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Percutaneous endoscopic gastrostomy tube-associated metastasis in pharyngo-oesophageal malignancy

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Introduction

A large proportion of patients with pharyngo-oesophageal carcinoma will either present with or develop dysphagia and odynophagia due to iatrogenic intervention or as a result of advancing disease. Gastrostomy tubes are an indispensable resource for maintaining nutrient intake in patients who are unable to take in adequate oral nutrition.¹⁻⁵ The optimum technique of gastrostomy placement in the setting of head and neck malignancy remains controversial. Currently, the most commonly used method of establishing enteral feeding in this patient subset is the minimally invasive 'pull' percutaneous endoscopic gastrostomy (PEG) technique, first described by Gauderer *et al.* in 1980.^{2,3} In addition to the usual complications of PEG tube insertion, patients undergoing this procedure for head and neck cancer are at risk of developing malignant seeding of the PEG stoma site.^{1,2,4,5} The first reported case of a cancer metastasising to a gastrostomy stoma was reported by Alagaratnam in 1977.⁶ This phenomenon became relevant to otolaryngologists in 1989 when Preyer and Thul established a link between upper aerodigestive cancer and stomal recurrence post PEG tube placement.⁷ Subsequently, a study published by Thakore *et al.* identified only two cases of gastric metastasis occurring without a history of PEG tube implantation in the setting of

pharyngo-oesophageal carcinoma.⁸ On average, 10,000 PEG tubes per year are placed in patients with pharyngo-oesophageal malignancy in the United States. This statistic, along with a mean survival time of only 4.3 months in confirmed cases of metastasis, illustrates the importance of determining the exact relationship between PEG placement and stomal recurrence.^{1,9} Knowledge of the incidence, pathophysiology, clinical relevance and prevention measures of PEG-associated stomal metastasis in head and neck cancer patients remains extremely limited.

Case report

A 60-year-old male presented to his GP with persistent odynophagia. After several failed courses of antibiotics, the patient was referred to an otolaryngology clinic for further investigation. Pharyngoscopic examination revealed a large exophytic tongue mass beginning at the level of the circumvallate papillae and extending inferiorly to the level of the hyoid bone. Biopsy performed at this time revealed a squamous cell carcinoma (SCC). The patient underwent radiographic staging and was classified as T2N1M0. The decision was made to treat the patient with radiotherapy alone. The patient was fitted with a PEG tube before the initiation of treatment in order to maintain adequate nutritional status with the anticipated pharyngeal discomfort and oedema. The PEG

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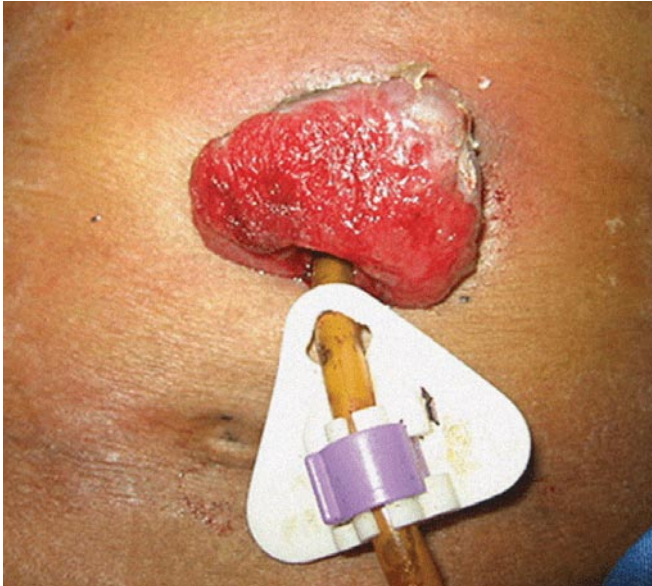


FIGURE 1: Stomal site squamous cell carcinoma, similar to the one seen in the patient.²⁶

