VIA MEDICA

CASE REPORT

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Skeletal muscle metastasis from oesophageal adenocarcinoma — case report and literature review

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ABSTRACT

The most common sites of metastases from oesophageal carcinoma are lymph nodes, liver, lungs, and bones. Metastases to skeletal muscles are very rare and are characterised by extremely poor prognosis. A 62-year-old man with advanced oesophageal adenocarcinoma underwent chemoradiotherapy. More than six months after the primary diagnosis, the patient presented with distant solitary metastasis to the skeletal muscle of the left lower leg. He complained of severe pain and swelling of the left lower leg. Radiological and pathological examination confirmed metastatic character of the lesion. The patient was qualified for radiotherapy.

Metastases to skeletal muscle are very rare, and no guidelines have been established for the treatment for these patients. It seems that chemotherapy and radiotherapy can be considered as the best treatment modality for these patients.

Key words: oesophageal carcinoma, skeletal muscle metastasis, oesophageal adenocarcinoma

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Introduction

According to the International Agency for Research of Cancer (IARC), oesophageal cancer is currently the eighth most common cancer worldwide. In 2018, there were approximately 572,000 newly diagnosed patients, which accounted for 3.4% of all cancers, and approximately 509,000 patients died (5.3% of all cancer-related death) [1]. Oesophageal tumours are characterised by poor prognosis, and the five-year survival rate is around 10% [2]. Metastases of oesophageal cancer are most often located in the lymph nodes, liver, lungs, and bones. Skeletal muscles are a very rare location of metastases, and until now no guidelines for their treatment have been developed.

Case report

A 62-year-old man, with the history of obesity and nicotinism, was seen in the Oncologic Surgery Outpatient Clinic of The Maria Sklodowska-Curie Institute — Oncology Center in Warsaw in July 2018 with diagnosis of oesophageal cancer. Previously the patient repeatedly reported to the primary care physician due to gastroesophageal reflux. He was referred for endoscopic examination of the upper gastrointestinal tract in July 2018. An ulcerative infiltration of the middle-lower part of the oesophagus was found. The infiltration was also visualised in computed tomography (CT) of the chest. Histopathological examination of specimens collected during gastroscopy confirmed the diagnosis of poorly differentiated (grade 3) oesophageal adenocarcinoma. The imaging examinations: ultrasound (US) of the abdominal cavity, CT of the abdominal cavity and pelvis, and positron emission tomography (PET), revealed the infiltration of the thoracic oesophagus, spreading over 88 mm, from the level of the trachea bifurcation to the supracardiac area. The infiltration formed a conglomerate with the pathological lymph nodes of the subcarinal area on the left side, with the largest transverse dimension 76 mm × 40 mm. The features of mediastinal lymph node involvement — group 2L, 7, 8 (cT3 cN2/3 cM1) were demonstrated. The patient case was discussed at a multidisciplinary meeting in July 2018. The patient

was qualified to induction chemotherapy with response evaluation following the second cycle, followed by radical chemoradiotherapy and possible surgical treatment. Induction chemotherapy according to the FLOT scheme (docetaxel + oxaliplatin + 5-fluorouracil + calcium folinate) was initiated in August 2018. The patient received 100% of the planned dose with moderately good tolerance of treatment. After two FLOT cycles, the patient underwent PET examination (August 2018) and partial regression was observed. The patient was qualified for a definitive chemoradiotherapy (50 Gy in 25 fractions of 2 Gy in combination with chemotherapy according to the FOLFOX scheme — oxaliplatin + 5-fluorouracil + calcium folinate, every 14 days). Treatment was continued from September to December 2018. Due to grade G1 haematological toxicity and worsening of treatment tolerance, the dose of chemotherapy was reduced. Six chemotherapy cycles were given (two cycles with full doses of drugs and four cycles with reduced doses) comprising the full planned dose of radiation. After the completion of combination treatment (January 2019), the patient came to the Oncological Outpatient Clinic due to the appearance of tumour-like lesion of the left crus, which was accompanied by severe lower limb pain. A magnetic resonance (MR) examination (January 2019) revealed an abnormal, heterogenous solid mass with dimensions of 143 mm × 25 mm × 17 mm, located medially to tibia, approximately in the middle of tibial shaft, destroying the cortical layer of the bone asymptomatically (Fig. 1). In addition, there was evidence of oedema in the flexor digitorum longus muscle. The infiltration into the neurovascular bundle of the posterior tibial artery was excluded. Bone scintigraphy (February 2019) did not reveal other pathological changes. A core needle biopsy of the tumour lesion in the flexor digitorum longus muscle was performed. Histopathological examination confirmed poorly differentiated G3 adenocarcinoma. In an immunohistochemical study, tumour cells expressed CKAE1/AE3 and CDX2 (in some cancer cells). The staining for CK7, CK20, chromogranin A, CD56, and CK5/6 was negative. The patient was qualified for radiotherapy for the area of a single metastasis to the flexor digitorum longus muscle and the left tibia (with a total dose of 35 Gy, in five fractions of 7 Gy). Treatment was carried out from February 14 to March 4, 2019. The lower limb pain was reduced. In order to prevent bone fractures, treatment with denosumab was initiated (March 2019). Currently, the patient is under continuous follow-up.

