Case Report

Dermatomyositis and small cell carcinoma of the bladder

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Dermatomyositis (DM) is an idiopathic inflammatory myopathy, characterized by a distinctive rash and symmetrical proximal muscle weakness. Dermatomyositis has been reported in association with malignancies in 15% to 25% of patients,[1] most commonly with ovarian, lung, gastric, and breast carcinomas, as well as with melanoma, mycosis fungoides, Kaposi sarcoma, and other malignancies.[2,3] The malignancy is discovered before, simultaneously with, or after the diagnosis of DM in more or less equal proportions.

Few reports have linked DM to a genitourinary malignancy, notably transitional cell carcinoma. Small cell carcinoma of the bladder (SCCB), a rare entity that arises from stem cells or neuroendocrine cells within the urothelium, has not been hitherto described in association with DM. We present a case of sudden-onset DM associated with SCCB. This case demonstrates the diversity of dermatologic clinical manifestations of DM and presents the first report of this disease in association with SCCB.

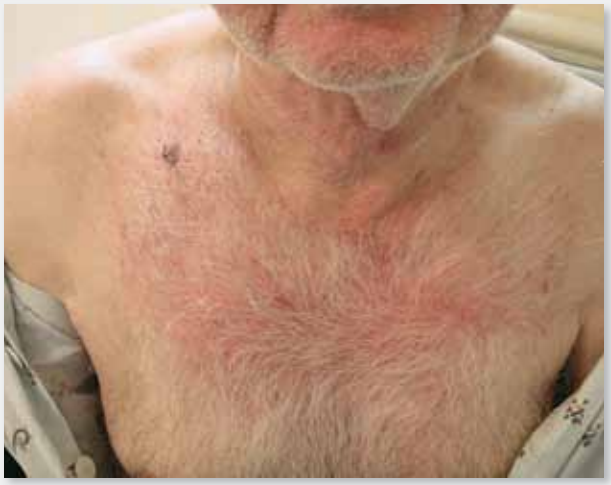
Case description

A 72-year-old man was admitted to our dermatology department with diffuse erythema on his scalp and face, periorbital swelling, and a fever of 38.5°C, all of which had developed abruptly over the previous 2 weeks. Past medical history was notable for prostatectomy owing to benign prostatic hyperplasia 15 years before.

Physical examination demonstrated erythema on the scalp and face, periorbital swelling associated with a violaceous complexion, and poikiloderma in a V-shaped distribution over the upper chest (**Figure 1**). Telangiectasias were noted on his proximal nail folds and hemorrhagic bullae were spotted on his fingers and palms (**Figure 2**). In addition, violaceous papules with slight scale were located on his proximal interphalangeal joints. Examination of his oral cavity revealed petechia on the upper palate and lips. Evaluation of muscle strength and deep tendon reflexes were notably normal at this point.

Laboratory results revealed the following: an elevated erythrocyte sedimentation rate and C-reactive protein level (33 mm/hr and 13 mg/L [normal 0 to 5 mg/L], respectively); leukocytosis of 14.08×10^9/L with left shift; serum glutamic oxaloacetic transaminase level of 475 IU/L (normal 7 to 40 IU/L); lactate dehydrogenase level of 760 IU/L (normal 100 to 260 IU/L); an elevated creatine phosphokinase (CPK) level of 10 471 IU/L (normal 10 to 190 IU/L); and an elevated fructose-bisphosphate aldolase level of 19.1 IU/L (normal 0 to 7.6 IU/L). Test results were positive for anti-Ro autoantibodies (32 U/mL, normal 0 to 20 U/mL) and reported an antinuclear antibody titre of 1:40, with a speckled pattern. Test results for anti–Jo-1, anti-DNA, and antineutrophil cytoplasmic antibodies were negative. Urinalysis showed microhematuria.

Figure 1. Diffuse macular violaceous erythema and telangiectasia in a V-shaped distribution on the upper chest



Clinical and laboratory data suggested a diagnosis of DM. Results of the patient's electromyographic (EMG) study were normal, most likely owing to the short duration of the disease and the lack of prominent muscle weakness.

