

CASE REPORT

Metastatic involvement of skeletal muscle from gastric adenocarcinoma

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Abstract

Gastric cancer represents the fifth most common cancer diagnosis worldwide and the third leading cause of cancer-related mortality. In the USA, the overall 5-year survival rate is 31%, with distant disease nearing 5%. The most common sites of metastasis are the liver and peritoneum. Skeletal muscle involvement has been rarely reported. Since clinical and imaging findings overlap with primary sarcomas, a confirmatory biopsy is required for diagnosis. Prognosis remains poor with treatment options including palliative chemotherapy, radiotherapy and surgical resection. We report the case of a 57-year-old female presenting with extensive involvement of skeletal muscle 10 years after achieving remission. In addition to illustrating the refractoriness and poor outcomes associated with muscle involvement, this case and comprehensive review of the literature highlights important characteristics of disease biology and tumor genomics that warrant detailed discussion and exposition to a wider audience.

INTRODUCTION

Gastric cancer is the fifth most common cancer diagnosis reported worldwide and the third leading cause of cancer-related mortality [1]. In the USA, the overall 5-year survival rate is 31%, with distant disease nearing 5% [2]. Up to 75% of patients can present with distant metastasis or lymph node involvement [3–4]. The most common sites of metastasis are the liver (48%) and peritoneum (32%) [5–6]. Other sites include the lung (15%), bone (12%), lymph nodes and adrenal gland [5–8]. Skeletal muscle involvement has been rarely reported.

CASE PRESENTATION

A 57-year-old Hispanic female with history of T3N1M0 poorly differentiated signet ring cell type adenocarcinoma of the GEJ, presented in late December 2018 with worsening abdominal and left lower-extremity pain. She had been treated initially in 2008 with two cycles of neoadjuvant DCF (docetaxel, cisplatin and 5FU) followed by total gastrectomy with D2 lymphadenectomy and roux-en-y reconstruction. Pathology done at that time showed a 10.5 cm poorly differentiated mucinous adenocarcinoma with transmural extension and invasion of the serosa and perigastric

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Table 1: Reported cases of skeletal muscle metastases from gastric carcinoma

Case	Year	Authors	Age (years)	Sex	Affected muscles
1	1962	Sato et al. [18]	N/A	N/A	Iliopsoas m.
2	1979	Treves and Barruch [19]	52	M	Psoas m.
3	1983	Obley et al. [20]	54	M	Paraspinal m.
4	1983	Fujiwara et al. [21]	74	F	NA
5	1984	Rosenbaum et al. [22]	54	M	Upper arm m., Femoral m.
6	1989	Arnold et al. [23]	59	F	Extraocular m.
7	1990	Porile et al. [24]	65	M	Sartorius m., Rectus femoris m.
8	1993	Sudo et al. [11]	61	M	Trapezius m.
9	1993	Van Gelderen [26]	47	F	Extraocular m.
10	1994	Toillon et al. [25]	58	M	Gastrocnemius m.
11	1996	Amano and Kumazaki [27]	57	M	Gastrocnemius m.
12	1997	Baude et al. [28]	N/A	N/A	Masseter m.
13	1998	Narvaez et al. [29]	49	M	Psoas m.
14	1998	Pestalozzi and von Hochstetter [30]	72	F	Gastrocnemius m.
15	1998	Pinto et al. [31]	N/A	N/A	NA
16	2001	Oba et al. [7]	70	M	Lumbar m., iliopsoas m.
17	2002	Kondo et al. [8]	64	F	Gluteus maximus m., Adductor magnus m.
18	2003	Varma et al. [32]	72	M	Anterior femoral m.
19	2004	Tuoheti et al. [9]	48	M	Shoulder muscle.
20	2004	Tuoheti et al. [9]	89	M	Gluteal muscle.
21	2006	Bese et al. [33]	60	M	Paravertebral m.
22	2008	Souayah et al. [34]	49	M	Lateral rectus m.
23	2009	Tougeron et al. [10]	71	M	Deltoid m.
24	2011	Sakuma et al. [35]	64	F	Gluteal m.
25	2012	Gogou et al. [17]	N/A	N/A	Femoral m.
26	2014	Pergolini et al. [36]	67	M	Adductor m.
27	2014	Lourenço et al. [15]	68	M	Upper thigh m.
28	2015	Koga et al. [16]	71	M	Latissimus dorsi m., transverse abdominal m., iliopsoas m., femoral m.
29	2017	Temido et al. [37]	42	M	Extraocular m.
30	2019	Aguirre et al.	57	F	Right Quadratus lumborum m. and Psoas m., left gluteus maximus m., vastus lateralis m., obturator internus m. and piriformis m.

