

Dermatomyositis associated with malignancy: A report of 3 cases

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ABSTRACT

The association between dermatomyositis (DMS) and various types of malignancies has been reported in several studies, with an estimated frequency of 20-25%. DMS may precede, accompany or follow the diagnosis of malignancy. In the present report, we have discussed three cases of dermatomyositis associated with malignancy. In the first case, DMS preceded the diagnosis of gastric adenocarcinoma while in the second and third cases, it followed the diagnosis of ductal carcinoma of the breast and transitional cell carcinoma of the bladder respectively. In all three patients, cutaneous and musculoskeletal features of DMS showed very good response to the treatment, irrespective of the course of malignancy.

Key words: Dermatomyositis, ductal carcinoma of breast, gastric adenocarcinoma, transitional cell carcinoma of bladder

INTRODUCTION

Dermatomyositis (DMS) is a rare inflammatory disease with musculocutaneous manifestations. Despite few reports to the contrary, DMS is widely accepted as a definite risk factor for internal malignancy, with rates varying from 10% to 50%.^[1] The type of malignancy also varies considerably with sex and geographic location, with ovarian and breast carcinoma predominating in women and lung cancer in men, worldwide.^[2] Asian studies have reported nasopharyngeal carcinoma as the most common type of malignancy associated with DMS.^[3,4] With reports of varied types of carcinomas associated with DMS, malignancy screening can be time consuming and expensive, but should be mandatory.

rash, Figure 1a and b]. Similar erythema and hyperpigmentation were also present on the neck, chest, shoulders and back [Shawl sign, Figure 1 c and d]. Erythematous hyperpigmented papules were present on the knuckles and both elbows [Gottron's papules, Figure 1e and f]. Musculoskeletal examination revealed proximal muscle weakness of shoulder and hip girdles. Skin biopsy from the erythematous lesion on the forehead revealed atrophic epidermis, focal basal cell vacuolar degeneration, dermal edema, mild perivascular lymphocytic infiltrate and abundant mucin in the dermis [Figure 2a and b]. Blood investigations of the patient revealed raised erythrocyte sedimentation rate (ESR), elevated titers of muscle enzymes (LDH and CPK-MM) and electromyography (EMG) showing first-degree muscle disease, confirming the diagnosis of dermatomyositis. Rhinolaryngoscopy of the patient revealed articular defects of vocal cords due to bulbar muscle palsy [detailed investigations are mentioned in Tables 1 and 2]. The patient was simultaneously investigated for underlying malignancy. Barium swallow of the patient showed esophageal motility disorder, computed tomography (CT) scan of the abdomen revealed thickening in the pyloric region, causing mild luminal compromise, esophago-gastro-duodenoscopy (OGDscopy) showed presence of gastric ulcer at the pyloric antrum and biopsy from

CASE REPORTS

Case 1

A 36-year-old male presented with complaints of itchy red lesions over the periorbital area, forehead and malar area associated with photosensitivity since 3 months, painless swelling around both eyes since 1 month and pain over the shoulder and hip region, nasal twang of voice and difficulty in deglutition since 2 days. Cutaneous examination of the patient revealed periorbital erythema, edema and hyperpigmentation [Heliotrope

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Figure 1: Cutaneous examination of case 1. (a and b) Heliotrope rash and periorbital edema, (c) "V" sign, (d) "Shawl" sign and (e and f) Gottron's papules

