

A WOMAN WITH PARANEOPLASTIC DERMATOMYOSITIS AS A HERALD FOR BREAST CANCER IN A RURAL KENYAN HOSPITAL: A CASE REPORT

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Abstract: Dermatomyositis is an idiopathic inflammatory myositis usually manifesting with proximal myopathy involving both upper and lower limbs and characteristic dermatologic signs including gottron papules and heliotrope sign. In >20% of cases, dermatomyositis is associated with various cancers whose specific types often reflecting the general distribution of cancers in the population. Such paraneoplastic dermatomyositis may be diagnosed before, concurrently with, or after the cancer diagnosis. We present a case of a woman in rural Kenya with paraneoplastic dermatomyositis diagnosed before advanced breast cancer, to underscore the importance of searching and surveillance for associated malignancy in all cases of dermatomyositis.

Keywords: Dermatomyositis, dermatomyositis and breast cancer, gottron papule, heliotrope rash, Kenya, paraneoplastic dermatomyositis, proximal myopathy.

1. CASE SUMMARY

Presenting illness and physical examination

A 66-year-old lady, married mother of 11 children from Narok, Kenya; first presented to us in late May 2021 with a 6-month progressive history of both upper and lower limbs proximal weakness leading to being bed-bound in the 2 months prior to presentation. She could not raise her hands above the shoulders to make her hair, brush her teeth, nor wash her face. She was unable to rise from a sitting or squatting position. She had associated hyperpigmented itchy maculopapular rashes, distributed over the knuckles of both hands, proximal thighs, shoulders, around both eyes with significant swelling around the eyes. She had vague lower limb joint pains but no associated joint swelling, with progressive edema of both legs, progressive dysphagia, and diffuse muscle pains. She had no chest symptoms. Prior to this, she had been a healthy nomadic pastoralist, with no personal or family history of malignancies, and had never been admitted to hospital before for any reason.

Clinically, she was quite sick-looking, emaciated, with conjunctival injection bilaterally, oral thrush, with general debility. She was febrile at Temperature 38.3°C, Blood pressure 102/69mmHg, Pulse rate 110bpm, SPO2 97% in room air, Random blood sugar 120mg/dl. Skin examination showed hyperpigmented pruritic maculopapular rashes (with scaling in some areas) distributed over the knuckles of both hands, proximal lateral thighs bilaterally, proximal antero-lateral shoulders bilaterally, over the upper back, and bilateral periorbital regions with bilateral periorbital edema (both eyes were nearly closed from the edema). Musculoskeletal exam showed significant proximal myopathy of both upper and lower limbs, swollen tender right arm, Bouchard and Heberden nodes on the finger joints (consistent with associated age-related primary osteoarthritis) with no features of mechanics hands or Raynaud phenomenon, no synovitis, no features of carpal tunnel

syndrome, with range-of-motion across all joints limited by severe muscle pains; mild pitting grade 2 bipedal edema more on the right leg. She was lucid, with normal cranial nerve exam, had reduced muscle bulk and tone globally, no unilateral weakness, with further neurological exam limited by the muscle pains. Additionally, she had a lipomatous swelling in the right axilla, hyperpigmented macules on the right breast but no obvious breast masses palpable bilaterally, no nipple discharge or regional lymphadenopathy. She had severe epigastric tenderness with no abdominal organomegaly, normal S1 and S2 heart sounds, no features of heart failure, and had transmitted breath sounds bilaterally. She was at class IV functional status as per World Health Organization (symptomatic at rest).

