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Commentary: Pigmented spot during esophagoscopy—a mole or melanoma?

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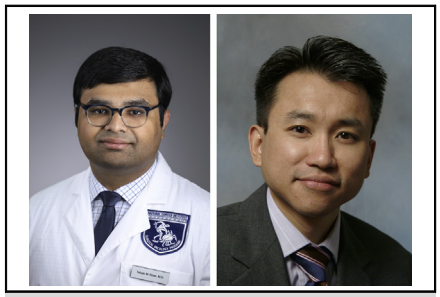

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CENTRAL MESSAGE

Surgical resection accompanied by systematic lymphadenectomy and adjuvant therapy may improve survival for primary malignant melanoma of the esophagus, which remains a diagnostic dilemma.

Primary malignant melanoma of the esophagus (PMME) is a very rare noncutaneous tumor first described in 1906 but not histopathologically proven until 1952.[1] It is thought to arise in this organ from the anomalous migration of neural crest cells during development. The world literature contains fewer than 350 cases of reported PMME.[2] Consequently, a standard-of-care treatment approach for this disease remains largely undefined, although surgical intervention is a mainstay for this serious cancer, with poor overall survival rates.

Dai and colleagues, in this issue of the *Journal*, assess outcomes of 70 patients from 10 hospitals accrued over a 20-year period with locally advanced PMME.[3] This report represents the largest case series of surgically treated PMME to date. As the authors highlight, there is a significant diagnostic challenge posed by PMME. Pathologic workup correctly identified less than half of patients preoperatively. Compounding this dilemma, a handful of patients in their series presented with no pigment at all (amelanotic melanoma). The authors' experience reminds clinicians to have a high index of suspicion for PMME when the expected histologies common to esophageal cancer are not encountered during routine workup, prompting more extensive tests such as melanoma-specific staining to obtain a correct diagnosis. A major observation from this study is that more than 50% of patients presented with lymph node metastasis regardless of stage differences, although, consistently, the greater the number of surgically dissected lymph nodes ($\geq$12), the more favorable was prognosis. Finally, the use of adjuvant therapy in these surgical patients correlated with improved survival, although due to limited subgroup numbers and diverse therapeutic modalities, the authors could not extensively explore this aspect of care. Most intriguingly, in the context of systemic therapies for melanoma, the modern success of small molecule targeted therapy (ie, BRAF plus MEK inhibitors[4]) and immune checkpoint inhibition (ie, anti-PD-1 alone or in combination with anti-CTLA-4 immunotherapy[5]) lend optimism to how multimodality care could potentially be improved for this rare tumor. Integrating these agents as adjuvants to surgical treatment or perhaps exploring their role in a neoadjuvant setting are logical next steps to consider.

The paucity of PMME, reliably and consistently diagnosed, will practically deny any future attempts at prospective, much less large-scale, evaluations of multimodality therapeutic interventions. For now, we look to this reference data set presented by Dai and colleagues for clinical guidance. They have emphasized the importance of curative intent resection combined with some kind of adjuvant therapy toward being able to achieve better survival for patients with this aggressive disease.

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THOR

Commentary: All that glitters is not gold

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CENTRAL MESSAGE

A retrospective study of patients treated by a variety of strategies is discussed. With recent knowledge gained in melanoma, the risk factors and optimal treatment strategies remain to be defined.

The authors submit results on the surgical treatment for primary melanoma of the esophagus (PMME) to provide new knowledge where little is known. This study collects data from multiple institutions from 1998 to 2018.[1] Approximately 53% of patients with PMME were initially misdiagnosed with other types of esophageal cancer. Given the small tissue sample size and poor differentiation, preoperative diagnosis was a challenge. Treatment of all patients followed strategies for esophageal cancer at the time they occurred. Current risk factors such as depth of invasion, subtype, and mutations associated with primary melanoma were not collected but data associated with esophageal cancers were. Positron emission tomography was not in routine use. Forty-one patients (58.6%) underwent a Sweet esophagectomy, rarely performed today, 17 (24.3%) a McKeown, 9 (12.9%) an Ivor–Lewis, and 3 (4.3%) a transhiatal. Despite the study reaching 2018, there is no mention of minimally invasive esophagectomy as a surgical approach, even though the companion video is of a minimally invasive esophagectomy. Remarkably, there was no operative mortality and surgical complications, grades II-IV, were low at 19.9%. This is particularly impressive, considering the study spans evolution in perioperative care and surgical techniques dating back to 1998.

Sex, presence of lymph node metastasis, extent of lymph node dissection, and postoperative therapy are reported as independent factors affecting prognosis. Although a more extensive lymph node dissection was associated with improved survival, it was not statistically significant. The impact of lymphadenectomy is a current point of controversy in patients with primary melanoma. Two randomized prospective studies have demonstrated no 10-year survival benefit in sentinel node positive patients undergoing lymphadenectomy.[2,3] In the current study, those patients who received adjuvant treatment from a variety of regimens also had improved survival, although few had initial therapy specific to melanoma, and even fewer had radiation therapy. Today, therapy for melanoma is rapidly evolving, with the introduction of several targeted therapies that have demonstrated significant improvement in survival even in late staged patients.[4]

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