

Occult Esophageal Squamous Cell Carcinoma Presenting with Multiple Bony Osteolytic Lesions Clinically Mimicking Multiple Myeloma: A Diagnostic Dilemma

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Abstract

Keywords

- ▶ esophageal squamous cell carcinoma
- ▶ dysphagia
- ▶ multiple myeloma

Bone metastasis as an initial presentation of esophageal carcinoma is uncommon. In the absence of typical presentations like dysphagia, these cases may lead to diagnostic dilemmas both for the clinicians and pathologists. Here, we report a case of disseminated metastasis of esophageal squamous cell carcinoma to the bone in a 47-year-old female, who presented with multiple osteolytic lesions and clinically mimicking multiple myeloma. A detailed diagnostic work-up established the diagnosis of esophageal squamous cell carcinoma.

Introduction

Esophageal cancer is one of the fatal cancers worldwide with a 5-year survival rate of 40% for localized tumors and 4% for tumors with advanced distal metastasis.¹ Histological types, grade, and stage are important factors in esophageal cancer prognosis. Regional and distant metastases have a profound impact on survival and outcome.¹ The most common sites of esophageal cancer metastases are lymph nodes, lung, liver, bones, adrenal glands, and brain.¹ Although bone metastasis of esophageal carcinoma is known, metastasis to the bone as an initial presentation is uncommon.^{2,3} Bone metastasis of esophageal carcinoma presenting with osteolytic lesions may clinically mimic multiple myeloma (MM) leading to delay in diagnosis.³ Here, we present a case of disseminated metastasis of esophageal squamous cell carcinoma (ESCC) to the bone in a 47-year-old female, who presented with multiple osteolytic lesions, clinically mimicking MM.

Case Report

A 47-year-old female was admitted to hospital with an abrupt onset of left forearm pain with limited range of motion in the left hand. She had 6-month history of generalized weakness,

decreased appetite, and backache. There was no history of trauma. She had no other significant past history.

On examination, her vitals were stable. She had pronounced lumbar kyphoscoliosis. No other peripheral lymphadenopathy or any organomegaly was detected. The rest of the systemic and general physical examinations were unremarkable.

The patient was found to have anemia with hemoglobin of 7.7 g/dL with normocytic normochromic morphology of the red blood cells, deranged renal parameters with a creatinine of 2.8 mg/dL, and hypercalcemia with a corrected calcium level of 16.8 mg/dL. The parathyroid hormone level was 20.2 pg/mL, which was normal. The Mantoux test was negative. Her skeletal survey revealed a pathological fracture of left humerus with multiple lytic lesions in the skull, dorso-lumbar vertebrae, and iliac bones (▶ Fig. 1A–C). A provisional diagnosis of MM was maintained after ruling out hyperparathyroidism.

The bone marrow aspirate was diluted; however, it showed an increase in plasma cells. Serum electrophoresis did not reveal any monoclonal peak. Bence Jones protein was not detected in the urine. At this point, the diagnosis of MM was in doubt. Bone marrow biopsy revealed myelofibrosis with infiltration by pleomorphic cells (▶ Fig. 1D). On immunohistochemistry