Diagnostic workup

Her initial etiological and baseline workup included a normal complete blood count, elevated ESR 45mm/hr., negative malaria test, normal renal function, normal thyroid profile, negative HIV test, negative VDRL for syphilis, negative rheumatoid factor, urinalysis showed many leucocytes consistent with a urinary tract infection, and a random blood sugar 120mg/dl (normal range 72-200mg/dl). She had negative anti-nuclear antibody (ANA) and negative anti double stranded DNA antibody (ds DNA). A creatinine kinase was not possible to obtain, but the SGOT (serum glutamic-oxaloacetic transaminase) was elevated at 156u/L (normal ≤ 40 u/L). Doppler ultrasound of both upper and lower limbs showed no features of deep venous thrombosis but marked soft tissue swelling noted on the right arm. A screening abdomino-pelvic ultrasound was normal (no space-occupying lesions seen), with a screening breast ultrasound showing a 1.62cmx1.86cm hypoechoic mass in the right breast at 11 o'clock position. VIA/VILI screening test was negative for cervical neoplastic changes. Upper gastro-intestinal endoscopy showed mild esophageal candidiasis with antral gastritis. Core biopsy of the breast mass was done, with histology showing features of lipoma with no atypia. Skin biopsy of the right breast showed active, chronic, non-specific dermatitis with reparative changes and no atypia or neoplasm seen. Muscle biopsy was taken from the right deltoid muscle (weakest muscle group per her clinical presentation), with histology showing patchy perivascular lymphocytic infiltrates, no granuloma or giant cells, no atypia or neoplasm noted; with conclusion of non-specific chronic myositis.

Management and follow-up

The patient was diagnosed clinically with dermatomyositis on the basis of progressive symmetrical proximal myopathy involving both upper and lower limbs; the characteristic skin findings of gottron papules (hyperpigmented rash on the knuckles), heliotrope rash (the hyperpigmented rash around both eyes with concomitant periorbital edema), sleeve and shawl signs (hyperpigmented rashes on bilateral proximal arms and over the upper back respectively) and holster signs (hyperpigmented rash on proximal thighs)-see figure 1 below showing some skin manifestations of dermatomyositis by Larazou et al[1]. Additionally, she had significant diffuse muscle pains, fever with elevated ESR of 45mm/hr., elevated serum transaminase (SGOT 156u/L), and compatible (though limited) skin and muscle biopsy results. She was started on steroid therapy with initial intravenous dexamethasone 8mg twice daily, then oral prednisone @1mg/kg/day in a single morning dose (with gastroprotection using omeprazole and osteo-protection using calcium and vitamin D oral supplements); methotrexate starting dose of 10mg with folate 5mg weekly; ciprofloxacin for the urinary tract infection, omeprazole for the antral gastritis, fluconazole for the oropharyngeal-esophageal candida, analgesics, with comprehensive multidisciplinary supportive therapy.



Figure 1: Specific skin manifestations in dermatomyositis:

- A. Heliotrope rash.
- B. Shawl rash.
- C. Gottron sign.
- D. Mechanic's hands.

She was discharged home on a wheelchair after 10 days of inpatient management and reviewed 2 weeks later. By then, the proximal myopathy had greatly improved to the point where she was able to lift both hands above the head, wash, dress, and feed herself independently, though she was still on a wheel chair. The muscle pains and edema had subsided, the heliotrope rash had almost resolved, and she was much stronger. Her steroid and methotrexate doses were adjusted appropriately. She defaulted on her subsequent clinic appointments (but continued methotrexate and prednisone) and came back 3 months later, with the proximal myopathy almost totally resolved, and now fully functionally independent. However, it was noted in this visit that the right breast was now diffusely swollen, with ipsilateral axillary lymphadenopathy (1-2cm lymph nodes). Mammography and repeat breast biopsy were recommended, but the patient and her family requested for more time to source for funds.

She got lost to follow-up for about 16 months, and returned in February 2023, having defaulted on all her medications. The right breast by then had features of an advanced breast cancer with peau d'orange (orange peel appearance), inverted nipple, skin ulcerations, multiple 2-4cm ipsilateral axillary lymphadenopathy with lymphedema of the right arm, and the breast was firmly fixed to the chest wall muscles (see figure 2 showing advanced breast cancer, by Nguetack et al[2], much similar to our patient). The proximal myopathy and skin manifestations of dermatomyositis had recurred, was wheelchair-bound, and markedly wasted. A repeat breast biopsy later showed infiltrating ductal carcinoma, grade III with lymphovascular space involvement and perineural invasion. The hormonal receptor status was not done yet due to financial constraints. Meanwhile, palliative therapy was initiated; but she succumbed to the complications of the breast cancer 3 months later.



