

# Docetaxel-induced Acute Myositis

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Docetaxel (Taxotere®), obtained from the European yew *Taxus baccata*, is a widely used chemotherapeutic agent active against a variety of solid tumors including breast, lung, ovarian, gastric, head and neck, and prostate cancers. The drug is administered intravenously on a weekly or three-weekly schedule. Its main side effects include myelosuppression, fatigue, myalgias, arthralgias, fluid retention, peripheral neuropathy, paronychia, and lacrimation [1]. Myositis, however, has rarely been reported.

We describe a breast cancer patient who developed severe acute myositis while on treatment with docetaxel.

## PATIENT DESCRIPTION

In November 2020, a 62-year-old female patient with a past medical history of essential hypertension and type II diabetes mellitus underwent a left breast lumpectomy for an infiltrating duct carcinoma, T2N0M0, grade 2, estrogen receptor positive, HER2 negative, Ki 67 30%. An Oncotype DX test revealed a recurrence score of 38, indicative of the need for the administration of adjuvant chemotherapy.

The first course of the combination of docetaxel, 75 mg/m<sup>2</sup> and cyclophosphamide 600 mg/m<sup>2</sup>, both on day one, was delivered in early January 2021; a second course was administered 3 weeks later, as planned. Approximately 4 days later the patient complained of bilateral painful,

swollen thighs, with hyperalgesia on superficial palpation of both thighs. A neurological examination did not disclose any focal findings.

The pain increased gradually and by day 25 of the course the patient was admitted to our institution with severe pain limiting the motion of her lower limbs. Creatine phosphokinase (CPK) level was 1729 U/L, increasing to 3122 U/L a day later (normal range 20–180 U/L). An ultrasound of the quadriceps muscle showed small hypoechogenic areas dispersed between muscle fibers with edema, findings compatible with myositis.

Treatment of 60 mg/day prednisone was started, resulting in an improvement in the edema and in a decrease of the CPK within one day to 2813 U/L and within one week to 1250 U/L; however, without substantial pain relief. A magnetic resonance imaging (MRI) of the thighs revealed marked symmetric muscular edema involving the rectus femoris, vastus lateralis and the semitendinous muscles compatible with an extensive myositis [Figure 1]. An electromyography test did not show electrophysiological changes usually observed in myositis. A muscle biopsy was not obtained.

An extensive autoimmune and paraneoplastic serology workup was obtained: ANA, anti-Smith ab, SSA, SSB, anti-ribosomal p ab, RNP ab, anti-JO1 ab, anti-SCI-70 ab, anti-CENP-B ab, anti-Mi-2, anti-PM-scl ab, anti-PL-7 ab, anti-PL-12 ab, SRP ab, Ku ab, and anti-GAD were all negative.

At the last follow-up appointment in April 2021, the CPK had gradually decreased to normal levels (127 U/L). The patient continued to feel bilateral proximal lower limbs pain; however, it was

controlled with analgesics, and she was not taking prednisone.

The administration of docetaxel was discontinued in view of the clinical picture and due to laboratory and radiological findings compatible with a drug-induced myositis. The patient refused further chemotherapy and was prescribed adjuvant hormone therapy with letrozole, an aromatase inhibitor.

## COMMENT

Myositis is defined as an inflammatory process that damages muscle fibers, which are then unable to contract. It may result in pain, tenderness, and most prominently, in weakness. A wide range of possible etiologic factors have been identified including autoimmune disorders such as dermatomyositis and polymyositis; viral, bacterial, or parasitic infections; drug effects as in the case of statins, colchicine, or hydroxychloroquine; metabolic disorders; or strenuous exercise [2].

Although docetaxel may cause myalgias and arthralgias, myositis resulting from exposure to this drug represents a rare complication. Available publications on this adverse event are based on single case reports [3,4,5].