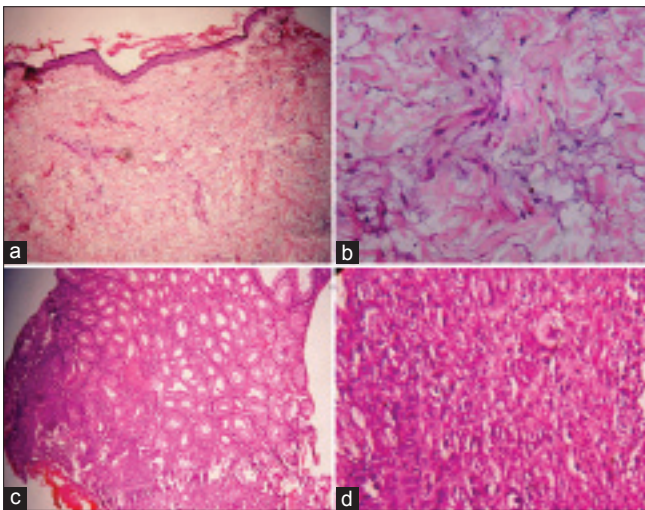


Figure 2: Case 1: (a) Skin biopsy, 100×; hematoxylin and eosin (H and E) stain: Atrophic epidermis, focal basal cell vacuolar degeneration, dermal edema, mild perivascular lymphocytic infiltrate and abundant mucin in the dermis. (b) Skin biopsy, 400×, H and E stain: Dermal edema and abundant mucin in the dermis. (c) Biopsy from gastric ulcer, 100×; H and E stain: Normal gastric glands and transition zone showing malignancy. (d) Biopsy of gastric ulcer, 400×; H and E stain: Tumor cells mainly arranged in solid sheets with paucity of glandular structure and mitotic activity suggestive of poorly differentiated adenocarcinoma

the gastric ulcer confirmed the diagnosis of poorly differentiated adenocarcinoma of the stomach [Figure 2c and d]. The patient was diagnosed as DMS associated with poorly differentiated

Investigations	Case 1	Case 2	Case 3
Hemoglobin (males 13-18gms/dl females 12-15gms/dl)	11.8	12.4	14.6
CBC (4000-11000/cmm)	8900	11400	11,000
ESR (female: 1-25 mm/hr Male: 0-17 mm/hr)	50	50	25
Serum creatinine (0.6-1.2 mg/dl)	0.8	1	0.8
Serum bilirubin (0.3-1 mg/dl)	0.6	0.72	0.9
SGOT (0-42U/L)	110	160	533
SGPT (0-42U/L)	25	30	208
Urine examination	WNL	WNL	30-40 RBC/hpf 8-15 Transitional Epithelial Cells 3-5 pus cells/hpf
CPK-MM (N-24 to 195 IU/L)	1518	2322	1966
LDH (N-105 to 331U/L)	1166	382	1362
ANA	Negative	Negative	Positive 4+

CBC: Complete blood count, ESR: Erythrocyte sedimentation rate, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, WNL: Within normal limits, CPK-MM: Creatinine phosphokinase muscle specific isoenzyme, LDH: Lactate dehydrogenase, ANA: Antinuclear antibody

gastric adenocarcinoma. The patient received oral prednisolone 1.5 mg/kg/day with low potent topical corticosteroids and

sunscreen. The patient's skin lesions and muscle symptoms showed excellent response [Figure 3a-f] to the treatment with reduction in the titers of muscle enzymes [Table 3]. After clinical improvement, prednisolone was tapered gradually and the patient was referred to an oncologist for management of gastric adenocarcinoma. Unfortunately, the patient was lost to follow-up.

Case 2

A 65-year-old married female, operated case of carcinoma of the right breast (*in situ* ductal carcinoma), presented with

complaints of sudden appearance of swelling and redness over the right breast since 2 weeks. The swelling was associated with appearance of red-colored minimally itchy lesions on the forehead, cheeks, nape of neck retroauricular area and pinna since 6 days. The patient also developed generalized swelling all over the body since 2 days with difficulty in raising her arms above the head and getting up from the squatting position. Cutaneous examination of the patient revealed violaceous erythema over the periorbital area, forehead, malar area, chin ([Figure 4a], pre- and postauricular area [Figure 4b and c] and

