

Chapter

Skeletal Muscle Metastases to the Flexor Digitorum Superficialis and Profundus from Urothelial Cell Carcinoma and Review of the Literature

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Abstract

Urothelial cell carcinoma (UCC) metastases to skeletal muscle are extremely rare and usually found in patients with advanced stage cancer. The most common sites of bladder cancer metastases are lymph nodes, lung, liver and bones. Muscle is an unusual site of metastases from a distant primary cancer, due to several protective factors.

We present a rare case of 76-year-old patient with metastases in the flexor digitorum superficialis (FDS) and flexor digitorum profundus (FDP) muscles, 2 years after a radical cystectomy for invasive UCC of the bladder. This case is the first description of a forearm lesion, with an extensive infiltration of the volar compartments of the forearm and the first one with a clear functional impairment.

Introduction

UCC is the most common primary malignancy of the urinary tract, accounting for more than 90% all bladder cancers, and may affect its entire length, from renal pelvis to bladder [1]. UCC is usually a tumour of older patients, with the average age of presentation of 65 years, with a strong male predilection (M:F = 4:1) [1].

Skeletal muscle metastases from bladder cancer are very rare. In the English literature, only five studies reported [2-6] on skeletal muscle metastases from UCC with clinical-radiological findings.

The case that we present is the first report of metastases involving the FDS and FDP muscles after an invasive UCC of the bladder.

The authors have obtained the patient's informed written consent for print and electronic publication of the case report.

Case report

A 76 year-old male presented to the general practitioner with gross hematuria and urinary frequency. The ultrasound (US) imaging and the cystoscopy revealed a mass in the bladder. A transurethral resection was undertaken and an invasive carcinoma (T3, N0, M0) was found at the histological examination. Three cycles of neoadjuvant chemotherapy were performed with cisplatin and gemcitabine.

Four months later, a radical cystectomy and an ileal conduit urinary diversion was performed. 1year after, a complete thoracoabdominal computed tomography (CT) was negative for metastases.

18 months later, the patient presented a persistent anterior right forearm pain, resistant to analgesic, at first underestimated by the general practitioner and treated as tendonitis.

The patient was referred to our hand surgery unit six months later for persistent pain of the right forearm and a painful flexion contracture of the proximal interphalangeal joints of the fingers (Figure 1) with the clinical suspicion of chronic compartmental syndrome .



Figure 1: Clinical presentation of the flexion contracture of the fingers of the right hand.

The consequent clenched fist position was not passively reducible. Spasticity was also supposed, but there was no evidence of hyperactive response to quick stretch of the long fingers [7].

The Magnetic Resonance Imaging (MRI) revealed a irregular lesion of 7.5 cm x 2.7 cm x 2.1cm in the superficial and deep volar compartment of the forearm with ring-enhancing (Figure 2). The lesion was infiltrating the muscular body of the FDS and FDP.

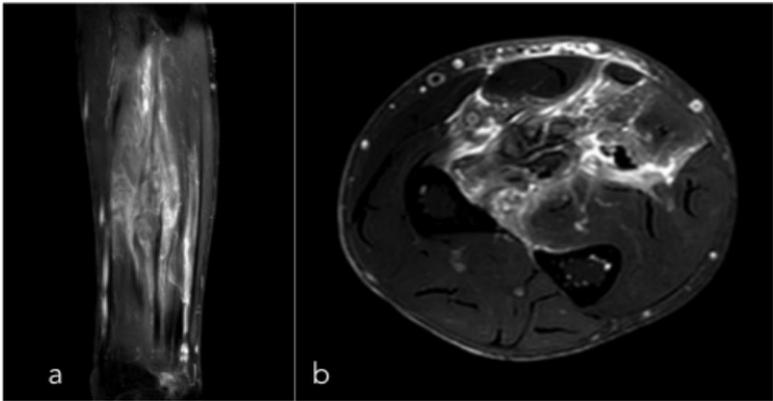


Figure 2: MRI of the right forearm (a- coronal view, b- axial view) : infiltrating lesion of the superficial and deep volar compartment of the forearm with a widespread edema.