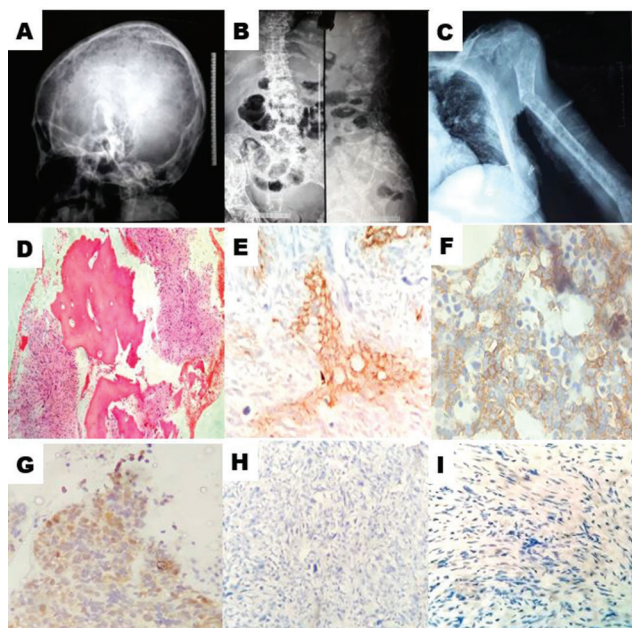


Fig. 1 Multiple lytic lesions of the (A) skull, (B) dorso-lumbar vertebrae and iliac bones. (C) Fracture left humerus. (D) Bone marrow biopsy showing myelofibrosis with infiltration by pleomorphic cells (H and E, 4 \times). The pleomorphic cells positive for cytokeratin AE1/AE2 (E), CK5/6 (F), and p63 (G) (IHC, 400 \times) and negative for CD38 (H) and CD138 (I) (IHC, 400 \times). IHC, immunohistochemistry.

(IHC), these cells were positive for cytokeratin AE1/AE2, CK5/6, CK7, and p63 (\rightarrow Fig. 1E-G). The tumor cells were negative for CK20, CD45, CD38, and CD138 (\rightarrow Fig. 1H,I). Based on these findings a diagnosis of poorly differentiated carcinoma metastasis to bone marrow from the upper gastrointestinal tract was made. Upper gastrointestinal endoscopy revealed an esophageal ulcer measuring 2 \times 1 cm, which was 20 to 22 cm from the upper incisors. Histopathological examination of the biopsy from the esophageal ulcer showed features suggestive of poorly differentiated squamous cell carcinoma (\rightarrow Fig. 2A). The tumor cells were positive for cytokeratin (\rightarrow Fig. 2B). Thus, a final diagnosis of a disseminated bone marrow metastasis from ESCC was made. In the meantime, the general condition of the patient deteriorated rapidly, and she expired after 4 weeks of hospital admission.

Discussion

ESCC, which is a predominant histologic subtype of esophageal cancer, has an overall 5-year survival rate of 14%.⁴ Metastases of ESCC to the bone are uncommon and vary from 1 to 14% in autopsy series.⁵ In clinical practice, bone metastases of esophagus cancer occurred infrequently. Radiologically bone metastases in esophageal carcinoma are detected in 1.6% of all cases with distant metastases.⁵ The detection rate has improved with positron emission tomography using F-18 FDG (fludeoxyglucoseF18 injection).⁵ Micrometastases of esophageal carcinoma to bone marrow are detected in 20.9% of the cases by light microscopic examination and 30.2% of cases by cytokeratin IHC.² Usually

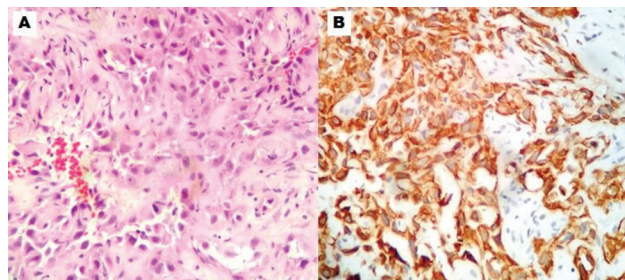


Fig. 2 (A) Esophageal biopsy showing esophageal squamous cell carcinoma (H & E, 400 \times). (B) Tumor cells positive for cytokeratin (IHC, 400 \times). IHC, immunohistochemistry.

bone metastases are osteolytic in nature, mixed patterns like osteolytic-osteoblastic and osteolytic-osteosclerotic are also reported.^{3,5}

The various other malignancies, which present with osteolytic metastases, are malignant melanoma, renal cell carcinoma, gastric carcinoma, colorectal carcinoma, hepatocellular carcinoma, thyroid carcinoma, and small cell lung carcinoma.³ Like other malignancies, spine is the most common site of bone metastases in esophageal carcinoma.⁵ In the present case, a panel of IHC markers helped in ruling out other malignancies. The tumor cells in the bone marrow biopsy were negative for HMB45 (ruled out malignant melanoma), CD10 (ruled out renal cell carcinoma), CK20 (ruled out colorectal carcinoma), HepPar1 (ruled out hepatocellular carcinoma), and thyroid transcription factor-1 or TTF1 (ruled out thyroid carcinoma). Negative immunoreactivity for leukocyte common antigen ruled out lymphoma whereas negative immunoreactivity for CD38 and CD138 ruled out plasma cell dyscrasia like MM. Infections like tuberculosis can also present with osteolytic bony lesions.³ In the present case, tuberculosis was ruled out as there was no fever and the Mantoux test was negative.