Table 2: Special investigations in cases

	Case 1	Case 2	Case 3
USG	Abdomen: Prominent portal veins	Right Breast: Edema of skin and Subcutaneous tissue Abdomen: Normal	Abdomen And Pelvis: Urothelial Carcinoma involving prostate and 1×3.2 cm sized lesion noted at bladder base and prostate
Barium swallow	Esophageal motility disorder	Not done	Not done
CT scan (abdomen)	Thickening in pyloric region, causing mild luminal compromise	Normal	Ill defined mildly enhancing lesion at the bladder base extending into the prostate
Pet scan	No evidence of metastasis	No evidence of metastasis	No evidence of metastasis
Rhino laryngoscopy	Articular defects of vocal cords due to bulbar muscle palsy	Normal	Bulbar muscle palsy
OGD scopy	Gastric ulcer	Not done	Not done
Electromyography	1 st degree muscle disease	Myopathic denervation	Consistent with myositis

USG: Ultrasonography, CT: Computed tomography, PET scan: Positron emission tomography, OGD scopy: Oesophago-gastro-duodenoscopy



Figure 3: Improvement in skin lesions of dermatomyositis after 2 weeks of treatment with oral steroids. (a) Heliotrope rash and periorbital edema before treatment. (b) Resolution of lesions after treatment. (c) Erythema over neck, chest and arms before treatment. (d) Resolution of the erythema over neck, chest and arms after treatment. (e) Erythematous and poikilodermatous lesions on the back and shoulders (Shawl sign) before treatment. (f) Resolution of erythematous lesions on the back, leaving behind dyspigmentation after treatment

both the breasts [Figure 4d and e]. Systemic examination of the patient revealed generalized edema and musculoskeletal system examination revealed proximal muscle weakness affecting the limb girdles. Laboratory investigations of the patient revealed raised ESR and markedly elevated muscle enzymes (LDH, CPK-MM) [Tables 1 and 2]. Electromyography showed presence of myopathic denervation consistent with polymyositis, while a muscle biopsy from the quadriceps muscles revealed inflammatory myositis. Skin biopsy from the erythematous lesion revealed atrophic epidermis, focal basal cell vacuolar degeneration and dermal edema [Figure 4f], suggesting the diagnosis of dermatomyositis. The patient was simultaneously

investigated for the recurrence of operated ductal carcinoma of the breast and metastasis. Ultrasonography of the right breast showed edema of the skin and subcutaneous tissue with fluid collection in the subcutaneous tissue without evidence of any mass. Positron emission tomography (PET) scan of the whole body did not reveal recurrence of previous malignancy or metastasis. The patient was diagnosed as dermatomyositis associated with treated ductal carcinoma of the breast and was initially started on oral prednisolone 1.5 mg/kg/day. But, in the absence of satisfactory improvement, subcutaneous injection methotrexate 15 mg/week was added. The patient showed excellent improvement in skin lesions and muscle function within 2 weeks [Figure 5a-f] with reduction in titers of muscle enzymes [Table 3]. The dose of oral steroids and methotrexate was tapered slowly without recurrence of the disease, leading to complete discontinuation of the treatment at the end of 4 months.

Table 3 : Improvement in the muscle enzymes

Cases	CPK-MM (muscle specific) (N-24 to 195 IU/L)		LDH (N-105 to 33 IU/L)	
	Before treatment	After 1 month of treatment	Before treatment	After treatment
1	1518	759	1166	753
2	2322	413	382	284
3	1966	212	1362	274

CPK-MM: Creatinine phosphokinase muscle specific isoenzyme, LDH: Lactate dehydrogenase

Case 3

A 58-year-old married male presented with complaints of swelling and redness of the periorbital area, face, trunk and upper extremities since 2 months, difficulty in raising limbs and getting up from squatting position since 15 days and nasal twang of voice



Figure 4: (a) Cutaneous examination of case 2 showing violaceous erythema over the periorbital area (heliotrope rash), forehead, malar area and chin. (b and c) Erythematous plaques on the pinnae and pre- and postauricular areas. (d) Erythema and edema of both the breast, more on the right side than on the left. (e) Scar of previous surgery on the right breast surrounded by erythema. (f) Skin biopsy from the erythematous lesion on the forehead. 400x, Hematoxylin and eosin showing atrophic epidermis, focal basal cell vacuolar degeneration and dermal edema