tube was inserted without complication on July 6, 1999, via the endoscopic 'pull' technique, which involved passing a guidewire through the oropharynx. During the endoscopic procedure, the patient's stomach and oesophagus were well visualised and unremarkable. The patient began his radiotherapy regime two weeks after the PEG procedure and received a total of 7,920cGy of radiation to the tongue base and left and right cervical areas over a period of six weeks. There was no residual disease noted after the completion of radiotherapy and the PEG tube was removed one month later without any apparent complications. Shortly thereafter, the patient returned to his GP with vague discomfort and intermittent bleeding around the site of the previous gastrostomy. The site appeared inflamed and firm (Figure 1). A course of co-amoxiclav was prescribed, but the patient's condition failed to improve. A punch biopsy of the area was taken and analysis revealed that the lesion was an SCC. CT/PET restaging scans identified a solitary mass in the anterior gastric wall, which extended through the left rectus abdominis muscle into the subcutaneous fat and skin (Figure 2). The location of the lesion was consistent with the site of the previous gastrostomy tube. The histology of the tumour was reviewed at an oncological board meeting and it was found to be consistent with that of the patient's primary tongue base malignancy. It was theorised that the tumour somehow seeded to the stoma site as a result of PEG tube placement.

The tumour was resected during an extensive operation that included a Billroth II gastrectomy, a 10cm excision of the abdominal wall and an exploratory laparotomy. Post-operation pathological analysis of the specimen found an SCC with clear margins measuring 9x5x3cm that had involved the stomach, abdominal wall and skin. Remarkably, all nine regional lymph nodes were negative, so no adjuvant therapy was initiated.¹⁰

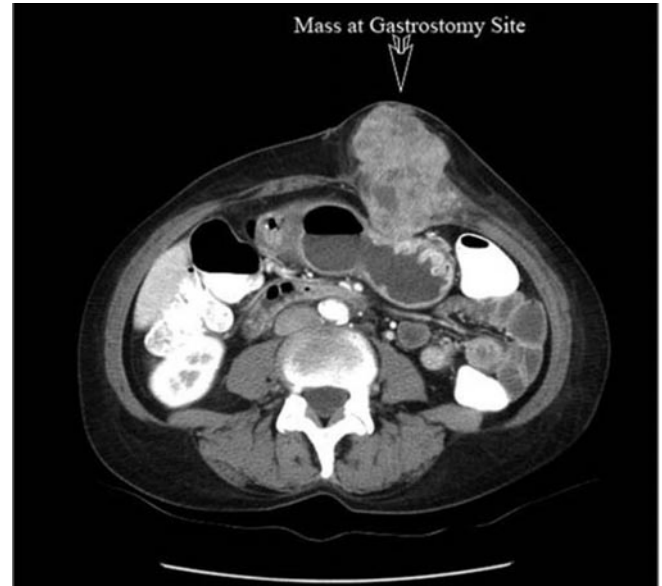


FIGURE 2: CT scan of another patient revealing mass infiltration from the stoma site into the abdominal and gastric walls.²⁷

Discussion

The mechanism by which these malignancies metastasise to the PEG tube stoma site remains controversial. There are three commonly suggested hypotheses. First, the PEG tube may be directly contaminated with viable malignant cells as it traverses the pharynx, which are subsequently implanted in the stomach and abdominal wall at the gastrostomy site.^{1,11-17} Second, it is theorised that the malignant cells that slough off continually are ingested and take root in the tissue surrounding the PEG tube.² Third, it is postulated that malignant cells arrive at the stoma site by the conventional means of haematogenous or lymphatic dissemination.^{4,18,19}

The implantation of malignant cells during both diagnostic and interventional surgical procedures is a well-recognised occurrence.^{8,11,20,21} The direct implantation theory is widely accepted in head and neck cancer patients because it is very simplistic, and studies show that stomal recurrences are most frequently observed when the trans-oral 'pull' method of PEG tube placement is used.^{1,22} The trans-oral approach causes the PEG tube to come into direct contact with the tumour, which may dislodge viable malignant cells as it traverses the upper aerodigestive tract. It is plausible that during the endoscopic procedure, the movement of the tube down the oesophagus may act as a vector for the direct implantation of malignant cells to the port site. Others argue that it is not clear whether stomal recurrences are actually caused by the 'pull' technique or if they are simply observed more because this technique is employed in up to 98% of head and neck cancer patients who require enteral feeding.¹

Despite the popularity of the direct implantation hypothesis, it cannot be ruled out that the malignant cells are reaching the stoma site via haematogenous or lymphatic spread. Studies

