

A Case of Dermatomyositis with Secondary Sjögren's Syndrome- Diagnosis with Follow-up Study of Technetium-99m Pyrophosphate Scintigraphy

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Abstract

Purpose: To report a case of dermatomyositis (DM) with secondary Sjögren's syndrome (SS) and propose the clinical application of technetium-99m pyrophosphate (^{99m}Tc-PYP) scan.

Case Report: A 50-year-old woman had progressive proximal muscle weakness of bilateral thighs, myalgia, tea-colored urine, and exercise intolerance for 6 months. Physical examination showed malar rash, V-sign, periungual erythema, and mechanic hands. Neurological assessment showed symmetric pelvic-girdle weakness, myopathic face, waddling gait, but preserved deep tendon reflex and sensory functions. DM was diagnosed on the basis of typical rashes and serum creatinine kinase elevation (7397 IU/L). Aside from myopathic symptoms, dry eye and mouth were reported. Thorough autoantibody searches showed positive anti-SSA/Ro antibody (198 U/ml). Both Schirmer's test and sialoscintigraphy were positive, leading secondary SS as diagnosis. Initial ^{99m}Tc-PYP scan revealed increased radiouptake in the muscles of bilateral thighs, compatible with clinical assessment. Follow-up scan three months later shows abnormal but attenuated radiouptake at bilateral thighs, in the presence of nearly-complete clinical recovery.

Conclusion: DM with secondary SS in adult is a unique disease entity, with predominantly myopathic symptoms and satisfactory therapeutic response as its characteristics. Our serial muscle imaging studies suggest that ^{99m}Tc-PYP scan is at once anatomically-specific and persistently-sensitive to microstructural damages within inflammatory muscles, enabling clinician to monitor disease activity and therapeutic response.

Key Words: Dermatomyositis, Sjögren syndrome, ^{99m}technetium pyrophosphate scan

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INTRODUCTION

Inflammatory myopathy is a group of disease that involves chronic muscle inflammation, accompanied by muscle weakness, exercise intolerance, and variable extra-muscular organ involvement⁽¹⁾. They comprise a heterogeneous entity of disorders, including dermatomyositis (DM), polymyositis, and inclusion body myositis. Prevalence of inflammatory myopathies in Western society varies with different countries, ranging from 4.9 to 42.1 per 1,000,000 persons⁽²⁾. In Taiwan, the prevalence is about 2.9 per 100,000 persons⁽³⁾.

Being the largest group of acquired and potentially treatable myopathies⁽⁴⁾, the importance of early recognition will increase, as will the need for supplementary tools for targeting pathological muscle and tracking therapeutic responses. Since serum muscle enzyme levels does not always correlate with muscle strength, muscle images appear as novel candidates for objective assessment of disease activities⁽⁵⁾. Muscle scan provides information of inflammation severity as well as exploration of gross musculature, enabling to localize target pathological muscle in a noninvasive manner. As not all the cases would receive confirmatory muscle biopsy in clinical

practice, muscle scan may shed the light for differential diagnosis⁽⁶⁾, prognosis prediction⁽⁷⁾, and disease activity monitoring⁽⁵⁾. Judicious diagnosis not only assists proper management in therapeutics but remarks notion for occult malignancy⁽⁸⁾. In Taiwan's cohort, DM patients carried a higher risk of malignancies than polymyositis (12.8% vs. 7%), mostly in nasopharynx, lung and breast⁽⁹⁾. It is therefore frequent the case that laborious workup for occult malignancy being commenced on subject with DM, well-known as the clinical precursor of cancer⁽¹⁰⁾.

Aside from the linkage to cancer, DM is at sometimes associated with other extraneural connective tissue diseases, making it an attractive disease entity⁽¹¹⁾. The major reports of overlapping syndrome include rheumatoid arthritis, scleroderma, and lupus erythematosus⁽¹²⁾. Cases associated with Sjögren's syndrome (SS) were limited. Herein we presented a case of DM with secondary SS and discussed their underlying pathogenesis.

CASE REPORT

A 50-year-old woman was admitted to the ward with 6 months history of progressive lower limbs weakness, resulting in problems on climbing upstairs and rising from