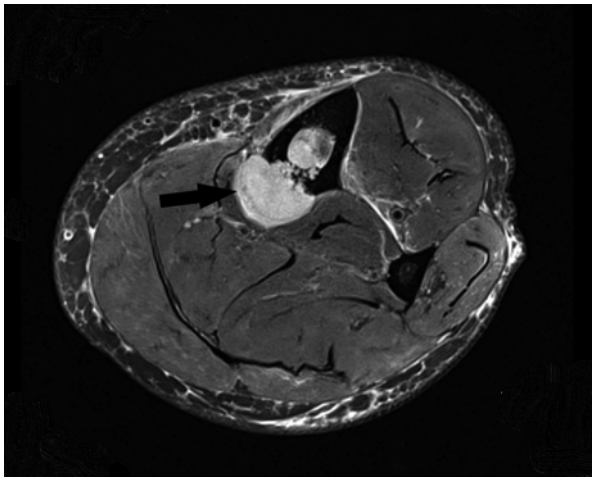

Figure 1. Axial magnetic resonance image of the left lower leg. The metastasis of the oesophageal adenocarcinoma to the flexor digitorum longus muscle with infiltration of the tibial bone

Discussion

Oesophageal cancer metastases are most commonly located in lymph nodes, lungs, pleura, liver, stomach, peritoneum, kidneys, adrenal glands, bones, and brain [3]. Metastases to skeletal muscles are very rare and usually locate in the muscles of the lower limb. The reason for the rare occurrence of oesophageal cancer metastases in this location is not fully understood. Some authors suggest that it may be associated with rich blood supply, systolic activity, frequent pH changes, and the production of lactic acid in skeletal muscles, which inhibit the development of cancer cells in this area [4].

A systematic literature review was carried out using PubMed. There were 25 articles in which clinical cases of patients with oesophageal cancer metastases in skeletal muscles were presented (Table 1). Most patients had metastases in skeletal muscles of the lower limb — thigh and lower leg. The most common clinical signs accompanying the diagnosis were pain and the presence of palpable tumour-like lesions. In our patient, metastasis was found in the left crus muscle and was diagnosed very shortly after completion of combination therapy due to primary oesophageal adenocarcinoma. The patient reported severe pain in the lower limb, intensifying during movement.

Diagnosis of skeletal muscle metastasis is difficult, and it is often misdiagnosed in physical examination and imaging examinations as sarcoma or other soft tissue pathologies [4]. Ultrasound is used to differentiate solid and cystic lesions [5], while PET is considered to be a more specific study than computed tomography in imaging lesions in skeletal muscles.

Wu et al. and Sohda et al. used a PET/CT imaging technique to diagnose metastasis of oesophageal adenocarcinoma to skeletal muscle. In the presented patient, a PET study performed in August 2018 showed no pathologies in the skeletal system. The lesion was visualised by magnetic resonance and finally confirmed by histopathological and immunohistochemical examination.