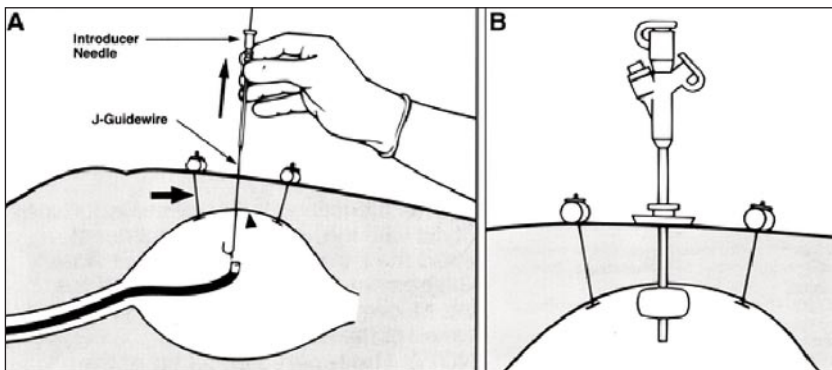


FIGURE 3: An illustration of the transabdominal 'introducer' technique for gastrostomy tube placement.¹³

conducted on animal models have demonstrated that traumatised tissue is more susceptible than healthy tissue to the deposition of circulating malignant cells.^{8,23} The increased circulation and angiogenesis that occurs in injured tissues, along with the increased density of platelets and collagen, provides an ideal micro-environment for tumour cell adherence and growth.²³ This theory is supported by several cases where patients developed metastasis to their stoma sites after open and radiologically placed gastrostomy, during which no equipment came into contact with the primary malignancy.^{8,24} The natural shedding of tumour cells into the lumen of the gastrointestinal tract can account for metastasis at PEG tube sites whether the tube is placed radiologically, trans-abdominally or trans-orally. However, it seems unlikely that tumour cells can survive the acidic pH of the stomach long enough to take root at the gastrostomy site.¹⁸ Cruz *et al.* recommended that the use of proton pump inhibitors be contraindicated in head and neck cancer patients, as they hypothesised that acid suppression may provide a more favourable environment for tumour growth.¹

Developing preventive measures for PEG-associated metastasis will remain a challenge until our knowledge of the pathogenesis of this complication grows. Analysis of previous cases of stomal metastasis has revealed an increased risk in patients with poorly differentiated, advanced stage pharyngo-oesophageal SCCs when compared to other head and neck cancers.²² Moreover, patients who underwent PEG tube placement prior to the initiation of therapy were found to be at increased risk, presumably because the gastrostomy tube had a higher likelihood of being contaminated with viable malignant cells.²⁵ One study advocated the administration of systemic chemotherapy around the same time as PEG tube placement in all head and neck cancer patients, based on the rationale that chemotherapy would decrease the circulating load of malignant cells and would make it more difficult for any tumour cells dislodged during the procedure to seed the PEG site.²⁵ Perhaps the greatest controversy with regard to the prevention of stomal metastasis is the method used to place the PEG tube. Regardless of the technique's relative importance in the spread of malignancy, it has been shown that gastrostomy procedures that bypass the oropharynx, such as the introducer (Figure 3)

and SLiC techniques, are associated with a 39% decrease in the incidence of complications, such as abscess and cellulitis, in head and neck cancer patients.¹³ As the location of these tumours leads to varying degrees of aerodigestive obstruction and subsequent bacterial overgrowth, it is thought that the trans-oral 'pull' approach exposes the apparatus to these bacteria, leading to a higher rate of complication.¹³ However, these procedures are more technically difficult, which may account for their less frequent use.

Conclusion

The use of PEG tubes in the setting of pharyngo-oesophageal malignancy allows patients to maintain adequate nutritional intake. However, the procedure is not without risks, the most serious of which may be the malignant seeding of the stomach and abdominal wall at the gastrostomy site. It may be that reported cases of PEG-associated metastasis underestimate the true incidence of this complication, which may be as high as 1%.¹ Physicians should be aware of this complication, as prognosis is quite poor.²² Furthermore, clinicians must educate patients on this complication prior to the insertion of a PEG tube in the setting of head and neck malignancy as part of proper management and informed consent.

The mechanism of metastasis to the gastrostomy site remains unclear. It may be that both haematogenous spread and sloughing off into the gastrointestinal tract play a role in this disease process. Regardless of the method of spread, a trans-abdominal approach such as the introducer technique should be indicated in all patients with active head and neck malignancy because it is safe, bypasses viable malignant cells and is associated with fewer complications in this patient group.¹³

Approval and consent

In collaboration with the board of physicians from ENT Consultants located in St. John's Newfoundland, a proposal for this case report was submitted to and approved by the research ethics board of the Memorial University of Newfoundland (MUN). The patient granted his consent for the authors to review all relevant medical files and submit a written case report based on information retrieved from MUN's database.

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