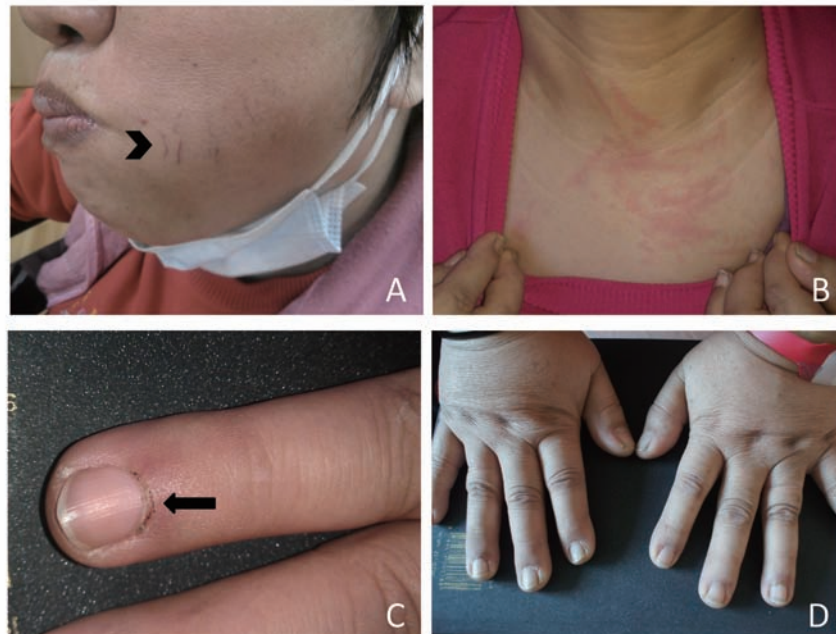


Figure 1. Maculopapular rashes over cheeks (Figure 1A, arrowhead), V sign (Figure 1B), periungual erythema (Figure 1C, arrow), and mechanic hands (Figure 1D) are main skin changes in this case..

the chair. Although maintaining ability to comb hair or lift objects above the head, she needed strong assistance whenever standing up from squat position. She also had general soreness, tea-colored urine, and fatigue, mostly worsened with strenuous activity. Neither difficulty with swallowing nor body weight loss was ever experienced. She retained continence on voiding and defecation and had no sensory complaints other than myalgia.

On physical examination, she had maculopapular rashes over cheeks, extending to involve at anterior chest wall (V sign), and visible at periungual areas as well (Figure 1). Sclerodacty and mechanic hands were also noted (Figure 1). Apart from very mild soreness on deep pressure toward the quadriceps, other muscle bulk remained non-tender and normal in appearance. Neurological examination showed myopathic face and waddling gait. There was decreased muscle power of iliopsoas 4/4, gluteal maximus 4/4, quadriceps 4/4, hamstrings 4/4, gastrocnemius 4+/4+, tibialis anterior 5-/5- bilaterally in the Medical Research Council of Great Britain grading but normoreflexia throughout. Evaluation

of mental status, sensory, and cerebellar system were normal.

On review of past history, she had no suspicious toxin exposure, including lipid-lowering agents, steroid, alcohol, and illicit drugs. She had no prolonged fever, body weight loss, lymphadenopathy, or insect bite. None of her family members presented similar symptoms or gait problems. Tentative diagnosis was proposed of myopathy, most probably DM.

Ancillary tests showed elevation of creatinine kinase (CK) 7397 IU/L (ref.: 26-192 IU/L), myoglobin 1565 ng/mL (ref.: 7-64 ng/mL), lactic dehydrogenase (1417.8 IU/L; ref.: 81-234 IU/L), aspartate transaminase (265 IU/L; ref.: 15-37 IU/L), and alanine aminotransferase (204 IU/L; ref.: 0-45 IU/L), reflecting the state of muscle damages. Thyroid function, cortisol level, HbA1c, hepatitis, and human immunodeficiency virus screening were all unremarkable. Electromyography disclosed poor recruitment but no increased muscle activity. The technetium-99m pyrophosphate ($^{99m}\text{Tc-PYP}$) scan revealed relatively increased radiouptake in the muscles