N/A not available, F female, M male.

adipose tissue. One in 27 lymph nodes was positive. She underwent adjuvant chemoradiation with capecitabine and had an uneventful follow-up. She was in remission until December 2017 at which time she was noted to have ascites and hematochezia. Findings on paracentesis were consistent with peritoneal carcinomatosis. Follow-up colonoscopy showed colonic and rectal erosions with biopsies returning as metastatic poorly differentiated gastric adenocarcinoma. She had completed four cycles of FLOT (oxaliplatin, docetaxel, 5-fluorouracil, leucovorin) prior to being admitted for urgent workup.

CT of the abdomen and pelvis obtained on admission showed an infiltrative soft tissue mass centered in the right quadratus lumborum with extension into the right psoas and right paraspinal muscles (Fig. 1). Follow-up MRI of the left femur demonstrated aggressive mass lesions within the left gluteus maximus and the left vastus lateralis extending into the posterior compartment of the thigh, strongly suggestive of metastatic involvement (Fig. 2). Tissue biopsy confirmed metastatic poorly differentiated adenocarcinoma involving fibromuscular tissue (Fig. 3). HER2/neu and PD-1 studies were negative. Palliative radiotherapy was started for symptomatic relief with a planned dose of 20–30 Gy. Tissue samples were sent for next-generation sequencing (NGS) which characterized the mass as MS-Stable with low tumor mutational burden (TMB: 5 Muts/Mb) and a

distinctive genomic profile showing FGFR3 amplification and mutations in BRAF G596S, MLL2 F603fs*327 and TP53 R175H. The patient agreed to hospice care and expired 3 months after discharge.

DISCUSSION

Skeletal muscle metastases from any primary tumor are rare occurrences with a reported incidence of 0.03 to 0.16% [9]. Though extremely uncommon, metastases usually stem from lung (25%), genitourinary (22.3%), gastrointestinal (21%) and breast primaries (8.2%) [9–13]. Metastatic infiltration is usually multifocal and adjacent to the trunk (paravertebral muscles, gluteus and thigh) and lower limb, followed by the arm, abdominal wall and chest [9–13].

From a physiological perspective, it is difficult to explain why skeletal muscle is only rarely affected by metastatic seeding from hematogenous dissemination given its high vascularity and total mass accounting for nearly 50% of total body weight [8, 10]. It is hypothesized that dynamic variability in muscular blood flow, mechanical movement during active exercise and endogenous production of lactic acid may act as protective measures against said outcomes [7, 14–15].

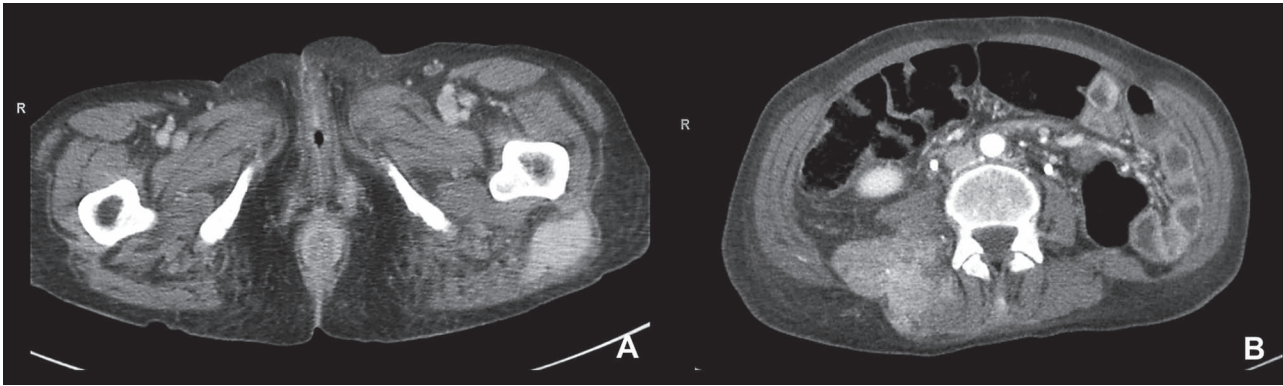


Figure 1: CT scan of pelvis with contrast [axial views]. Contrast-enhanced soft tissue mass compromising the left gluteal maximus and measuring 2.5×4.5 cm (A). There is also a contrast-enhanced soft tissue mass adjacent to the right side of the L4 vertebra that involves the quadratus lumborum muscle and causes edema of the psoas muscle (B). The mass measures 5.9×3.2 cm in diameter.

