JAMA Dermatology Clinicopathological Challenge

Rapidly Progressive Stiffness and Nodularity of Both Hands in a Middle-aged Woman

Pin-Hsuan Chiang, MD; Ren-Feng Liu, MD

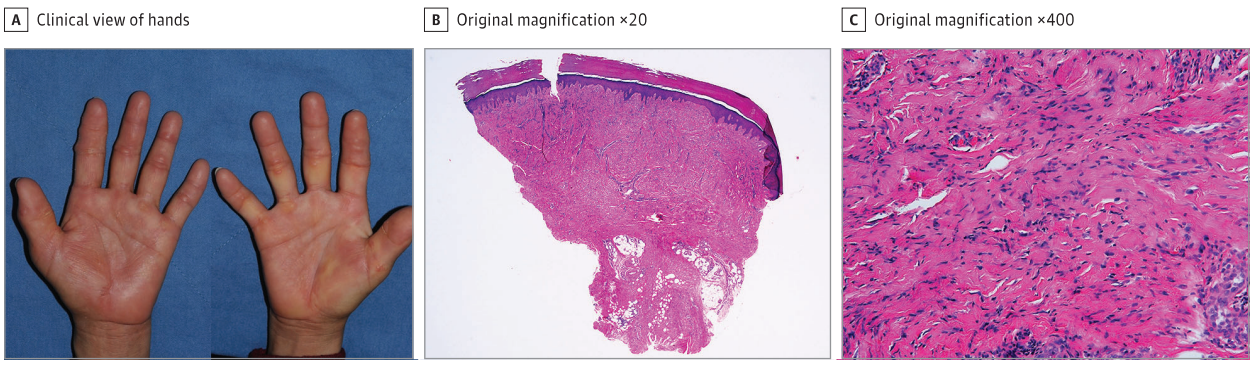

Figure. A, Clinical image of erythematous and edematous changes of bilateral hands and multiple nodules on palms and interphalangeal joints. B and C, Hematoxylin-eosin–stained specimen showing increased fibroblasts with fibrosis from dermis to subcutis.

A woman in her late 40s presented with rapidly progressive redness and stiffness of both hands, accompanied by 2 months of multiple finger joint and right shoulder pain. Results of autoimmune serology, including antinuclear antibody, C3 and C4, rheumatoid factor, and Scl-70 antibody tests, were negative. Raynaud phenomenon was not seen. There was an absence of nailfold capillary changes and distal digital pitting.

The patient was treated with nonsteroidal anti-inflammatory drugs, systemic steroid therapy, and disease-modifying antirheumatic drugs (ie, hydroxychloroquine), but symptoms persisted. Two weeks after treatment initiation, multiple tender nodules developed over the palms and interphalangeal joints, and flexion contractures continued (**Figure**, A). Incisional skin biopsy of the palmar nodules (Figure, B and C) and computed tomography (CT) were performed. Results of the CT demonstrated bilateral ovarian tumors with highly suspect peritoneal metastases.

WHAT IS YOUR DIAGNOSIS?

A. Dupuytren contracture

B. Fibroblastic rheumatism

C. Palmar fasciitis and polyarthritis syndrome

D. Scleroderma

Quiz at jamacmelookup.com

Diagnosis

C. Palmar fasciitis and polyarthritis syndrome

Microscopic Findings and Clinical Course

Histopathologic examination revealed increased fibroblasts with fibrosis from dermis to subcutis (Figure, B and C). The fascia was not included in the biopsy specimen.

For the ovarian cancer, the patient received neoadjuvant chemotherapy with carboplatin and paclitaxel at 3-week intervals for 3 cycles. Results of the follow-up CT showed partial regression in the left ovarian tumor and a stationary right ovarian tumor. The patient underwent debulking surgery with bilateral salpingo-oophorectomy. The pathology of the ovarian tumors demonstrated high-grade serous carcinoma. Regarding her hands, the patient reported partial resolution of swelling, pain, and nodularity, but no improvement in flexion contractures.

Discussion

Palmar fasciitis and polyarthritis syndrome (PFPAS) is a rare paraneoplastic disorder that was first described in 1982 by Medsger and colleagues.[1] The most common cancer underlying PFPAS is ovarian cancer, followed by pancreatic and gastrointestinal cancers and breast and lung cancers.[2] This syndrome predominantly affects women aged 50 to 70 years.[2] The pathogenesis of PFPAS is unknown, but a hypothesis is that PFPAS results from profibrotic factors, such as transforming growth factor-β produced by tumor cells.[1,3]

Patients with PFPAS present with sudden-onset erythema and thickening and pain in bilateral hands followed by nodular fasciitis and flexion contracture that lead to limited range of motion.[2,4] Polyarthritis usually develops symmetrically and affects the metacarpophalangeal and proximal interphalangeal joints and wrists.[2] Involvement of the shoulder, knee, ankle, and foot joints also has been

reported.[1] Histopathologic features of PFPAS demonstrate increasing fibroblasts, from dermis to subcutis and even deeper.[5] The epidermis is usually unaffected.