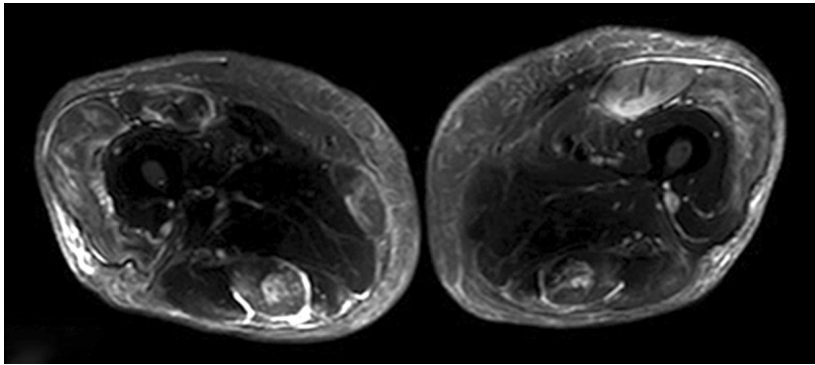
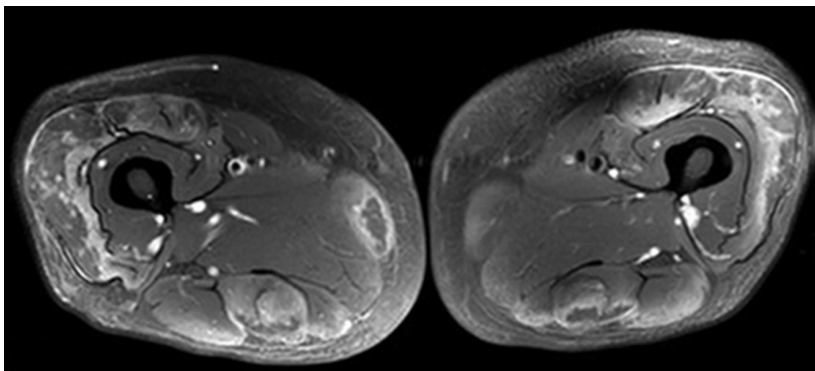
The clinical presentation of our patient fits well with the description of this complication. Most patients have been female with a background of diabetes mellitus and most presented with a breast carcinoma, frequently non-metastatic.

Myositis usually develops early in the course of treatment with docetaxel, mostly during the second or third cycle and the most prominent, and frequently only, complaint has been, as in our case,

**Figure 1.** MRI of both thighs

MRI images at mid-thigh level showing marked symmetrical patchy muscle edema involving all compartments accompanied by fascial planes edema with post-IVGAD enhancement, compatible with extensive acute myositis and fasciitis

MRI = magnetic resonance imaging

**[A]** Transverse STIR**[B]** Post-IVGAD T1FS

severe bilateral thigh pain with limitation of lower limb motion.

The CPK level is elevated at diagnosis and prompt pain relief usually follows a short course of high-dose steroids. This relief did not occur in our patient, as prednisone resulted in only moderate improvement. In patients in whom steroids fail to obtain the desired relief, other possible therapeutic interventions may include opioid and non-opioid analgesics. In refractory cases, methotrexate and intravenous immune globulin have been used [3].

The differential diagnosis of docetaxel-induced myositis includes

paraneoplastic syndromes such as polymyositis, necrotizing myopathy, and peripheral nerve vasculitis, diabetic sensorimotor polyneuropathy, polymyalgia rheumatica, and pyomyositis [4]. These possibilities were excluded in our patient based on clinical presentation, laboratory findings of an elevated CPK level, and results of the imaging tests including ultrasound and MRI, which were consistent with multifocal myositis in the background of recent exposure to docetaxel-based chemotherapy. Of note, cyclophosphamide, which was given concomitantly with docetaxel, has not

been associated with myositis. Moreover, our patient was not exposed to other known myositis-inducing drugs, such as statins.

The mechanism by which docetaxel causes an acute myositis has not been fully elucidated. Possible muscle injury may result from a direct toxic effect, interference with neuromuscular transmission, or a docetaxel-induced increase in the intramuscular level of certain cytokines such as interferon gamma, tumor necrosis factor, and interleukins 2 and 6 [5].

### CONCLUSIONS

Docetaxel is a widely used chemotherapeutic agent in a variety of solid tumors. Clinicians should be aware that, although rare, acute myositis may result from its administration. This complication should be suspected in patients who develop bilateral, symmetric thigh pain with muscle weakness and an elevated CPK level, particularly in women with breast cancer who are diabetic.

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Art is how we decorate space; music is how we decorate time.

Jean-Michel Basquiat (1960–1988), American artist