

Carcinoma of the Gall Bladder Presenting as Dermatomyositis

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Abstract

Dermatomyositis (DM), manifested as paraneoplastic syndrome, is not a very common clinical entity but its association with various internal malignancies is well-documented in literature. We present such a case of DM associated with characteristic skin lesions and subacute onset of proximal muscle weakness, acquired from a very rare malignancy like adenocarcinoma of gall bladder. ©

INTRODUCTION

Dermatomyositis is a rare disorder of skeletal muscles with inflammation and necrosis of muscle fibres, and characteristic rash in skin. When it occurs in older age groups, it is very often associated with malignancy like lung, breast, ovary and stomach. This syndromic (paraneoplastic) manifestation comprises of 8% of all cases of myositis. The malignancies may antedate or postdate the onset of muscle involvement by up to 2 years. The incidence of paraneoplastic syndrome is higher in patients of DM with advanced age and this is why a meticulous search of underlying malignancy should be performed in all such cases, as the resection of tumour is sometimes associated with remission of myositis.

We present here such an association and to the best of our knowledge, no case of DM due to underlying carcinoma of gall bladder has reported so far from India, and this is the second report of this kind in world literature where the first case was documented by Yiannopoulos G in 2002.¹

CASE REPORT

A 44 years old female patient, housewife by occupation, was reported to our Institute for evaluation of gradual onset, slowly progressive bluish-purple discoloration of face with few scattered itchy lesions in upper limbs for the preceding 3 months. She also had mild weakness of shoulder and pelvic-girdle muscles present for the last 2 weeks. She did not disclose any past history of prolonged fever, malaise, arthralgia/

arthritis, anorexia, appreciable weight loss, recent vaccination, Raynaud's phenomenon, cough, haemoptysis, haematemesis/melaena, haematochezia, oral ulcer, alopecia, jaundice, drug intake (e.g., penicillamine, clofibrate, statins, corticosteroids, emetine, colchicine, chloroquine or zidovudine), lump in the breast or pain in the abdomen. She was non-smoker, non-hypertensive, non-diabetic, and did not give any history of exposure. There was no history of loss of consciousness, headache, vomiting, seizures, sensory dysfunction, distal limb muscles or, bladder and bowel involvement. She had difficulty in squatting and combing her hairs but she could work well until recently without fatigue.

On Examination

Physical examination on admission revealed a middle-aged, average built individual with mild pallor but without having pyrexia, jaundice, clubbing or lymphadenopathy. The pulse rate was 84/min, regular, normal and equal in all the four limbs. The JVP was normal and her blood pressure was 130/85 mm of Hg, both supine and standing. The temperature was 37°C, and respiration 20/min. The skin lesions in the face were bluish-purple in colour, which was chiefly distributed over forehead, and upper and lower eyelids. The whole of the face was moderately puffy and erythematous with severe periorbital oedema. The skin lesions were also distributed over anterior and posterior part of neck and chest, shoulders, lower back, arms and forearms; these lesions were of mixed character like maculopapular eruptions, diffuse erythema and scaling eczematoid dermatitis; and were slightly itchy and photosensitive (Figs .1 and 2). Erythematous papules were present over the knuckles (Gottron 'sign); subcutaneous calcification was not seen.

During the hospital stay, she developed definite weakness of proximal group of muscles of all the four

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Fig. 1: Puffy face with a bluish-purple hue, periorbital oedema, and eczematoid skin lesions in forehead, neck, shoulder, arm, elbow and forearm; diffuse erythema is noted in anterior chest.



Fig. 2: Mixed skin lesions of maculopapular eruptions, diffuse erythema and scaling eczematoid dermatitis.

limbs without any involvement of distal group. Neither the muscle weakness showed any diurnal variation nor any change in degree of weakness after repeated use. Gradually, she showed evidence of loss of weight; within a very short time, she developed nasal intonation with occasional regurgitation, and dysphagia to both solid and liquid food.

