

Case Report

Docetaxal induced scleroderma like disease

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Abstract

Scleroderma like skin disease is a rare entity among the drug induced dermatological manifestations. It is attributed to various drugs and recently to certain oncological medications especially taxanes. Despite being an efficacious chemotherapeutic agent, it results in scleroderma like skin lesions rarely it resolves in some patients if detected early with omission of the culprit drug with or without steroids. Despite its rarity in literature untreated cases develop severe functional limitation due to skin fibrosis. After an exploration of literature search herein we report the first case of *docetaxal* induced scleroderma in a Sri Lankan which was detected and promptly treated with steroids successfully. We report this case to make clinicians aware about this condition when encountered with a patient having skin fibrosis with background history of chemotherapy, the possibility of a drug induced scleroderma.

Keywords:

Scleroderma, taxanes, Docetaxal

Introduction

Drug induced scleroderma like disease is a relatively rare condition which occurs following administration of a drug which resembles scleroderma like pattern and improves once the causative drug is withdrawn, some patients require steroids and in some patients, it may remain depending on the patient's characteristics.

Various drugs can cause scleroderma like lesions and morphea like plaques. Literature has revealed bleomycin, tryptophan and vitamin K₁. Recently chemotherapeutic agents have been detected to cause such lesions. Taxane based agents, gemcitabine,

tegafur uracil and immune check point inhibitors are notorious to cause such drug induced fibrotic lesions. (1)

This condition differs from systemic sclerosis by the absence of internal organ involvement, raynauds, nailfold capillary abnormalities and negative antinuclear antibodies. Though the exact mechanism is yet to be elucidated there were some mechanisms proposed such as dermal fibrosis, granulomatous inflammation, endarteritis, vascular thrombosis, increased production of type1 procollagen which are provoked by different drugs.(1)

Case History

A 62-year-old known Sri Lankan patient with invasive ductal breast carcinoma T₂N₁M₀ with ER +, PR+ and HER2- negative underwent wide local excision and axillary clearance who was given chemotherapy with 4 cycles of doxorubicin, cyclophosphamide and 4 cycles of Docetaxal and started with Exemestine. While waiting for radiotherapy she presented with thickening of skin, difficulty in opening mouth, affected hand function. Therefore, she was not given radiotherapy and referred from oncology clinic to Rheumatology clinic for evaluation.

On inquiry she had malaise, swelling and stiffness of hands and face. She didn't have oral ulcers, patchy alopecia, arthritis, photosensitivity rashes, urinary abnormalities, gastro oesophageal reflux disease or dysphagia, any altered bowel habit or cough. She never experienced Raynaud's phenomenon.

On examination, there was hyper pigmented skin over the face with moderate skin thickening; she was afebrile, pale and not icteric. There was no palpable lymphadenopathy or no clubbing. There were skin

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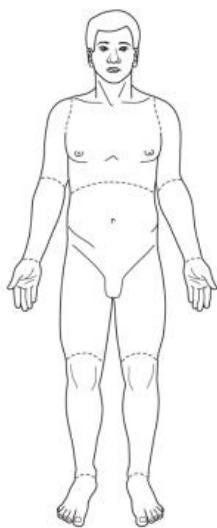
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thickening and hardening, dermal oedema on face, hands and feet. There were no ulcers or pruritus. She had mild trismus with microstomia. Her fingers were swollen with severe thickening of skin and stiffness therefore her hand function was significantly affected and she was unable to fully flex the fingers. Nails didn't show any changes and there was no telangiectasia. She didn't have active arthritis or tendinitis. Bed side swallowing assessment was normal. Her respiratory and cardiovascular system examinations were unremarkable and she was normotensive. On abdominal examination

there was no hepato-splenomegaly or ballotable masses. Nervous system examination was unremarkable. Her feet were showing moderate skin thickening with limited toe movements.

Modified Rodnan skin score (MRSS) is used for measurement of skin thickness in scleroderma clinical trials. (2)

Her MRSS was 19 initially, and after steroid therapy it was 7 at the 6th week of treatment.



	Right				Left			
Fingers	0	1	2	3	0	1	2	3
Hands	0	1	2	3	0	1	2	3
Forearms	0	1	2	3	0	1	2	3
Upper Arms	0	1	2	3	0	1	2	3
Face			0	1	2	3		
Anterior Chest			0	1	2	3		
Abdomen			0	1	2	3		
Thighs	0	1	2	3	0	1	2	3
Legs	0	1	2	3	0	1	2	3
Feet	0	1	2	3	0	1	2	3
Column Totals								
Total:								
Key:	0 – No Thickening 1 – Mild Thickening 2 – Moderate Thickening 3 – Severe Thickening							
Notes:								

Figure 1- Modified Rodnan skin score (MRSS) - obtained by clinical palpation of 17 different body areas and subjective averaging of thickness of each site. A maximum point of this scoring is 51.