The natural course of esophageal carcinoma involves the esophagus primarily with extension to the adjacent structures.⁶ So, the symptoms appear when these anatomical structures are involved leading to dysphagia, dysphonia from laryngeal paralysis, weight loss followed by substernal and/or epigastric pain, and regurgitation.⁶ Dysphagia is a typical presentation of esophageal carcinoma present in more than 80% of the cases.^{6,7} However, dysphagia occurs only when two-thirds of the esophageal lumen is involved.⁷ A deep infiltrating tumor can metastasize to adjacent organs without producing dysphagia.³ Cases of esophageal carcinoma presenting with bone pain due to bone metastasis and without any complaint of dysphagia are extremely rare.⁵ The lack of dysphagia in the present case could be explained by the non-stenotic pattern of the lesion. Comparison of the present case with some of the cases reported in the literature is enumerated in \rightarrow Table 1.^{3,5-9}

Cases of occult carcinomas presenting with osteolytic bone metastasis may clinically mimic MM.³ The diagnosis of MM requires the presence of \geq 10% clonal plasma cells in the bone marrow or biopsy proven plasmacytoma along with evidence of end-organ damage such as hyper

Table 1 Table showing comparison of the present case with some of the cases reported in the literature

Authors	Age (y)/sex	Histological type of esophageal carcinoma	Site(s) of bony metastasis	Nature of bone metastasis
Alvarez Diaz et al ³	59/M	Adenocarcinoma	Cervical and dorso-lumbar vertebrae, left humerus, ribs and right femoral neck	Osteolytic and osteoblastic
Reezae and Bradaran Rahimi ⁵	60/F	ESCC	Left femur	Osteolytic
	42/F	ESCC	Left tibia	Osteolytic
	24/M	ESCC	Left iliac bone	Osteolytic
	60/F	ESCC	Cervical vertebrae	Osteolytic
	40/M	ESCC	Ribs	Osteolytic-sclerotic
Shewchuk et al ⁶	59/F	ESCC	Right femur, left iliac bone, and skull	Osteolytic
Viaro et al ⁷	58/M	Epidermoid carcinoma	Cervical vertebrae	Osteolytic
Singh et al ⁸	37/M	ESCC (post esophagectomy for ESCC)	Right calcaneus	Osteolytic
Sánchez-Jiménez et al ⁹	63/M	Adenocarcinoma	Left maxilla	Osteolytic
Present case	47/F	ESCC	Skull, dorso-lumbar vertebrae iliac bones, and left humerus	Osteolytic

Abbreviation: ESCC, esophageal squamous cell carcinoma.

Calcemia, Renal dysfunction, unexplained Anemia, and Bony lytic lesions (CRAB).¹⁰ There are reports of MM presenting with an esophageal ulcer.¹⁰ The present case had features of end-organ damage like hypercalcemia, renal dysfunction, anemia, and bony lytic lesions, which led to the clinical suspicion of MM. Bone marrow biopsy with negative monoclonal peak and urine Bence Jones protein helped in ruling out MM. Upper gastrointestinal endoscopy and biopsy from the esophageal ulcer helped in confirming the diagnosis of ESCC.

Such cases are managed symptomatically as chemotherapy and radiotherapy do not improve survival.³

Occult esophageal carcinoma presenting with osteolytic bone metastasis may clinically mimic MM. Typical clinical presentations like dysphagia, dysphonia, substernal and/or epigastric pain, and regurgitation may not be present in these cases leading to diagnostic dilemma both for the clinicians and pathologists.

Conflict of Interest

None declared.

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