEG placement when used in patients with head and neck cancer. Recognition of direct implantation as even a possible mechanism of tumor dissemination should prompt all physicians involved in the care of patients with head and neck cancer to take every effort to eliminate this route of spread. Measures should include treatment of the squamous cell carcinoma before instrumentation of the upper aerodigestive tract, enteral access procedures that do not contact the area of the malignancy, such as laparoscopic or open gastrostomy techniques, or the “push” method of PEG tube placement.

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