A surgical explorative excision (Figure 3) of the lesion was performed with a resection en bloc of the FDS of the long fingers. The deep infiltration of the FDP and partially of the median nerve avoided a radical primary resection.

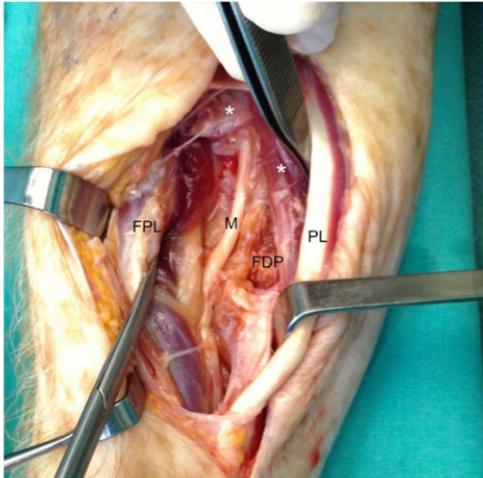


Figure 3: Intra-operative findings. (*) Flexor digitorum superficialis partially resected, (PL) Palmaris longus, (FPL) Flexor pollicis longus, (M) Median nerve, (FDP) Flexor digitorum profundus

The pathology reported a skeletal muscle metastasis compatible with a high grade UCC positive to the CK7, p63, GATA3, AE1/AE3 markers and negative to the CK20 (Figure 4-5).

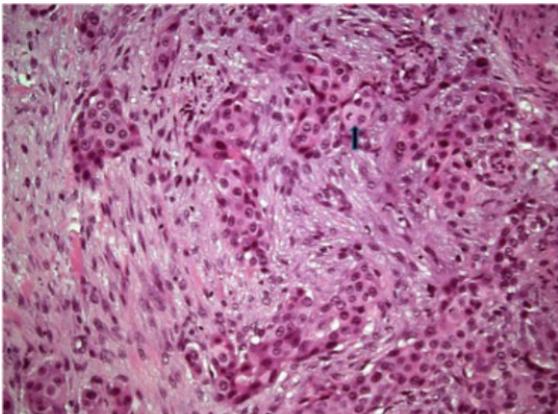


Figure 4: Nests of polygonal cells surrounded by stroma reaction of transitional cell carcinoma (arrow: mitotic figure), higher magnification. H&E x200.

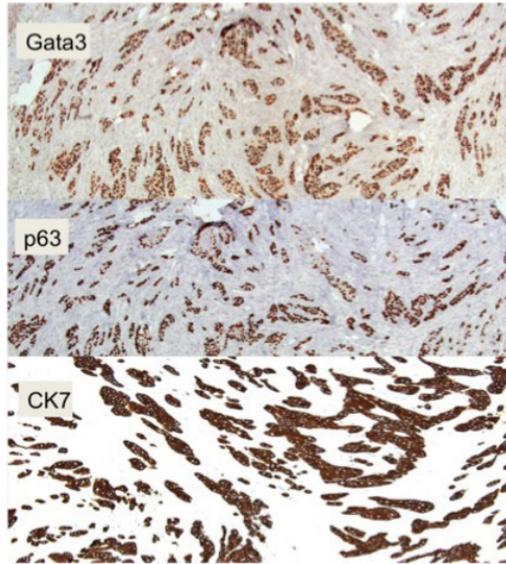


Figure 5: Immunohistochemistry: CK7, p63 and GATA3 expression in malignant cells, consistent with transitional cell differentiation

A Pet/CT whole body (Figure6) showed a metastatic progression of the cancer, with ectopic lesions to the right forearm, the left sacroiliac joint, and the chest wall.