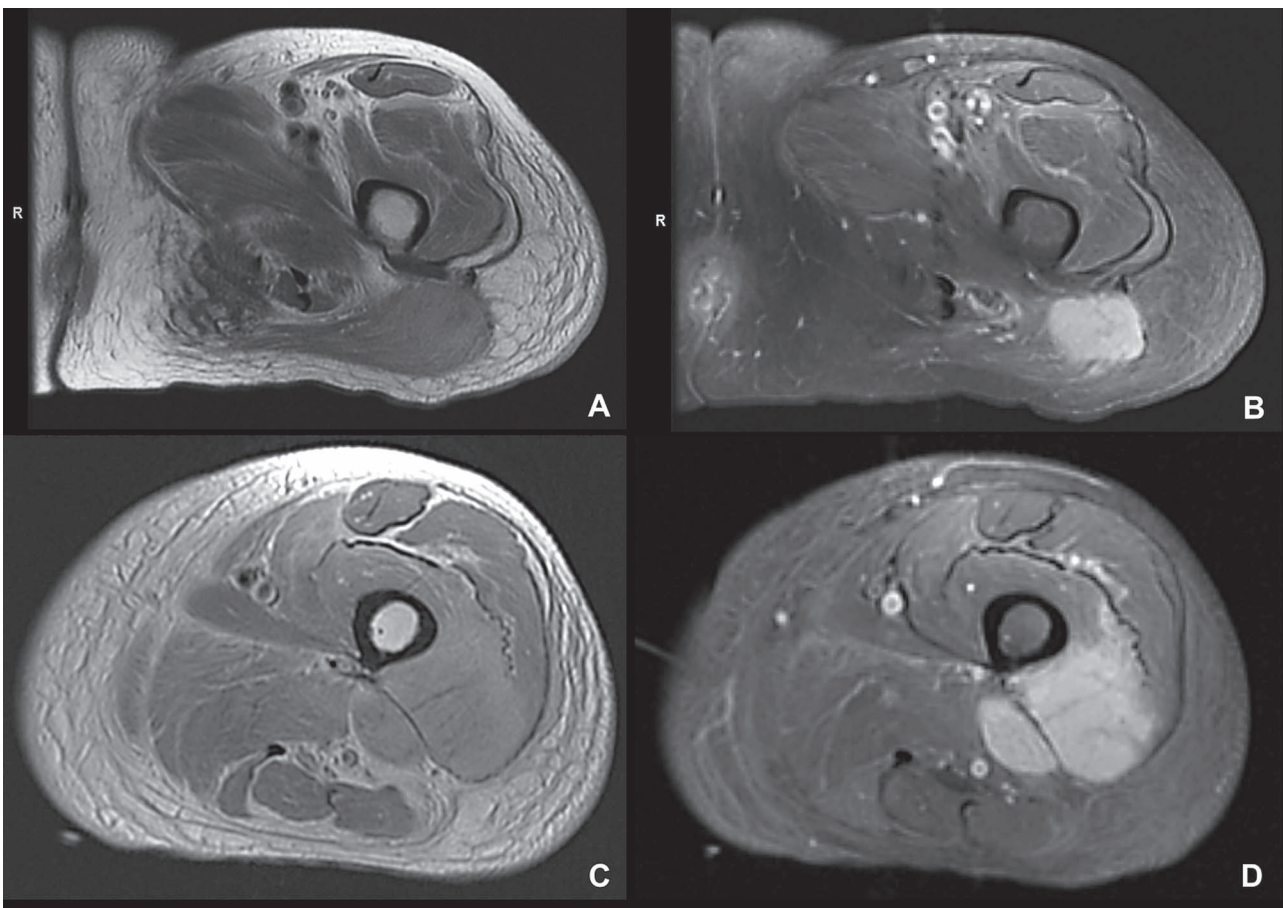


Figure 2: Gadolinium-enhanced T1-weighted and T2-weighted MRI s of the pelvis [axial views]. T1-weighted images show a mass with isointense signal and poorly-defined margins in the left gluteus maximus measuring $4.8 \times 3.0 \times 4.7$ cm (A), as well as a poorly defined isointense mass within the deep aspect of the left vastus lateralis muscle (C). On T2-weighted images (B & D) these lesions appear hyperintense with well-defined margins (no areas of central necrosis are evident).

Only 30 cases of muscle involvement from a gastric primary have been reported in the literature since the 1960s (Table 1) [7–11, 15–37]. The vast majority of patients in these reports are males ($n = 19$, 63%) with females accounting only for 27% of cases ($n = 8$). There were three instances in which gender was not reported. Mean age at diagnosis was 61 (ranging from 42 to 89 years). In most reported instances, muscle metastases developed with synchronous hepatic and/or lung involvement.

Our case is similar in presentation to the one by Koga *et al.* in that widespread muscle infiltration occurred in the absence of liver or lung involvement [16].