Figure 5: (a) Heliotrope rash, periorbital edema and erythematous lesions on the forehead, malar area and chin before treatment. (b) After treatment. (c) Erythema over the right pinna and pre- and postauricular areas before treatment. (d) After treatment. (e) Erythema over the left pinna and pre- and postauricular areas before treatment. (f) After treatment. (g) Erythema and edema over both the breasts before treatment. (h) After treatment

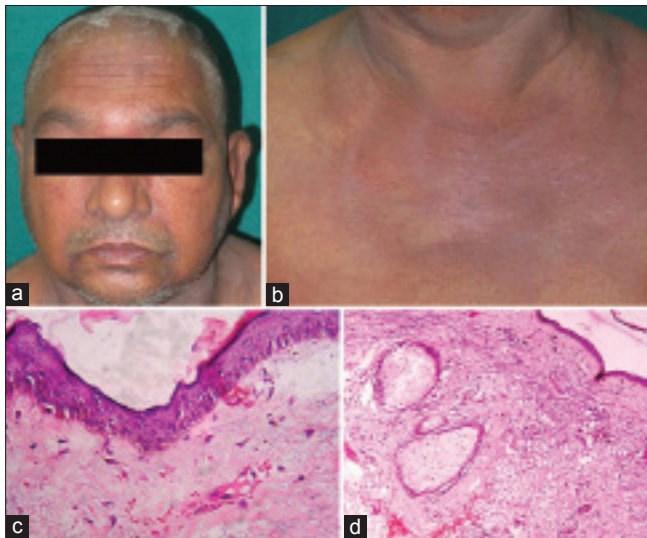


Figure 6: (a) Cutaneous examination of case 3: Heliotrope rash and periorbital edema. (b) Erythema over the "v" area of the neck (i.e., "V" sign) and upper chest. (c) Skin biopsy, 400x, hematoxylin and eosin (H and E): Showing atrophic epidermis, basal cell vacuolar degeneration, dermal edema and perivascular inflammatory infiltrate. (d) Skin biopsy, 400x, H and E: Showing atrophic epidermis, basal vacuolar degeneration, dermal edema and perivascular inflammatory infiltrate with abundant mucin in the dermis

and nasal regurgitation of the food since 1 day. The patient was apparently alright 3 months ago, when he developed increased frequency of micturition, urgency and reddish discoloration of urine lasting for 3-4 days. The patient was investigated and



Figure 7: (a) Cutaneous examination of case 3: Heliotrope rash and periorbital edema before treatment. (b) Resolution of heliotrope rash and periorbital edema after 2 weeks of treatment. (c) Erythema over the "v" area of the neck (i.e., "V" sign) and upper chest. (d) Resolution of erythema over the "v" area of the neck and upper chest after 2 weeks of treatment

diagnosed to have high-grade transitional cell carcinoma of the urinary bladder with extension to prostate on biopsy of the prostate. Cutaneous examination of the patient revealed confluent

macular violaceous erythema and edema of the periorbital area, forehead and malar area [Figure 6a] with erythematous rash on the neck, chest [Figure 6b] and back. Systemic examination of the patient revealed generalized edema and musculoskeletal system examination revealed weakness of the muscles of limb girdles.