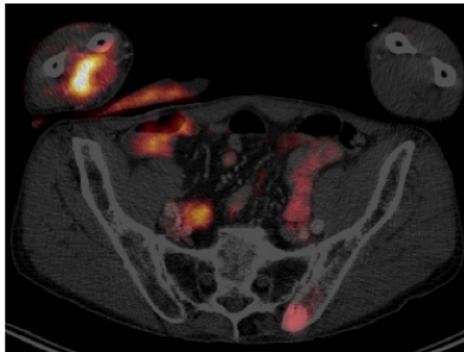


Figure 6: A Pet/CT whole body showed an advanced stage of the cancer, with multiple metastasis in the right forearm, in the left sacroiliac joint and the chest wall.

For a local pain control, a palliative chemotherapy was administered with carboplatinum and gemcitabine. Then, 5 cycles of 4Gy radiotherapy were then performed in the forearm (20 Gy).

At 4 months postoperatively, the patient showed a recalcitrant flexion contracture of the long fingers without local pain in the right forearm.

Five months after the surgical excision, the patient died for the progressive deterioration of the general conditions.

Discussion

Metastases to the skeletal muscle from distant primary lesions are rare, and usually found in case of advanced stage of cancer. Muscles are an unusual site of metastases even though they represent almost the 50% of the total body mass [3] and are highly vascularized [4]. Several defensive factors have been proposed to create a hostile environment against metastases such as muscle pH, muscle motion, ability to remove lactic acid accumulation that plays a role against tumor neovascularity [6-8]. Magee et Rosenthal [9] in 2002 reported that a previously documented local trauma seems to be a risk factor for development of metastasis , probably for an imbalance of local physiological and mechanical factors.

Several studies from autopsies report rates of muscle metastases oscillating from 6% to 17,5% [10,11]. These data underline the frequency of asymptomatic skeletal muscles metastases, most of all in advanced stage of a malignancy. The majority of these metastases are microscopic lesion undetectable with CT scans and MRI [4,5].

Skeletal muscles metastases from UCC are, however, very rare and to our best knowledge, only 9 cases have been reported in the english literature [2-6].

The great muscles, such as the erector spinae, psoas, and gluteals are the most common sites of metastatic involvement (Table 1) . Nabi

et coll [3] reported metastases to psoas, rectus abdominis, adductor of the thigh. Doo [5] and Katafigiotis [6] described two metastases to sartorius, while Nagao [4] proposed the case of one in the gluteus maximus.

Ekici et al [2] described the first case of upper limb metastasis in a deltoid muscle. Our case is the first description of a forearm lesion, with an extensive infiltration of the volar compartments of the forearm and the first one with a clear functional impairment.

Usually, the clinical presentation of all the reported cases in literature [2-6] is a localized and painful muscular swelling (Table 1). In our case, the patient complained of a bothersome flexion contraction of the fingers with muscular pain, at first assumed as chronic compartmental syndrome.

Radiologic Exams

Nabi et al [2] emphasize that every localized muscular mass in patients affected previously from transitional cell carcinoma should be considered to be a metastasis and should be investigated.

Skeletal muscle metastases are frequently incidental findings on CT of the chest or abdomen. The CT scans show an increase in ring-shaped enhancement with hypoattenuation of the inner part. MRI findings, although not specific, show low to intermediate signal intensity in the T1-weighted image and uniform high-signal intensity in the T2-weighted image (Table 1).

Treatment

Fine-needle aspiration biopsy with ultrasonographic guidance should be advisable to determine skeletal muscle metastases from UCC.

In our case, we removed the lesion en bloc for diagnosis and treatment, according to Ekici et al. [2] Katafigiotis et al. [6] that reported good results in terms of pain control with en bloc excision.

Nabi et al. [3] reported that the mean survival rate after receiving chemotherapy was 8 months (min 6 - max 12), while Katafigiotis reported a survivorship of 7 months after chemotherapy and radiotherapy.

