Hong Kong College of Physicians

Case report for AIM Interim Assessment

Name of candidate (print and sign):
Hospital and Unit: **Specialty other than AIM:**
Name of supervisor (print and sign):
Date(s) and place (hospital) of patient encounter: Aug 2018
Date of report submission: 10th March, 2021

Case report

Title: Anti-TIF1 gamma associated dermatomyositis

Case history:

An 81-year-old male with background history of type II diabetes mellitus, hypertension and hyperlipidaemia, was admitted to our hospital for erythematous rashes (Figure 1). He presented with gradual onset of patchy erythematous skin changes over face, bilateral eyelids, limbs, extensor surfaces of joints and trunk in the course of two weeks. Skin changes were followed by progressive, symmetrical proximal muscle weakness, with difficulty to lift heavy objects and climb upstairs. He attended our hospital emergency department as he started to develop multiple episodes of choking with fluid intake.

He had no arthritis, mucositis or alopecia. There was no associated abdominal pain, haematochezia or changes in bowel habits. He had no cough, shortness of breath or haemoptysis. He denied any constitutional symptoms or fever.

On physical examination, patient had periorbital heliotropic rash, Gottron papules over the interphalangeal extensor surfaces of bilateral hands. Violaceous rash was seen over sun- exposed area including face, neck and extensor surface of the upper limbs. There was also evidence of periungual telangiectasia and hoarseness of voice. A focused neurological examination demonstrated bilateral proximal muscle weakness over both upper and lower limbs.

Laboratory results showed patient has anaemia with haemoglobin level 8.5g/dL (reference 13.2-17.2 g/dL) , white cell and platelet count was normal. Biochemical tests including renal function, liver function test and bone profile was unremarkable. Creatinine kinase level was 2266 U/L (ref 39-308 U/L). There was elevated carcinoembryonic antigen (CEA) level 13 ug/l (reference < 4.7 ug/l).

Electromyography demonstrated early myopathic changes. Muscle biopsy was performed, showing evidence of focal atrophy. Skin biopsy over the anterior upper chest wall showed orthokeratosis with focal mildly flattened epidermis, smudging of interface and focal papillary oedema, mild dermal lymphohistiocystic infiltration which were in keeping with dermatomyositis. Anti-transcription intermediary factor 1 gamma (anti-TIF1-γ) was strongly positive.
The diagnosis of dermatomyositis (DM) was established based on the clinical and laboratory findings.
The presence of anti-TIF1-γ autoantibodies raised the concern of paraneoplastic dermatomyositis. Oesophageal-gastro-duodenoscopy and colonoscopy were done as anaemia workup, both findings were unremarkable. Positive Emission Tomography-Computer tomography (PET-CT) of whole body was negative for primary malignancy. He was clinically deteriorated during the hospital stay with repeated choking, subsequently required nasogastric tube for feeding.

He was started on high dose intravenous methylprednisolone, followed by oral prednisolone 60mg daily and methotrexate 15 mg once per week. In view of progressive muscle weakness, dysphagia and elevated creatinine kinase despite high-dose steroid, Intravenous immunoglobulin (IVIG) was finally administered. However, he was refractory to multiple lines of immunosuppressive therapy including repeated courses of IVIG. The patient eventually succumbed due to severe pneumonia.

Discussion and literature review

In this case study, we reported a case of anti-transcription intermediary factor 1 gamma (anti-TIF1-γ) associated dermatomyositis (DM). Anti-TIF1-γ Ab is one of the

myositis-specific antibodies that is associated with immune-mediated myopathy, with positive correlation to paraneoplastic type of DM.
Although in our reported case, neoplastic lesions were not identified from endoscopic and imaging point of views, proactive search of underlying neoplasm is mandatory for all DM cases with positive anti-TIF1-γ autoantibodies.

Dermatomyositis is an idiopathic inflammatory myopathy. The pathogenesis of DM is not well understood, but it is believed to be complex and multifactorial.
Patients usually presented with dermatological manifestations, such as periorbital heliotrope rash, interphalangeal Gottron papules, pruritic violaceous rash, facial erythema, poikiloderma over sun-exposed area and periungual erythema [1], [2].
Myopathy usually followed dermatological manifestations, with classical features of progressive, symmetrical, proximal muscle weakness. Laboratory findings include elevated creatinine kinase level which correlates with the disease activity of the myopathy. The diagnosis of dermatomyositis is based on the combination of clinical features, pattern of muscle involvement, muscle enzymes level, electromyographic findings, muscle and skin biopsy analysis [3].
DM is also associated with other systemic involvements, including interstitial lung disease, oesophageal dysmotility , myocarditis and arthritis.