Figure 2

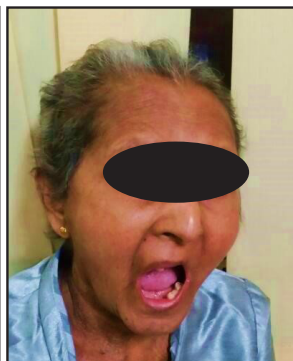


Figure 3



Figure 4



Figure 5

Figure 2,3,4,5, -Facial, hand and feet dermal oedema and significantly affected mouth opening, hand function

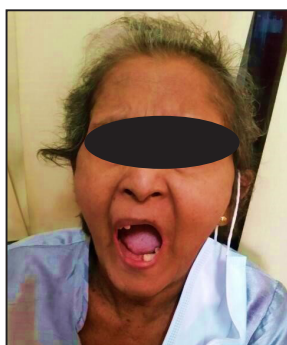


Figure 6



Figure 7



Figure 8

Figure 6,7,8, - After 6 weeks resolution in oedema and hand function started to appear.

Diagnostic assessment

Full blood count showed white blood cells 14,000/mm³ with neutrophil leucocytosis, haemoglobin 9.8g/dL, platelets 330,000. Her CRP was 2.9; ESR was 48mm/1st hour. CPK was normal. Calcium and other electrolytes were normal. UFR showed few pus cells, no RBC and trace albumin. Liver function tests revealed AST 46, ALT 53, INR 1.1, APTT 35s, total bilirubin 18micromol/L, indirect bilirubin 10 micromole/L, direct bilirubin 10 micromole/L, total protein 62mg/dL, albumin 40mg/dL, globulin 22mg/dL, gamma-GT 64. Fasting blood sugar was 96mg/dL. Blood urea 8 mmol/l & serum creatinine 112 mmol/l.

Hand X-ray and chest X-ray were unremarkable. 2D ECHO was normal. ANA, Rheumatoid factor, Anti SCL-70 were negative.

Skin biopsy was not done as she has not given consent and as she was on chemotherapy with the risk of poor wound healing and its consequences.

Therapeutic approach

For the invasive ductal breast carcinoma she was given chemotherapy with 4 cycles of doxorubicin, cyclophosphamide and 4 cycles of Docetaxal. She was started on exemestane which is an aromatase inhibitor as she had Estrogen Receptor positivity and as she was a post-menopausal woman. After the completion of chemotherapy while waiting for radiotherapy, she presented with the scleroderma like disease. Radiotherapy was not given.

We opted to manage her with multidisciplinary approach incorporating the care of oncologist, physiotherapist and occupational therapist with our Rheumatology input. As patient was anxious initially, she was reassured and explained about the need for investigations. Then with the enlightenment of the possibility of Docetaxal induced scleroderma like disease, she was given the explanation. She was started on oral prednisolone 20 mg daily.

She was monitored regularly. She was offered physiotherapy to improve the mobility and strength of muscles of hand and feet. Occupational therapy was

arranged to facilitate her hand function with modified gadgets for brushing and eating. Gait training was given to prevent contracture formation. She was given local applications including moisturizers and emollients. Prednisolone was gradually tailed off. Improvement in symptoms noted at around 6 weeks after the commencement of prednisolone. Radiotherapy was not given as it is contra-indicated due to scleroderma like disease.

She was followed up in rheumatology and oncology clinics. Currently she is functionally independent.

Discussion

Scleroderma is thickening of skin which is the pathognomonic feature of systemic sclerosis. It could be either limited cutaneous or diffuse. It is a multi-system rheumatological disease. The 2013 ACR EULAR classification criteria for scleroderma states hallmark features of systemic sclerosis are fibrosis of skin and/or internal organs, presence of specific antibody and vasculopathy.

Skin thickening of the fingers extending beyond metacarpophalangeal joints is virtually enough for diagnosing as scleroderma. There are 7 features considered in the absence of the above. They are skin thickening of fingers, fingertip lesions, telangiectasia, nailfold capillaroscopic abnormality, Interstitial Lung Disease, Pulmonary Arterial Hypertension, Raynaud's Phenomenon, Antibodies associated with Scleroderma. Skin biopsy is not necessary unless there is a suspicion of another disorder. Scleroderma can predate the malignancy or it can follow the malignancy.

There are no diagnostic criteria for drug induced scleroderma like disease. It is correlating the temporal association with drug and the clinical pattern of involvement. Therefore it is a comprehensive decision. For the clinical evaluation of skin thickness MRSS is used as reference in most of the trials worldwide.

Drug induced scleroderma differs from systemic sclerosis by the absence of internal organ involvement and negative serology. There are some drugs implicated in the drug induced systemic sclerosis

among them chemotherapeutic agents are becoming popular nowadays. Analgesics, immune check point inhibitors, neurological drugs, appetite suppressants and gadolinium based contrast agents are other agents.

Despite its effectiveness in improving survival docetaxel has numerous side effects in various systems in the body. There are dermatological adverse effects noted following treatment with docetaxel such as acute generalized exanthematous pustulosis (AGEP), cutaneous lupus erythematosus, erythema multiforme, palmar-plantar erythrodysesthesia, scleroderma-like skin lesions, Steven-Johnson syndrome, and toxic epidermal necrolysis. (1)

Prevalence of scleroderma-like disease has been reported less frequently in literature. In Sri Lanka there are no reported cases up to now as per our knowledge.

Conclusion

When a patient with features of scleroderma is encountered always it must be born in mind regarding a secondary process which is reversible when promptly detected and treated otherwise it can adversely affect the functional capacity of the patient. Despite it is rarity we wanted to bring out the topic which is an enigma to be sorted.

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Consent

Consent was obtained from the patient for publishing the photography and the case.