Chemotherapy with or without the addition of local radiotherapy has been reported as an efficient treatment in skeletal muscle metastases [3-5]. In the study of Nabi et al [3], all patients had palliative chemotherapy with mitomycin, vincristine, adriamycin and cyclophosphamide. Ekici et al [2] used cisplatin, methotrexate and vinblastine. Katafigiotis et coll [6] administered 6 cycles of gemcitabine and cisplatin. In our case, a Carboplatinum and Gemcitabine protocol has been adopted (Table 1).

Nabi et coll [3] used in two patients a local palliative radiotherapy of 35 Gy. Our patient received 5 cycles of 4Gy radiotherapy (20 Gy) with good pain control.

Chemotherapy and radiotherapy are usually the preferred palliative treatment method. Surgical resection should be proposed in case of compressive effect of the metastasis, even though en bloc excision can improve pain control in painful muscle metastases [3, 5].

Table :1

| No. | Study | Age | Initial stage of disease | Initial treatment received | Clinical presentation | Radiological presentation - Localisation | Treatment received | Follow up |
|-----|---------------------------------|-----|--------------------------|--|---|--|---|-------------------|
| 1 | <i>Nabi et al.</i> | 65 | T3N0M0 | Radical cystectomy with sigmoid neobladder | Localized swelling on medial aspect of thigh with pain | CT showing ring- enhancing lesion in the left adductor of the thigh | Palliative chemotherapy | Died at 8 months |
| 2 | <i>Nabi et al.</i> | 27 | T3BN2M0 | Radical cystectomy with ileal conduit | Persistent back ache with limp | CT with enlarged swollen left psoas | Palliative chemotherapy with localized radiotherapy | Died at 6 months |
| 3 | <i>Nabi et al.</i> | 62 | T3AN0M0 | Radical cystectomy with sigmoid neobladder | Persistent swelling in anterior abdominal wall | CT showing ring- enhancing lesion in left rectus abdominis | Palliative chemotherapy | Died at 12 months |
| 4 | <i>Nabi et al.</i> | 70 | T3BN2M1 | None | Left limp with backache | CT with enlarged swollen left psoas | Palliative chemotherapy with localized radiotherapy | Died at 8 months |
| 5 | <i>Nabi et al.</i> | 36 | T3AN1M0 | Radical cystectomy with ileal conduit | Pain in the back | CT with swollen left psoas with areas of low attenuations | Palliative chemotherapy | Died at 6 months |
| 6 | <i>Doo et al</i> | 45 | T2N0M0 | Transurethral resection | Left tight pain | MRI – T1 slight high signal, T2 high signal with strong enhancement in left sartorius | Palliative chemotherapy with localized radiotherapy | No data available |
| 7 | <i>Katafjiotis et al</i> | 51 | T2N0M0 | Radical Cystectomy and prostatectomy an urinary diversion with ileal conduit | Left tight pain and localized mass | MRI – No data available. Left sartorius | Resection, radiotherapy, chemotherapy | Alive at 7 months |
| 8 | <i>Ekici et al</i> | 41 | T3N0M0 | Chemotherapy | Fixed mass on the deltoid muscle, painless | MRI – No data available. Right deltoid muscle | Resection, chemotherapy | Died at 9 weeks |
| 9 | <i>Nagao</i> | 63 | T3N1M1 | Chemotherapy and radiotherapy | Swelling localized on the right gluteus | Ct with slight enhancement, Gluteus maximus | No data available | No data available |
| 10 | <i>Fusetti, Guidi, Lucchina</i> | 76 | T3N0M0 | Radical cystectomy with ileal conduit | Painful flexion contracture of the proximal interphalangeal joints of the fingers | MRI - T2 high signal with strong enhancement of the flexor digitorum superficialis and profundus | Resection, chemotherapy | Died at 5 months |

Conclusion

Muscular localized swelling and lumps in patients with positive clinical history for UCC need to be taken as possible skeletal metastases. Radiological findings and a biopsy may help to study the lesion and to determine the most suitable treatment.

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