Table 1. Publications addressing oesophageal carcinoma patients with metastases to the scelatal muscles

Number	Author	Age	Gender	Metastases location
1.	Schultz et al. (1986)	ND	ND	Gluteus minimus muscle
2.	Miura et al. (1998)	58	M	Left shoulder
3.	Pretorius et al. (2000)	62	M	Right vastus lateralis muscle
	Pretorius et al. (2000)	ND	ND	ND
4.	Rehman et al. (2002)	71	M	Right thigh
5.	Lekse et al. (2003)	78	F	Inferior rectus eyeball muscle
6.	Wu et al. (2005)	67	M	Right gluteus minimus muscle
7.	Koike et al. (2005)	ND	ND	Deltoid muscle
8.	Heffernan et al. (2006)	67	F	Right infraspinatus muscle
9.	Hayata et al. (2009)	61	F	Gluteus maximus muscle
	Hayata et al. (2009)	58	M	Right forearm
10.	Norris et al. (2009)	58	M	Right iliacus muscle
11.	Hsieh et al. (2011)	58	M	Left psoas muscle
12.	Uygur et al. (2011)	62	F	Right temporal muscle
13.	Lu et al. (2012)	71	M	Left erector spinae
14.	Cincibuch et al. (2012)	64	M	Left quadriceps muscle
	Cincibuch et al. (2012)	76	M	Right gluteus minimus muscle
	Cincibuch et al. (2012)	57	M	Right subscapularis muscle
	Cincibuch et al. (2012)	42	M	Iliacus muscle
	Cincibuch et al. (2012)	60	M	Numerous metastases (including the gluteus maximus muscle)
15.	Matsutani et al. (2013)	72	M	Left triceps muscle
16.	Leuzzi et al. (2013)	65	M	Right paraspinal muscles
17.	Sohda et al. (2014)	49	M	Left thigh
18.	Maruzen et al. (2015)	45	M	Left thigh
19.	Domínguez et al. (2015)	53	M	Left gluteus medius muscle
20.	Thumallapally et al. (2016)	73	M	Left rectus eyeball muscle
21.	Azadeh et al. (2016)	65	M	Right iliacus muscle
22.	Fujimoto et al. (2017)	77	M	Left forearm
23.	Saito et al. (2017)	56	M	Left shoulder
24.	Mendiola et al. (2018)	61	M	Left iliopsoas muscle
25.	Abiad et al. (2019)	19 patients treated from 1997 to 2017 with metastases to skeletal muscle		

M — male; F — female; ND — no data

El Abiad et al. analysed 1341 patients treated for oesophageal cancer. Only 25 of them had distant metastases to soft tissues (skeletal muscles and/or subcutaneous tissue). The average age at diagnosis of metastasis was 64 years, and the average time from the diagnosis of primary oesophageal cancer until the metastasis was diagnosed was 9.6 months. In the presented patient it was 62 years and less than seven months, respectively.

El Abiad et al. showed that the incidence of soft tissue metastases was related to the histological subtype of oesophageal cancer. Adenocarcinoma far more frequently spreads to skeletal muscles and subcutaneous tissue (85%) than squamous cell carcinoma of the oesophagus (15%).

To date, no harmonised guidelines have been developed for the treatment of patients with oesophageal cancer metastases to skeletal muscles. Each patient

should be treated individually. When planning treatment, the clinical stage of primary disease, the patient's performance status and general condition, as well as prognostic factors should be considered [6].

Based on literature review, it can be seen that the majority of patients were treated with chemotherapy. In other patients, radiotherapy and/or surgical resection of the metastasis was used. It seems that patients with single metastasis in skeletal muscle should be resected or irradiated, whereas patients with multiple metastases should receive chemotherapy [6–8].

Regardless of the treatment used, patients with primary oesophageal cancer with distant metastases have a poor prognosis. The five-year survival rate is estimated at around 5% [4]. Diagnosis of metastases in skeletal muscle is usually associated with terminal stage of the disease and very poor prognosis [9]. The average survival time from the diagnosis of metastasis is 7.5–9 months [6, 8, 10, 12]. For comparison, the average survival time from the diagnosis of primary stage IV oesophageal cancer is 13 months [6].

Summary

Metastases of oesophageal adenocarcinoma to the skeletal muscles are rare, and so far no guidelines for their treatment have been developed. The occurrence of even a single, isolated metastasis in this area is associated with the terminal stage of the disease and is characterised by extremely poor prognosis. Due to the limited treatment options and the risk of complications, it seems that the use of chemo- or radiotherapy in these patients can bring significant benefits.

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