Paraneoplastic Dactylitis Leading to the Diagnosis of Ovarian Cancer

Tali Eviatar MD and Ori Elkayam MD

Department of Rheumatology, Tel Aviv Sourasky Medical Center, affiliated with the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

KEY WORDS: dactylitis, malignancy, ovarian cancer, paraneoplastic

IMAJ 2019; 21: 354–355

Paraneoplastic syndrome is a collection of signs and symptoms at locations remote from a tumor or its metastases. Dactylitis is a typical manifestation of psoriatic arthritis (PsA) and other forms of spondyloarthritis. The syndrome has also been described in gout, sarcoidosis, and sickle cell disease in children, as well as in mycobacterial, streptococcal, and brucellar infections [1]. We present a unique case of dactylitis suspected as being paraneoplastic in origin.

PATIENT DESCRIPTION

A 60-year-old woman with a past history of osteoarthritis was referred to our department with inflammatory pain of 2 weeks duration in the fingers of her left hand, right wrist, and first left toe. She had been prescribed a nonsteroidal anti-inflammatory drug by her family physician without improvement. Physical examination [Figures 1A and 1B] revealed dactylitis of the second finger and erythema, tenderness of the middle phalanx of the fourth finger of the left hand, and dactylitis of the first left toe. Her medical and family history was negative for psoriasis, gout, spondyloarthritis, and inflammatory bowel disease. She denied any systemic symptoms, including weight loss. Her blood tests, including infectious serology and cultures, were normal except for a mild increase in liver enzymes and C-reactive protein levels.

An abdominal ultrasound was conducted to rule out hepatic pathology. The results were within normal limits. She was prescribed 20 mg of prednisone, without significant improvement, and she started taking apremilast based on the presumed diagnosis of PsA sine psoriasis. Two weeks after starting apremilast, while still taking 5 mg of prednisone, she developed further worsening of the dactylitis, including the second, forth, and fifth fingers of her right hand, and arthritis of the elbow.

Arthrocentesis of the elbow disclosed inflammatory fluid (12,000 white blood cell count) without evidence of bacterial or mycobacterial infection. In view of the atypical presentation and the resistance to corticosteroids, she was sent for a full paraneoplastic workup.

Whole body computed tomography disclosed metastatic lesions in the abdominal and pelvic cavities, which were histologically confirmed as metastatic ovarian carcinoma. She underwent a total abdominal hysterectomy and bilateral oophorectomy with debulking of the tumor and started chemotherapy treatment.

COMMENT

We present a case of migratory dactylitis and arthritis, ultimately recognized as the paraneoplastic manifestation of metastatic ovarian carcinoma.

Dactylitis is highly suggestive of PsA, which is not classically considered a manifestation of malignancy. The malignancy rate reported in a prospective Canadian study of PsA patients was similar to that of the general population [2]. In contrast, a recent Japanese study [3], which included 115 PsA patients, reported a rate of malignancy of 16.5% before and 3.5% after the

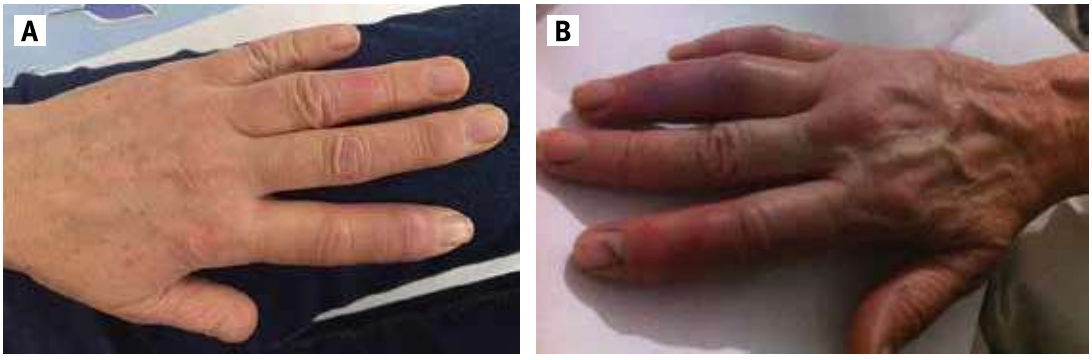

Figure 1. Physical examination of hands

[A] Left hand showing dactylitis of second digit and erythema of the middle phalanx of the fourth digit, which was tender to palpation

[B] Right hand showing dactylitis of second, fourth, and fifth digits

onset of arthritis. Most of those patients (83.5%) did not have psoriasis, and 80% presented with dactylitis. The investigators raised the possibility of a paraneoplastic syndrome in some patients.