Neurological survey disclosed that she was right handed individual with normal higher mental function and cranial nerves. There was no ptosis and pupils were 2.5 mm equal, reacting to light. She showed inability to get up from squatting position and combing her hairs. There was grade III muscle power at hips and shoulders, and power remained normal at elbows, wrists, knees and ankles. The proximal limb muscles were mildly tender and a bit inelastic in feel. There was neither any muscle atrophy nor contracture present. Plantar response was bilaterally flexor. Sensory functions, deep tendon reflexes, cerebellar functions, bladder and bowel functions, and gait were essentially normal. Examination of abdomen did not reveal any lump or hepatosplenomegaly. Rectal and vaginal examinations were within normal limits. There was no lump present in the breasts. The remainder of her physical examination was unremarkable.

A provisional diagnosis of dermatomyositis was made with a big query of paraneoplastic syndrome in mind (Bohan's classification Group III).

Investigations

We performed a battery of tests, which showed Hb 10 g/dl (normocytic-normochromic anaemia), total leucocyte count 13300/mm³ with differential count N₇₀L₂₅M₁E₄, ESR 110 mm in 1st hour (Westergren). Stool examination did not reveal occult blood. Urine was of



Fig. 3: Photomicrography showing segmental necrosis with focal destruction of sarcoplasm. Perifascicular atrophy and perivascular cellular infiltration by phagocytic and inflammatory cells. Endomysial and perimysial interstitial tissue shows mononuclear cells infiltrate. H and E x 350.

normal colour and devoid of myoglobin. Her serum bilirubin, urea, creatinine and sugar (PP) levels were respectively 0.6 mg/dl, 25 mg/dl, 0.6 mg/dl and 108 mg/dl. Other components of liver function tests revealed alkaline phosphatase 81 U/L, AST 190 U/L, ALT 66 U/L, γ -glutamyltransferase 156 U/L (normal 0-30 U/L), total protein 7.9 g/dl with serum albumin level 3.3 g/dl and globulin 4.6 g/dl. Chest X-ray, ECG, upper G.I. endoscopy, thyroid profile and serum electrolytes (sodium, potassium, calcium, phosphate, and magnesium) were within normal limits. Her C-reactive protein (CRP) was 680 μ g/dl (normal 6.8-820 μ g/dl), serum creatine kinase (CK) was 1659 U/L (upper normal 170 IU/ml), antinuclear factor (ANF) and antibody to (Jo-1) antigen were negative. Mammography, ELISA test for HIV, and blood for carcino-embryonic antigen and Ca-125 did not reveal any abnormality.

Electromyography demonstrated spontaneous activity (fibrillation potentials and positive sharp waves), and motor unit potentials which were of low amplitude, polyphasic and had an abnormally early recruitment (myopathic pattern). Nerve conduction velocity was within normal limits.

Ultimately ultrasonography (USG) of the abdomen was performed and it opened the Pandora's box by the presence of gall bladder calculi with hypoechoic mass there, and presence of multiple liver secondaries as well as periportal and peripancreatic lymphadenopathy.

Treatment

Meanwhile, oral prednisolone in a dose of 1 mg/kg/day was started and the patient gradually responded symptomatically, so far the proximal muscle weakness was concerned.

Histopathology

Biopsy of gall bladder mass — the USG-guided FNAC confirmed the gall bladder mass as adenocarcinoma.

Skin biopsy - moderate degree of hyperkeratosis with scattered pigmentation and sparse perivascular chronic inflammatory infiltrates.

Muscle biopsy - a muscle biopsy from upper thigh revealed segmental necrosis with focal destruction of sarcoplasm and invasion by phagocytic and inflammatory cells; perifascicular atrophy and perivascular cellular infiltration in few places. Endomysial and perimysial interstitial tissue showed mononuclear inflammatory cells infiltrate (Fig. 3).

In the context of adenocarcinoma of gall bladder, the surgeon was informed whether any kind of surgery could be possible in the patient. After discharge, oral prednisolone was continued in a gradually tapering dose. Our patient visited us at one month after being discharged from the hospital; she was continuing with oral prednisolone and consulted surgeon for the adenocarcinoma of her gall bladder. Since then, she was lost to follow-up.