A biopsy taken from the quadriceps muscle showed scattered necrotic and regenerative muscle fibres but failed to demonstrate perifascicular atrophy or inflammation, which are more specific to DM. Skin biopsy from the upper chest demonstrated vacuolar interface dermatitis with sparse, superficial, and deep lymphocytic infiltrates and abundant mucin (**Figure 3**), suggestive of DM.

An abdominal ultrasonography, performed as part of the paraneoplastic workup, demonstrated multiple metastases in the liver and hydronephrosis on the left

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Figure 2. Periungual telangiectasia and erythematous papules most pronounced over the proximal interphalangeal joints (ie, Gottron papules)

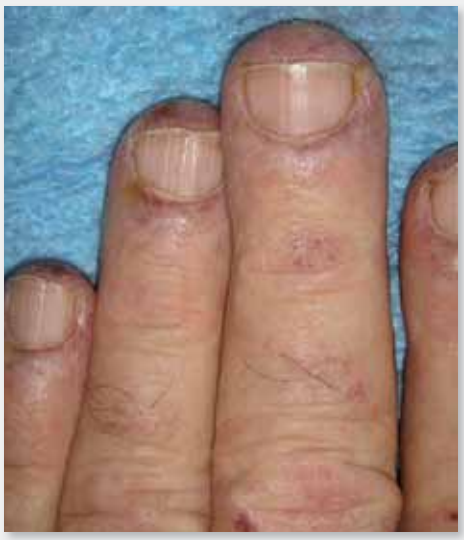
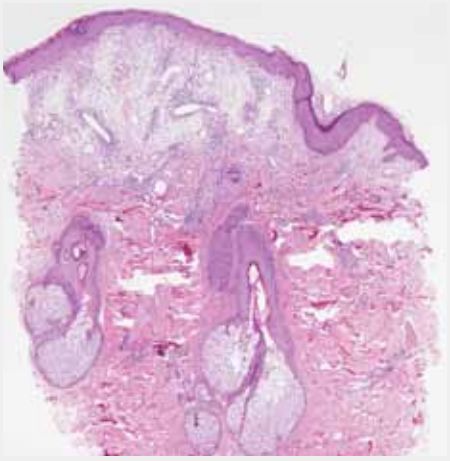


Figure 3. Vacuolar interface dermatitis with sparse superficial and deep perivascular and periadnexal lymphocytic infiltrates and abundant mucin deposits in the dermis (hematoxylin–eosin staining, original magnification x 40)



side. Computed tomography found, in addition to the above findings, a solid 2.7-cm lesion within a diverticulum in the left posterior bladder wall.

Cystoscopy-guided biopsy from the solid tumour in the diverticulum demonstrated poorly differentiated small cell carcinoma. Results of immunohistochemical stains were positive for cytokeratin 7, synaptophysin, and K167, and were negative for cytokeratin 20. Analysis of the material retrieved from an ultrasonography-guided biopsy of the liver lesions revealed similar findings.

Therapy with 1 mg/kg of prednisone was initiated, resulting in moderate improvement in the extent and intensity of the skin rash. Nevertheless, CPK levels continued to increase and the patient developed proximal limb muscle weakness and dysphagia over a 2-week period. Therapy with 25 g of intravenous immune globulin over 5 days was added, to no avail. A course of chemotherapy with cisplatinum and etoposide was then given, but muscle weakness progressed and respiratory insufficiency ensued, necessitating mechanical ventilation.

Two months after his initial presentation, the patient succumbed to pneumonia with Gram-negative sepsis and chemotherapy-induced neutropenia, which developed concurrently and failed to respond to treatment with broad-spectrum antibiotics.

Discussion

Dermatomyositis is an uncommon myopathy, characterized by a pathognomonic heliotrope rash (a purple-red, macular eruption of the eyelids and periorbital edema), Gottron papules (flat-topped, polygonal, and violaceous papules over the knuckles), and a symmetrical proximal muscle weakness. Other cutaneous features include poikiloderma in a photosensitive distribution, periungual telangiectases, and facial erythema.

On presentation, the patient did not fulfill the Bohan criteria for the diagnosis of DM.[4] Although he had the typical rash and elevated CPK levels, he failed to demonstrate muscle weakness and there was no evidence of muscle inflammation on biopsy or on the EMG study results. Notwithstanding, the distinctive dermatologic features and the renowned association of DM with malignancy prompted an immediate workup, which indeed revealed the condition to be paraneoplastic.