Clinically, muscle metastases present as painful palpable masses, in contrast to primary soft-tissue sarcomas [11, 13]. Since clinical and imaging findings overlap, a confirmatory biopsy is required for diagnosis [10]. Most skeletal muscle metastases are detected on CT imaging because of its routine

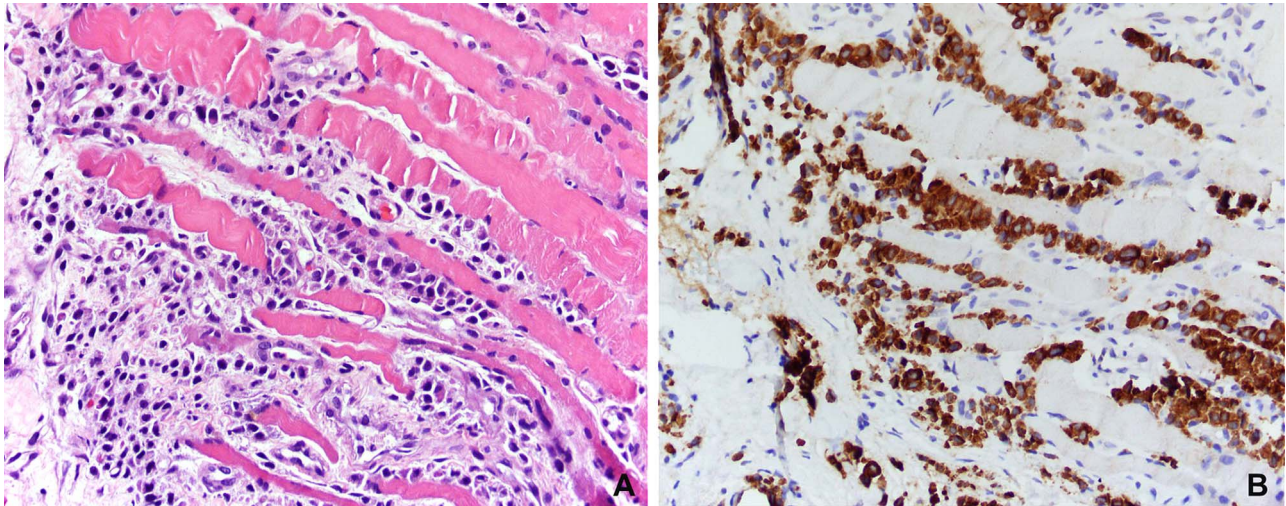


Figure 3: Tissue biopsy [left gluteus muscle mass]. (A) Poorly differentiated carcinoma invading skeletal muscle (H&E, 20 \times). (B) Keratin immunostain showing positive signet ring carcinoma cells (IHC, 20 \times).

widespread use. Nevertheless, MRI is considered the superior imaging modality to characterize muscle features [7, 9, 13, 15–17]. Per an extensive retrospective analysis of 461 patients conducted by Surov et al., most muscle metastases present as hyperintense lesions on T2-weighted imaging relative to its surrounding musculature and hypo- or isointense lesions with heterogeneous enhancement on T1-weighted modalities [38]. Both primary sarcomas and muscle metastatic disease exhibit similar features on MRI [11, 13]. On CT imaging, lesions exhibit a vast array of nonspecific radiological features. In the aforementioned study out of the 17 patients with a stomach primary, 41.2% presented as masses with homogenous contrast enhancement, 29.4% presented as diffuse infiltration with muscle swelling, 23.5% had intramuscular calcifications and only 6% ($n = 1$) presented as an abscess-like lesion [38]. There were no instances presenting as intramuscular bleeding on CT imaging. It is important to point out, though, that extensive perilesional enhancement with areas of central necrosis on gadolinium-DTPA (diethylenetriamine penta-acetic acid) enhanced MRI may be pathognomonic features of muscle metastasis as shown in a retrospective series of 12 patients by Tuoheti et al. [9].

Prognosis remains poor namely due to the presence of a widely metastatic disease and lack of effective treatment modalities [16–17]. Treatment options include palliative chemotherapy, radiotherapy and surgical resection for symptomatic relief. Chemotherapy is indicated for advanced disease with extensive metastatic burden [9, 13, 16]. Surgical excision may even prolong patient survival per some accounts, but the evidence is limited [9, 17].

In conclusion, skeletal muscle metastasis arising from a gastric primary is extremely rare and carries a poor prognosis. Any painful soft tissue mass in this patient population should raise immediate suspicion and warrants further analysis with MRI and biopsy. Proper identification is key so as to not delay treatment. NGS can prove to be particularly useful and provide invaluable information to guide potential targeted treatment on the basis of tumor-specific genetic profiling. Chemotherapy, radiation and surgical excision remain adequate palliative options for symptomatic relief.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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ETHICAL APPROVAL

No ethical approval was required for the drafting of this manuscript.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

GUARANTOR

L.E.A., M.G.-B. and B.A. are guarantors of this article.

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