DISCUSSION

A paraneoplastic neurological syndrome (PNNS) is a neurological disorder that is associated with a neoplasm which lies anatomically remote from it, ie, the syndrome is not due to direct effect of the tumour itself, metastasis, opportunistic infections, complications of drug or radiation therapy, or malnutrition. PNNS may precede or follow the identification of a neoplasm by weeks, months, or occasionally years and this relationship, till today, is ill-understood.^{2,3} The association between polymyositis-dermatomyositis (PM-DM) and malignancy was first suggested by Shy GM in 1962⁴ and of late, a number of studies have established the association.^{2,3} Any kind of malignancy may be associated with DM, most commonly lung, breast, ovary, stomach, colon and less commonly rectum, kidney, testis,

lymphoma, female genital tract and myeloproliferative disorders, and rarely melanoma, mycosis fungoides or Kaposi's sarcoma. The paraneoplastic syndrome with DM is linked most often with carcinoma of the lung and colon in men, and of the breast and ovary in women. Previously, it was believed that frequency of neoplasm in patients with DM was approximately 50% but subsequent studies revealed that the incidence was much less, and probably it is near about 20%. In elderly patients, particularly those with DM, the frequency of an associated neoplasia reaches 100% in some series. De Vere and Bradley reported that 29% of overall group of DM patients had an associated malignancy; this figure went up to 40% if the patient was over 40 years of age, and to 66% if the patient was both male and over 40.⁵

The term 'carcinomatous neuromyopathy', a non-inflammatory proximal myopathy, is often described to a syndrome with symmetrical proximal muscular weakness, which is associated with depressed tendon reflex; this is probably of neurogenic in origin.⁶ In the context of malignancy, a patient may have proximal weakness as part of general cachectic state.

Females are preferentially affected in DM associated with neoplasia. Classical heliotrope rash may not be evident but periorbital oedema is usually present. As in idiopathic DM, the involvement of skin over elbows, knees and knuckles (Gottron's sign) may be lacking. Other than clue from skin involvement, no biochemical or histological feature reliably diagnoses this paraneoplastic variant of PM-DM; the skin and muscle tissue do not contain tumour cells. The markers of inflammation like ESR and CRP are often normal and should not be relied upon, and even the serum CK may remain normal in chronic cases. EMG may be normal in 10% cases. Antibody against cytoplasmic tRNA synthetases (anti-Jo1) is present in less than 50% cases. Muscle biopsy, the gold standard for diagnosis, may not yield any result because the involvement may be patchy, and a single biopsy may be normal (especially, if small) necessitating repeat biopsy.

Though there is general agreement that DM is treated with corticosteroid or some other form of immunosuppression, it has been observed that in patients with malignancy, the myositis and the cutaneous manifestations are less responsive to systemic glucocorticoid therapy. The leading cause of death in these patients is metastatic spread of the malignancy rather than complications directly related to myositis..

Any kind of malignancy may be associated with dermatomyositis, but an association with gall bladder malignancy is extremely rare. Intense literature search reveals that, globally, our patient seems to be the second case report of such an association after Yiannopoulos G.¹ So far, only three cases of dermatomyositis associated with cholangiocarcinoma have been reported in literature.¹ Our idea in presenting this case is to highlight

gall bladder carcinoma, a rare cause of PNNS, remained undocumented from our country still recently. This case report also emphasizes that an adult-onset DM should always make the physician suspicious about underlying malignancy.

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Announcement

RSSDI – 2005

33rd Annual Conference

23rd, 24th and 25th September 2005, Bangalore

The highlights of the Conference include the following:

- The Conference Venue is in the midst of IT icons surrounded by greenery, go-karting etc.
- The Conference building is aesthetically designed to have an excellent acoustics.
- More than 3000 delegates are expected to attend.
- As part of the Conference, CME is also organized.
- Nationally and Internationally acclaimed faculties shall address the delegates using the state-of-the art audio-visuals.
- Parallel scientific sessions.
- Many pharma companies have agreed to display their products and services.
- The following is the delegate fees:

Category	Upto 28 th Feb 2005	Upto 30 th June 2005	Upto 31 st July 2005	From 1 st August 2005 & onsite registration
Member-RSSDI	2000	3000	4000	6000
Non-Member	2500	3500	4500	7000
PG Student	1500	2000	2500	3000
Accompanying persons	1000	2000	2500	3000
* CME (for all)	500	500	500	500

* Participation in CME needs a separate registration fee.

- Accommodation, transport and sight seeing shall be arranged on request.
- Accompanying children and spouses shall have fun time at the venue itself.

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