A variety of paraneoplastic syndromes have been reported in association with ovarian cancer, but there is a paucity of data on their incidence or prevalence. Those conditions include paraneoplastic neurologic (e.g., paraneoplastic cerebellar degeneration), endocrine, hematologic, dermatologic, ophthalmic, and rheumatologic syndromes (dermatomyositis and palmar fasciitis and polyarthritis syndrome [PFAPS]) [4,5]. PFAPS is characterized by painful swelling of both hands that progresses to flexion contractures, without dactylitis [5].

This unique case shows dactylitis as the presenting symptom of metastatic ovarian cancer. The red flag was the rapid evolution of multiple impressive dactylitis, despite treatment with corticosteroids. Patients presenting with dactylitis which do not fall into a characteristic diagnostic pattern may need to undergo an extended workup that includes a full investigation of a paraneoplastic condition.

Correspondence
Dr. T. Eviatar
Dept. of Rheumatology, Tel Aviv Sourasky Medical Center, Tel Aviv, 6423906 Israel
Phone: (972-3) 697-3668, **Fax:** (972-3) 697-4577
email: talieviatar@gmail.com

References

1. Healy PJ, Helliwell PS. Dactylitis: pathogenesis and clinical considerations. *Curr Rheumatol Rep* 2006; 8 (5): 338-41.
2. Rohekar S, Tom BD, Hassa A, Schentag CT, Farewell VT, Gladman DD. Prevalence of malignancy in psoriatic arthritis. *Arthritis Rheum* 2008; 58 (1): 82-7.
3. Hagiwara K, Suyama Y, Fukuda K. Clinical experience in 115 patients with arthritis and/or enthesitis who met the classification criteria for psoriatic arthritis (CASPAR) within the last two years-possible association with malignant disorders. *Mod Rheumatol* 2016; 26 (4): 625-9.
4. Viau M, Renaud MC, Gregoire J, Sebastianelli A, Plante M. Paraneoplastic syndromes associated with gynecological cancers: a systematic review. *Gynecol Oncol* 2017; 146 (3): 661-71.
5. Manger B, Schett G. Paraneoplastic syndromes in rheumatology. *Nat Rev Rheumatol* 2014; 10 (11): 662-70.

Capsule

The secret life of cediranib

Anti-angiogenic agents are used to inhibit the formation of new blood vessels that supply nutrients and oxygen to tumors. However, recent findings suggest that they can have additional anticancer effects. The antiangiogenic drug cediranib can sensitize tumors to poly (ADP-ribose) polymerase (PARP) inhibitors, which normally target tumors with defective DNA repair. **Kaplan** and co-authors determined that cediranib damages tumors both by interrupting their blood supply, inducing hypoxi a, and by directly affecting pathways involved in DNA repair, sensitizing cancer cells to PARP inhibitors.

Sci Transl Med 2019; 11: eaav4508
Eitan Israeli

Capsule

High mutational load gets a response

Cancers harbor many genetic mutations. Defects in DNA mismatch repair prevent tumors from repairing certain types of DNA damage and lead to a hypermutable genomic state known as microsatellite instability (MSI). Some tumors with a high degree of MSI may be treatable with PD-1 (programmed cell death-1) immunotherapy, but patient response is highly variable. **Mandal** and colleagues studied drivers of differential response to immunotherapy in these patients and found that MSI intensity and insertion-deletion mutations strongly affected therapeutic outcome.

Science 2019; 364 :485
Eitan Israeli

Capsule

BCAPing inflammasome activation

The phosphoinositide 3-kinase adaptor protein BCAP (B cell adapter for PI 3-kinase) limits macrophage responses to stimulation of Toll-like receptors. Inflammasomes are multiprotein complexes that activate the protease caspase-1 to process the proinflammatory cytokine interleukin-1β (IL-1β). **Carpentier** and colleagues identified a distinct role for BCAP in preventing excessive activation of inflammasomes. In macrophages, BCAP reduced active caspase-1 levels, IL-1β release, and cell death after exposure to the toxin nigericin or after bacterial infection. BCAP delayed caspase-1 activation by inflammasomes, and loss of BCAP promoted bacterial clearance in mice.

Sci Signal 2019; 12: eaau0615
Eitan Israeli