Rare paraneoplastic dermatomyositis secondary to high-grade bladder cancer

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The clinical presentation of bladder cancer typically presents with hematuria; changes in voiding habits such as urgency, frequency, and pain; or less commonly, obstructive symptoms. Rarely does bladder cancer first present as part of a paraneoplastic syndrome with an inflammatory myopathy. Inflammatory myopathies such as dermatomyositis have been known to be associated with malignancy, however, in a meta-analysis by Yang and colleagues of 449 patients with dermatomyositis and malignancy there were only 8 cases reported of bladder cancer.[1] Herein, we report a paraneoplastic dermatomyositis in the setting of a bladder cancer.

Case presentation and summary

A 65-year-old man with a medical history of hypertension and alcohol use presented to the emergency department with worsening pain, stiffness in the neck, shoulders, and inability to lift his arms above his shoulders. During the physical exam, an erythematous purple rash was noted over his chest, neck, and arms. Upon further evaluation, his creatine phosphokinase was 3,500 U/L (reference range 52-336 U/L) suggesting muscle breakdown and possible inflammatory myopathy. A biopsy of the left deltoid and quadriceps muscles was performed and yielded a diagnosis of dermatomyositis. He was treated with prednisone 60 mg daily for his inflammatory myopathy. The patient also reported an unintentional weight loss of 20 lbs. and increasing weakness and inability to swallow, which caused aspiration events without developing pneumonia.

The patient's symptoms worsened while he was on steroids, and we became concerned about the possibility of a primary malignancy, which led to further work-up. The results of a computed-tomography (CT) scan of the abdomen and pelvis showed right-sided hydronephrosis and hydrourteter with an irregular, soft-tissue density mass of 4.7 x 3.2 x 4.2 cm along the posterior wall of the bladder (Figure 1). A cystoscopy was performed with transurethral resection of a bladder tumor that was more than 8 cm in diameter. Because the mass was not fully resectable, only 25% of the tumor burden was removed. The pathology report revealed an invasive, high-grade urothelial cell carcinoma (Figure 2). Further imaging ruled out metastatic spread.

The patient was continued on steroids. He was not a candidate for neoadjuvant chemotherapy because of his comorbidities and cisplatin ineligibility owing to his significant bilateral hearing deficiencies. Members of a multidisciplinary tumor board decided to move forward with definitive surgery. The patient underwent a robotic-assisted laparoscoptic cystoprostatectomy with bilateral pelvic lymph node dissection and open ileal conduit urinary diversion. Staging of tumor was determined as pT3b N1 (1/30) M0, LVI+. After the surgery, the patient had resolution of his rash and significant improvement in his muscle weakness with the ability to raise his arms over his head and climb stairs. Adjuvant chemotherapy was not given since he was cisplatin ineligible as a result of his hearing loss. Active surveillance was preferred.

Four months after his cystoprostatectomy, he experienced new-onset hip pain and further imaging, including a bone scan, was performed. It showed metastatic disease in the ischium and iliac crest (Figure 3). The patient decided to forgo any palliative chemotherapy and to have palliative radiation for pain and enroll in hospice. He died nine months after the initial diagnosis of urothelial cell carcinoma.

Discussion

Dermatomyositis is one of the inflammatory myopa-

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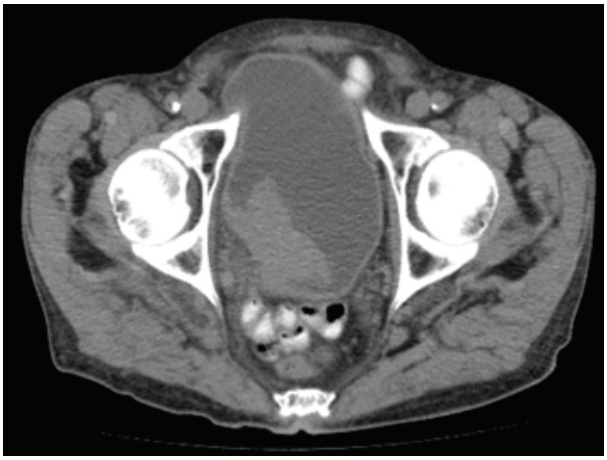

FIGURE 1 Computed-tomography scan of the abdomen and pelvis, revealing a right-sided hydronephrosis and hydrourteter with an irregular, soft-tissue density mass of 4.7 x 3.2 x 4.2 cm along the posterior wall of the bladder.

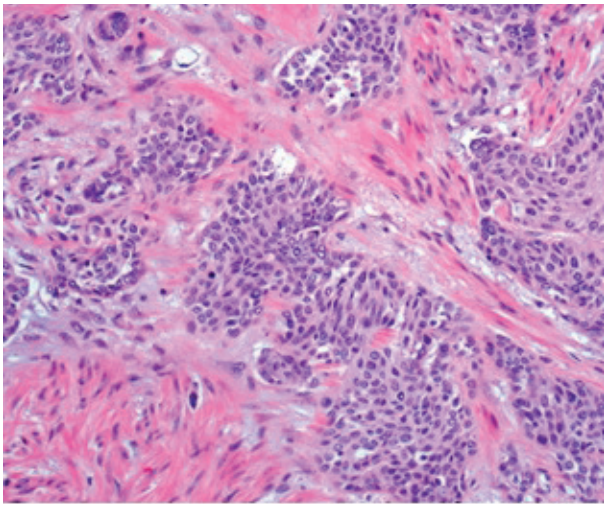

FIGURE 2 Invasive, high-grade urothelial cell carcinoma infiltrating the muscularis propria muscle bundles of the bladder.