In recent years, discovery of myositis specific autoantibodies (MSA) revealed DM is a heterogenous group of disorder, with each subtype demonstrates its unique clinical features, disease progression pattern, degree of systemic involvement and prognosis [4].

Assessment of myositis autoantibodies pattern is recommended for delineation of dermatomyositis subtypes, which is important not only prognostically but also serve as a guide for subsequent treatment. DM-specific antibodies include anti-synthetase, anti-signal recognition particle (anti-SRP), anti-Mi2, anti-melanoma differentiation associated protein 5 (anti-MDA5), anti NPX2, anti-TIF1-γ and anti- small ubiquitin-like modifier activating enzyme (SAE).

Anti-TIF1-γ antibody is a myositis specific autoantibody which can be found in patients with dermatomyositis [5]. Presence of this myositis specific autoantibody

confers a greater risk of developing solid and haematological malignancies, especially those presented in advanced age [6]. The positive predictive value of anti-TIF1-γ in identifying DM-related cancer is about 58%.

Positive anti-TIF1-γ Ab usually correlates with gastrointestinal cancer [7]. In our reported case although clinical evidence of malignancy could not be demonstrated, the severe debilitating dysphagia was in keeping with the anti-TIF1- γ related DM. Other key associations of Anti-TIF1-γ Ab include severe cutaneous disease with absence of arthritis, interstitial lung disease and Raynaud phenomenon [8]. These systemic involvements were also absent in our patient.

Glucocorticoid in conjunction of steroid sparing agent such as methotrexate, mycophenolate, azathioprine as well as rituximab remain the mainstay treatment for DM. IVIG can be used as last resort if refractory to the above therapies, especially in patients with severe oesophageal involvement causing dysphagia.

Tables and figures:

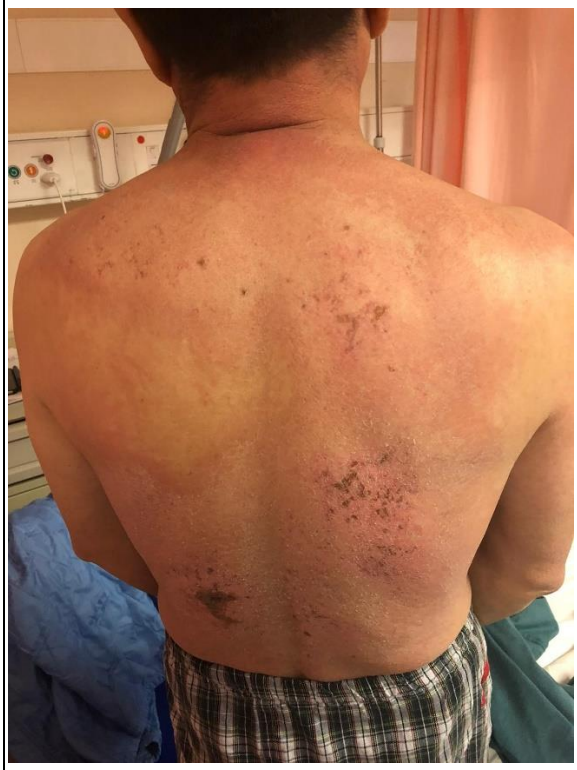

Figure 1.

Patchy erythematous rashes over the back (written consent had been obtained from the patient)

Reference(not more than 10):

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8. Fiorentino DF, Kuo K, Chung L, Zaba L, Li S, Casciola-Rosen L. Distinctive cutaneous and systemic features associated with antitranscriptional intermediary factor-1γ antibodies in adults with dermatomyositis. J Am Acad Dermatol. 2015 Mar;72(3):449-55. doi: 10.1016/j.jaad.2014.12.009. Epub 2015 Jan 14. PMID: 25595720; PMCID: PMC4351728.

No of words in Case History and Discussion (excluding references):____1085_____
(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

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(signature of Trainee)

Endorsed by Supervisor *

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(signature of Supervisor)