Figure 2: Advanced inflammatory breast cancer: see the characteristic peau d'orange with ulcerated nipple and areolar region.

(Nguetack et al, 2012)

2. DISCUSSION

Dermatomyositis and polymyositis are idiopathic inflammatory myopathies, both characterized by proximal skeletal muscle weakness and muscle inflammation (myositis). Dermatomyositis is further characterized by specific skin manifestations, including gottron papules (erythematous to violaceous papules occurring symmetrically over the finger knuckles) and heliotrope rash (erythematous to violaceous eruption on periorbital skin) both of which are characteristic for dermatomyositis[3]. In patients with dark skin, these may appear as hyperpigmented lesions; and may be accompanied with scaling and pruritus[4]. Other skin manifestations include poikiloderma on specific body parts (the shawl sign-the upper back, the V sign-along the V of the neck and upper chest; holster sign-the lateral thigh, sleeve sign-proximal lateral shoulders); nailfold changes with abnormal capillaroscopy; mechanics hands-abnormal hyperkeratosis and fissures on the lateral aspect of fingers and the palms; generalized erythroderma, etc.[5]. Our patient had the classical presentation of dermatomyositis, with prominent proximal myopathy and characteristic skin manifestations. Being a systemic disease, it may manifest in other body systems due to multiple pathways[6]. Diagnostic criteria for dermatomyositis by American College of Rheumatology/European League Against Rheumatism include both clinical and laboratory criteria[7]. Our patient met the diagnostic criteria for dermatomyositis. The main stay of dermatomyositis management is steroid therapy, together with steroid-sparing immunosuppressants, e.g. methotrexate, azathioprine, calcineurin inhibitors, mycophenolate mofetil etc. This is done in a multidisciplinary team. Our patient responded rapidly and progressively to steroids and methotrexate within a multidisciplinary management context, allowing for progressive tapering down of the steroid dosage.

Dermatomyositis is a well-recognized paraneoplastic disorder, with a strong association with malignancies/cancers (up to 20% in adults), whose spectrum generally mirrors that of the general population distribution[8]. For instance, population-based studies in Scandinavian countries found increased risk of ovarian, lung, breast, pancreatic and colorectal cancers in patients with inflammatory myopathies, especially dermatomyositis[9]. In the general Kenyan population, the 5 most common cancers are breast, cervical, prostate, esophageal and colorectal cancers[10]. It follows that paraneoplastic dermatomyositis will be associated with one of these malignancies. The cancer can be diagnosed before, concurrently with, or after the diagnosis of the dermatomyositis. In many studies, the cancer is diagnosed simultaneously with dermatomyositis, or during the first year following the dermatomyositis diagnosis[11]. Some of the risk factors in paraneoplastic dermatomyositis include older age at disease onset, dysphagia, cutaneous necrosis, and capillary damage on muscle biopsy.

With breast cancer being one of the top causes of cancer in Kenya, it is not surprising that our patient was eventually diagnosed with advanced breast cancer associated with the dermatomyositis. In this case, diagnosis was delayed by multiplicity of factors; principally, financial constraints. Interestingly, cancer-associated myositis has positively been linked to the occurrence of certain autoantibodies e.g. transcription intermediary factor (TIF)-1 gamma and nuclear matrix protein (NXP)-2. Conversely, the occurrence of some myositis-specific autoantibodies e.g. anti-synthetase, anti-Mi-2, anti-MDA5, anti-RNP etc., seem to confer a decreased risk of malignancy in dermatomyositis[12]. In the rural Kenyan context, paucity of basic diagnostic resources precludes any potentially revealing genetic analysis. A thorough screening for malignancy is thus an integral part of dermatomyositis diagnosis and management; and begins with a comprehensive history, physical exam and targeted laboratory and imaging tests.

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