thies with a clinical presentation of proximal muscle weakness and characteristic skin findings of Gottron papules and heliotrope eruption. The most common subgroups of inflammatory myopathies are dermatomyositis, polymyositis, necrotizing autoimmune myopathy, and inclusion body myopathy. The pathogenesis of inflammatory myopathies is not well understood; however, some theories have been described, including: type 1 interferon signaling causing myofiber injury and antibody-complement mediated processes causing ischemia resulting in myofiber injury.[2,3] The diagnoses of inflammatory myopathies may be suggested based on history, physical examination findings, laboratory values showing muscle injury (creatine kinase, aldolase, ALT, AST, LDH), myositis-specific antibodies (antisynthetase autoantibodies), electromyogram, and magnetic-resonance imaging. However, muscle biopsy remains the gold standard.[4]

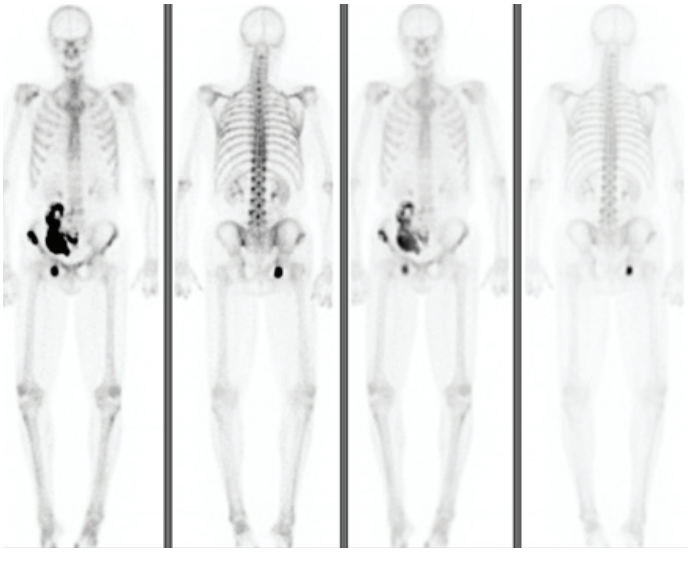

FIGURE 3 Skeletal scintigraphy (bone scan) showing diffuse metastatic lesions in the right acetabulum and ischium, right iliac crest, and left iliac bone.

The initial treatment of inflammatory myopathies begins with glucocorticoid therapy at 0.5-1.0 mg/kg. This regimen may be titrated down over 6 weeks to a level adequate to control symptoms. Even while on glucocorticoid therapy, this patient's symptoms continued, along with the development of dysphagia. Dysphagia is another notable symptom of dermatomyositis that may result in aspiration pneumonia with fatal outcomes.[5,6,7] Not only did this patient initially respond poorly to corticosteroids, but the unintentional weight loss was another alarming feature prompting further evaluation. That led to the diagnosis of urothelial cell carcinoma, which was causing the paraneoplastic syndrome.

A paraneoplastic syndrome is a collection of symptoms that are observed in organ systems separate from the primary disease. This process is mostly caused by an autoimmune response to the tumor and nervous system.[8] Inflammatory myopathies, such as dermatomyositis, have been shown to be associated with a variety of malignancies as part of a paraneoplastic syndrome. The most common cancers associated with dermatomyositis are ovarian, lung, pancreatic, stomach, colorectal, and non-Hodgkin lymphoma.[9] Although an association between dermatomyositis and bladder cancer has been established, very few cases have been reported in the literature. In the Yang meta-analysis, the relative risk of malignancy for patients with dermatomyositis was 5.5%, and of the 449 patients with dermatomyositis who had malignancy, only 8 cases of bladder cancer were reported.[1]

After a patient has been diagnosed with an inflammatory myopathy, there should be further evaluation for an underling malignancy causing a paraneoplastic process. The risk of these patients having a malignancy overall is 4.5 times higher than patients without dermatomyositis.[1] Definite screening recommendations have not been established, but screening should be based on patient's age, gender, and clinical scenario. The European Federation of Neurological Societies formed a task force to focus on malignancy screening of paraneoplastic neurological syndromes and included dermatomyositis as one of the signs.[10] Patients should have a CT scan of the chest, abdomen, and pelvis. Women should have a mammogram and a pelvis ultrasound. Men younger than 50 years should consider testes ultrasound, and patients older than 50 years should undergo usual colonoscopy screening.

The risk of malignancy is highest in the first year after diagnosis, but may extend to 5 years after the diagnosis, so repeat screening should be performed 3-6 months after diagnosis, followed with biannual testing for 4 years. If a malignancy is present, then treatment should be tailored to the neoplasm to improve symptoms of myositis; however, response is generally worse than it would be with dermatomyositis in the absence of malignancy. In the present case with bladder cancer, therapies may include platinum-based-chemotherapy, resection, and radiation. Dermatomyositis as a result of a bladder cancer paraneoplastic syndrome is associated with a poor prognosis as demonstrated in the case of this patient and others reported in the literature.[11]

Even though dermatomyositis is usually a chronic disease process, 87% of patients respond initially to corticosteroid treatment.[12] Therefore, treatment should be escalated with an agent such as azathioprine or methotrexate, or, like in this case, an underlying malignancy should be suspected. This case emphasizes the importance of screening patients appropriately for malignancy in patients with an inflammatory myopathy and reveals the poor prognosis associated with this disease.

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