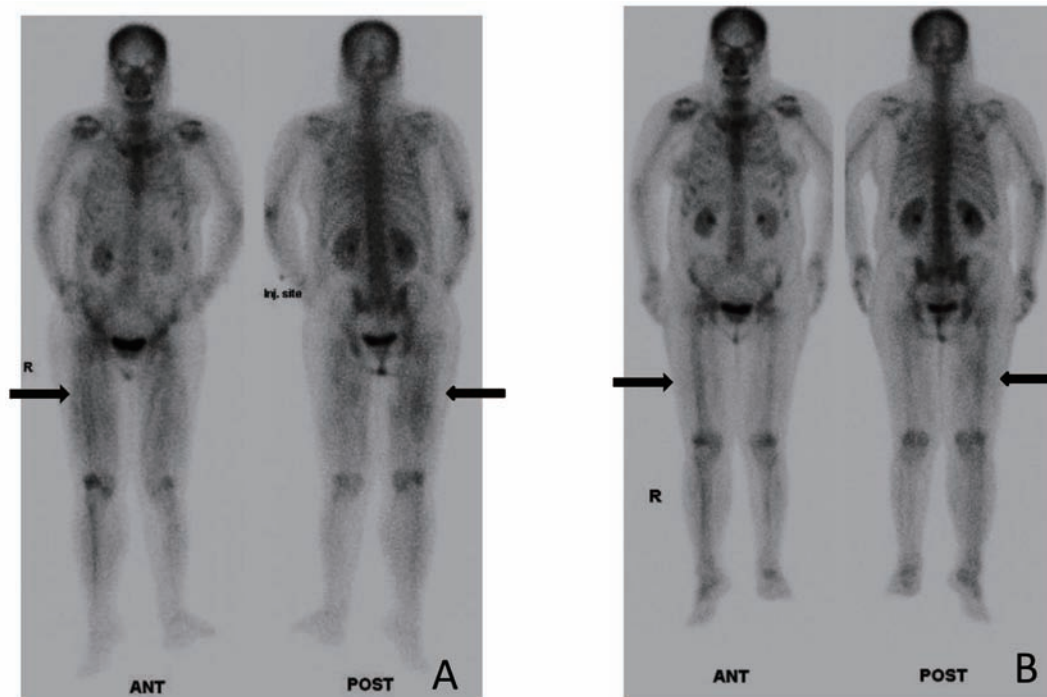


Figure 2. Initial $^{99m}\text{Tc-PYP}$ scan targets the damaged muscle bulk compatible with clinical assessment (Figure 2A, arrow). Follow-up scan three months later shows abnormal but attenuated radiouptake at bilateral thighs, in the presence of nearly-complete clinical recovery (Figure 2B, arrow)

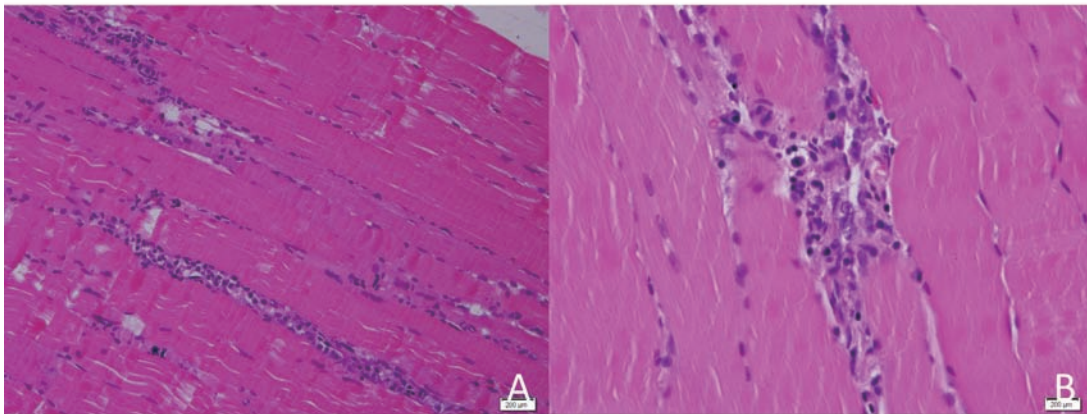


Figure 3. Muscle biopsy with hematoxylin and eosin stain showed lymphocyte-like cells infiltrating between the muscle bundles. A, Low magnification. B, High magnification.

	Muscle strength (Right/Left)	Muscle enzyme		Treatment
		Creatinine kinase (IU/L)	Myoglobin (ng/ mL)	
Pre-treatment	Iliopsoas 4/4 Quadriceps 4/4 Gastrocnemius 4+/4+	7397.5	1421.6	
Post-treatment 1 month	Iliopsoas 4+/4+ Quadriceps 4+/4+ Gastrocnemius 5-/5-	2538.0	795.3	Prednisolone 60mg QD
Post-treatment 2 months	Iliopsoas 5-/5- Quadriceps 5-/5- Gastrocnemius 5/5	1215.7	232.5	Prednisolone 35mg QD
Post-treatment 3 months	Iliopsoas 5-/5- Quadriceps 5-/5- Gastrocnemius 5/5	455.6	76.0	Prednisolone 20mg QOD

Table. Summary of Therapeutic Response and Muscle Enzymes Changes

of bilateral thighs, more advanced in the right side, and right lower leg (Figure 2). Biopsy of right gastrocnemius and quadriceps showed some lymphocyte-like cells infiltrating between the muscle bundles and some around the perivascular area (Figure 3). Neither necrosis nor obvious perifascicular muscle fiber atrophy was identified. The diagnosis of probable DM was made based on to criteria proposed by Bohan and Peter⁽¹³⁾. To clarify occult malignancy, investigation with aim of tumor screen was made. Colon fibroscopy was commenced due to abnormal carcinoembryonic antigen level 50.73 ng/mL (ref.: 0-3 ng/

mL). A villous adenoma, sized 1.5 cm, was explored then removed from proximal ascending colon.