Differential diagnosis of PFPAS includes Dupuytren contracture, scleroderma, fibroblastic rheumatism, intrinsic joint diseases, and rarely, diabetic cheiroarthropathy. Dupuytren contracture commonly occurs in White men of older age and is associated with diabetes mellitus, smoking, and alcohol consumption.[6] Although Dupuytren contracture and PFPAS have similar pathology, Dupuytren contracture can be clinically indolent for years, and its skin lesions affect the fourth and fifth fingers.[6] Patients with scleroderma usually have Raynaud phenomenon, a positive antinuclear antibody test, and nailfold capillary dilation and hemorrhage.[7] Also, microscopically, thickened and increased collagen fibers must be demonstrated.[8] Fibroblastic rheumatism is accompanied by sclerodactyly and Raynaud phenomenon; its histopathologic features are increased fibrosis and a loss of elastic fibers.[9,10] Also, patients with fibroblastic rheumatism often have a clinical response to immunosuppressive treatment.[9,10]

To our knowledge, there are currently no established PFPAS treatment guidelines. Nonsteroidal anti-inflammatory, systemic or intralesional corticosteroidal, and disease-modifying antirheumatic drugs have been reported to be ineffective.[2-4] During cancer treatment, about half of patients with PFPAS show gradual improvement of pain, edema, and redness of the hands.[3,4] However, joint contracture, which may substantially reduce the patient's quality of life, is usually irreversible.[2]

Cutaneous and musculoskeletal symptoms of PFPAS develop before other signs of cancer, by an average of 6 months and 8.6 months, respectively.[2,4] Moreover, PFPAS occurring after a cancer diagnosis and treatment may indicate the progression of the cancer.[2] Once PFPAS is suspected, complete cancer screening and early management can substantially improve the patient's prognosis and preserve hand function.

ARTICLE INFORMATION

Author Affiliations: Department of Dermatology, Chang Gung Memorial Hospital, Linkou, Keelung, and Taipei, Taiwan (Chiang, Liu); College of Medicine, Chang Gung University, Taoyuan, Taiwan (Chiang, Liu).

Corresponding Author: Ren-Feng Liu, MD, Department of Dermatology, Chang Gung Memorial Hospital, No. 222, Maijin Rd, Anle Dist, Keelung City, 20401, Taiwan (hiawathahaha@gmail.com).

Published Online: November 11, 2020. doi:10.1001/jamadermatol.2020.4386

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patient for granting permission to publish this information.

Self-assessment Credit: This article is eligible for journal-based self-assessment (1 credit) for Maintenance of Certification (MOC) from the American Board of Dermatology (ABD). After completion of an activity, please log on to the ABD website at www.abderm.org to register your credits. This may be done after each exercise or after accumulating many credits.

REFERENCES

1. Medsger TA, Dixon JA, Garwood VF. Palmar fasciitis and polyarthritis associated with ovarian carcinoma. *Ann Intern Med*. 1982;96(4):424-431. doi:10.7326/0003-4819-96-4-424

2. Manger B, Schett G. Palmar fasciitis and polyarthritis syndrome-systematic literature review of 100 cases. *Semin Arthritis Rheum*. 2014;44(1):105-111. doi:10.1016/j.semarthrit.2014.03.005

3. Kajikawa H, Sobajima T, Koiwai C, Ichigo S, Takagi H, Imai A. Palmar fasciitis with polyarthritis-associated ovarian cancer: case report and literature review. *Mol Clin Oncol*. 2018;8(2):292-295.

4. Martorell EA, Murray PM, Peterson JJ, Menke DM, Calamia KT. Palmar fasciitis and arthritis syndrome associated with metastatic ovarian carcinoma: a report of four cases. *J Hand Surg Am*. 2004;29(4):654-660. doi:10.1016/j.jhsa.2004.04.012

5. Yoshioka K, Fukumoto T, Sowa-Osako J, Tateishi C. Idiopathic palmar fasciitis and polyarthritis syndrome. *BMJ Case Rep*. 2019;12(11):e232954. doi:10.1136/bcr-2019-232954

6. Shaw RB Jr, Chong AK, Zhang A, Hentz VR, Chang J. Dupuytren's disease: history, diagnosis, and treatment. *Plast Reconstr Surg*. 2007;120(3):44e-54e. doi:10.1097/01.prs.0000278455.63546.03

7. Knobler R, Moinzadeh P, Hunzelmann N, et al. European Dermatology Forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin, part 1: localized scleroderma, systemic sclerosis and overlap syndromes. *J Eur Acad Dermatol Venereol*. 2017;31(9):1401-1424. doi:10.1111/jdv.14458

8. Asano Y, Fujimoto M, Ishikawa O, et al. Diagnostic criteria, severity classification and guidelines of localized scleroderma. *J Dermatol*. 2018;45(7):755-780. doi:10.1111/1346-8138.14161

9. Jurado SA, Alvin GK, Selim MA, et al. Fibroblastic rheumatism: a report of 4 cases with potential therapeutic implications. *J Am Acad Dermatol*. 2012;66(6):959-965. doi:10.1016/j.jaad.2011.07.013

10. Marconi IM, Rivitti-Machado MC, Sotto MN, Nico MM. Fibroblastic rheumatism. *Clin Exp Dermatol*. 2009;34(1):29-32. doi:10.1111/j.1365-2230.2008.02748.x