The case stresses a cardinal point: Not all diagnostic criteria need to be present on initial presentation of DM. Muscle weakness and EMG evidence of myopathy can take several weeks to develop. Moreover, DM might appear as sine myositis, with only the typical dermatologic attributes. It has been shown that the risk of malignancy in these patients, in which myositis develops more than 6 months after the onset of the dermatologic manifestations, is no different than in patients with the classic presentation.[5] Therefore, the absence of these features should not dismiss the diagnosis and should definitely not deter from a full paraneoplastic workup at the outset.

Dermatomyositis has been associated with malignancies such as ovarian, lung, gastric, and breast carcinomas. It is an example of a paraneoplastic syndrome, which is a reaction triggered by an altered immune system response to a neoplasm or by remote effects of tumour-derived factors. Several risk factors carry a higher risk of malignancy. These include older age of onset, abrupt

presentation, constitutional symptoms, and a grossly elevated erythrocyte sedimentation rate—all exemplified in our patient. In contrast to adult DM, pediatric cases are not typically associated with malignancy.

Few reports have linked DM to bladder cancer, notably transitional cell carcinoma.[6,7] Small cell carcinoma of the bladder is an uncommon tumour, first recognized in 1981, comprising less than 1% of all bladder carcinomas. The disease is more common in men, with most cases occurring in the seventh and eighth decades of life. The tumour arises either from stem cells within the urothelium or from neuroendocrine cells within the urothelium or the submucosa. Small cell carcinoma of the bladder carries a poor prognosis, with a median survival of 4 to 23 months.[8]

Small cell carcinoma of the bladder carries several similarities to its pulmonary counterpart, small cell lung carcinoma (SCLC): First, both are associated with cigarette smoking (between 50% and 79% of patients with SCCB are current or former smokers). Second, both diseases are presumed to arise from the neuroendocrine cells. Finally, paraneoplastic syndromes such as hypercalcemia, Cushing syndrome, and sensory neuropathy have been reported with SCCB and SCLC.

The mainstay of therapy for DM is tumour burden reduction or removal when present. Other therapies are empirical and include corticosteroids in combination with an immunosuppressive or cytotoxic agent. Azathioprine, methotrexate, cyclophosphamide, cyclosporine, mycophenolate mofetil, and chlorambucil have been used as steroid-sparing agents in various cases. Additional treatment options are plasmapheresis and intravenous γ-globulin.[9]

Conclusion

To the best of our knowledge, this is the first report of an association between SCCB and DM. The lack of previous such observations, as opposed to an abundance of reports connecting SCLC and DM, presumably stems from the rarity of the former tumour as opposed to the preponderance of lung carcinoma.

Dr Sagi is a practising physician, **Dr Amichai** is a Senior Physician, **Dr Barzilai** is Deputy Director, **Dr Shpiro** is a Senior Physician, **Dr Baum** is a Senior Physician and Lecturer, and **Dr Trau** is Director, all in the Department of Dermatology at the Sheba Medical Center at Tel Hashomer in Israel. **Dr Neimushin** is a practising physician and **Dr Lidar** is a Senior Physician and Lecturer, both in the Department of Internal Medicine F and Rheumatology Unit, at the Sheba Medical Center at Tel Hashomer.

EDITOR'S KEY POINTS

- Dermatomyositis (DM) is a well-known entity associated with various neoplasms.
- This case report of DM is unique, as it presents an association between DM and the rare small cell carcinoma of the bladder.
- This case demonstrates most of the classical clinical signs of DM and is characterized by an acute onset, eventually culminating in death.

POINTS DE REPÈRE DU RÉDACTEUR

- La dermatomyosite (DM) est un problème bien connu associé à divers néoplasmes.
- Ce rapport sur un cas de DM est unique, en ce sens qu'il présente une association entre la DM et un rare carcinome des petites cellules de la vessie.
- Ce cas met en évidence la plupart des signes cliniques habituels de la DM et se caractérise par une invasion brutale, culminant éventuellement par le décès.

Competing interests
None declared

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