To document any co-morbid autoimmune disease, we further clarify any constitutional symptoms in addition to comprehensive serology panel. The patient had dry eye and mouth in association with positive anti-SSA/Ro antibody level 198 U/ml (ref.: 7-10 U/ml) and relevant abnormal anti-nuclear antibodies titer (1:160; nucleolar pattern). Schirmer's test was positive [5 mm in 5 minutes (ou)]. Sialoscintigraphy showed salivary gland impairment. She was negative for complement, anti-double stranded

DNA, anti-SS-B/La, anti-Scl-70, and anti-Jo-1 antibodies. Secondary SS was diagnosed⁽¹⁴⁾. She got nearly-complete recovery with serum CK normalization (355.0 IU/L) three months after prednisolone therapy (Table). In the follow-up ^{99m}Tc-PYP muscle scan, abnormal signal of bilateral thighs persisted, but with attenuated radiouptake.

DISCUSSION

Although muscle pain is common in primary SS⁽¹⁵⁾, linkage between DM and SS has been focused onto juvenile form^(16, 17). Herein we present a case of adult-onset DM with SS, representing a unique disease entity contrast to previous literature^(11, 12). While most cases develop myopathic symptoms years after the diagnosis of SS⁽¹⁸⁾, our patient has muscle weakness as the initial symptom. We therefore regard the diagnosis of DM with secondary SS being properly made.

Although current opinion points anti-SSA/Ro as a myositis-associated rather than myositis-specific autoantibody⁽¹⁹⁾, discussion on its contribution to damages of muscle and/or vessels continues. Two types of anti-SSA/Ro antibodies, anti-SSA-52 kDa (aSSA52) and anti-SSA-60 kDa (aSSA60), have been identified. Although both constitute inflammatory state⁽¹⁹⁾, aSSA52 turns to be an independent surrogate marker for muscle damages^(20, 21). Whether high anti-SSA/Ro titer in our case contributes myopathy remains unsettled, as commercially available anti-SSA/Ro assay fails to detect aSSA52 and debatable cross reactivity between aSSA52 and aSSA60⁽²¹⁾.

^{99m}Tc-PYP, a commonly used medical radioisotope, is applied in functional studies of heart, skeletal muscle, bone, and tumors⁽²²⁾. With red and white cells binding biological behavior⁽²²⁾, the regions of tracer accumulation may correspond to areas of active muscle inflammation and severity of the muscle weakness as well⁽²³⁾. Mechanism leading ^{99m}Tc-PYP uptake includes extracellular fluid expansion, enhanced regional vascularity and permeability, and elevated tissue calcium concentration⁽²⁴⁾. It's therefore plausible to infer that inflammatory cells infiltration within muscle bundles and perivascular spaces in our pathology report launches into vascular permeability changes and secondary myocyte damages. It's also worthy to put note on the initial ^{99m}Tc-PYP scan of our case perfectly matched to clinical assessment, providing informative localization

of target muscles and diagnostic cue. As muscle biopsy in clinical practice is not feasible in all cases, ^{99m}Tc-PYP scan provides a supplementary noninvasive tool elucidating underlying pathogenesis. The follow-up ^{99m}Tc-PYP scan also verifies inflammatory process within the muscles, even in the presence of symptom remission and laboratory normalization. Aside from its sensitive characteristic, changes between initial and follow-up scans also suggest its potential role to monitor disease activity and therapeutic response.

Although serum muscle enzymes, such as CK and aldolase, have been applied as ancillary test as part of myopathy evaluation, their levels don't always correlate with clinical assessment. This is attributed by the facts that either disease chronicity or remnant muscle fiber amount may confound the results⁽²⁵⁾. With the regards to localization of muscle damage, they provide limited information compared to the image studies. Magnetic resonance imaging, which can clearly identify the soft tissue anatomy as well as the site of muscle inflammation, is more expensive and technically-demanded than muscle scan. Although with less image resolution, ^{99m}Tc-PYP scan provides an option for evaluating myopathy of less cost, but sensitive information in localization of pathological muscle. It is, however, prudent selection of image tools should be made on the basis that repeated ^{99m}Tc-PYP scans contribute radiation exposure of moderate degree.

There are some limitations in our case report. First, the pathology reports from two separate muscle bulks unveiled inflammatory reaction but no perifascicular atrophy. It is, however, the interpretation of biopsy is vulnerable to tissue sampling in mosaic pattern involvement commonly seen in DM⁽²⁶⁾. Second, the follow-up biopsy after treatment was not proceeded, mainly under ethic concern and remarkable clinical improving course.

In sum, we present an adult patient of DM with secondary SS, as dominant pelvic-girdle weakness with satisfactory response to steroid as its clinical phenotype. Although not pathognomonic, anti-SSA may contribute inflammatory cascade within damaged muscles and neighboring vasculatures. Our serial muscle imaging studies suggest that ^{99m}Tc-PYP scan is at once anatomically-specific and persistently-sensitive to microstructural damages within inflammatory muscles.

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