Laboratory investigations of the patient revealed raised ESR, positive antinuclear antibody test (ANA 4+) and markedly elevated muscle enzymes (LDH, CPK-MM). Electromyography showed presence of myopathic denervation consistent with polymyositis, while a muscle biopsy from the quadriceps muscles revealed inflammatory myositis. Urine examination of the patient showed 30-40 RBCs/hpf, 8 to 15 transitional epithelial cells and 3-5 pus cells/hpf [Tables 1 and 2]. Skin biopsy from the violaceous erythematous lesion revealed atrophic epidermis, basal cell vacuolar degeneration, dermal edema and perivascular inflammatory infiltrate with abundant mucin in the dermis [Figure 6c and d]. Ultrasonography of the abdomen and pelvis revealed 1 cm × 3.2 cm-sized mass at the bladder base, involving the prostate and suspected to be transitional cell carcinoma of the bladder. CT scan of the abdomen revealed ill-defined, mildly enhancing lesion at the bladder base extending into the prostate which on biopsy and immunohistochemistry confirmed the diagnosis of high grade transitional cell carcinoma. Rhinolaryngoscopy of the patient showed bulbar palsy. The patient was diagnosed as DMS associated with transitional cell carcinoma of the bladder and received oral prednisolone 1.5 mg/kg/day and subcutaneous injection methotrexate 15 mg/week in view of severity of skin and muscle involvement. Skin lesions of the patient showed complete resolution after 2 weeks of the treatment [Figure 7a-d], but muscle function recovery was monitored by fall in titers of muscle enzymes [Table 3]. Unfortunately, the patient died of sudden cardiac arrest while awaiting the surgery.

DISCUSSION

DMS is a connective tissue disease with characteristic cutaneous manifestations, and it is well known to be associated with various types of malignancies. The first suggestion that DMS was associated with malignancy was made by Sterz in 1916, and numerous cases have since been reported.^[5] It is widely accepted as a definite risk factor for internal malignancy, with rates varying from 10% to 50% in different studies.^[1]

The malignancy types vary in each country. Hill *et al.* reported DMS in strong association with ovarian, lung, gastric, colorectal and pancreatic malignancy in several Northern European countries, whereas Wong reported that nasopharyngeal carcinoma was as high as 75% in Hong Kong^[6] and Ang *et al.* reported a rate of 50% in Singapore.^[7] On the other hand, in Japan, gastric, lung, breast and ovarian malignancy were commonly associated with DMS (in order of frequency). Asian studies have shown nasopharyngeal carcinoma as the most common association.^[3,4]

Other malignancies associated with DMS included those of gastric, liver, cervical lymph node metastases of unknown origin, cholangial, esophageal, colonic, laryngeal, renal, tongue and lymphoma.

Several predictive factors of associated malignancy have been described over the years, with the age of the patient being the most important.^[8] The incidence is higher in patients with age more than 40 years^[9] and male sex.^[3,10] Other factors include raised ESR,^[11] skin lesions,^[12] muscle biopsy findings^[13] and muscle enzyme levels,^[3,14] cutaneous necrosis,^[10] interstitial lung diseases,^[3] amyopathic dermatomyositis,^[10] muscle biopsy findings,^[13] constitutional symptoms, rapid onset of disease and Raynaud's phenomenon.^[14]

Malignancy was often detected within the first year of onset of DMS. Zang *et al.* studied 115 cases of DMS with malignancy, in which malignancy preceded dermatomyositis in 14 cases, was diagnosed concurrently in 22 patients and in another 79 patients it appeared within 3 years after the DMS was diagnosed. Among them, malignancy was detected in 66 patients in the first year, 11 patients in the second year and only two patients in the third year.^[9]

The exact incidence of DMS with the three malignancies reported in our cases is not available, but breast malignancy has been increasingly reported in association with DMS in females,^[2] and there are isolated case reports of DMS associated with gastric and transitional cell carcinoma of the bladder. Two patients of DMS with transitional cell carcinoma of the bladder had presented with amyopathic dermatomyositis.^[15]

DMS associated with malignancy is generally more resistant to corticosteroid and cytotoxic therapies than idiopathic myositis.^[16] Dermatomyositis activity reflects the state of malignancy, and some reports have described improvement of DMS without immunosuppressive drugs after the resection of the malignancy.^[16-18] The overall survival rate was considerably worse when compared with other forms of myositis.^[19]

The unique features of our cases include appearance of associated undiagnosed gastric malignancy in a young patient of DMS in the first case and occurrence of DMS after diagnosis and treatment of underlying malignancy in the second case. Few important observations drawn from our cases are that the possibility of DMS should be kept in mind in patients of malignancy even if the malignancy is treated. Underlying malignancy should be ruled out even in young patients, as seen with our first case.

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