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CASE REPORTS

Palmar fasciitis and polyarthritis syndrome in patients with ovarian cancer—a case report and review of the literature

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Palmar fasciitis and polyarthritis syndrome (PFPAS) is a challenging clinical diagnosis characterized by the diagnosis of neoplasm with accompanying flexion contractures, inflammatory fasciitis, fibrosis, and generalized arthritis of the hands [6]. The differential diagnosis includes Dupuytren's contractures, rheumatoid arthritis, scleroderma, eosinophilic fasciitis, and reflex sympathetic dystrophy [3].

PFPAS has been implicated with neoplasms such as hematological malignancies [7] and cancers of the lung [9, 10], prostate [12], breast [11], pancreas [4, 7], and extraovarian adenocarcinoma [14]. There have been 15 reported cases of ovarian cancer-related PFPAS with variable presentations, times to diagnosis, surgical interventions, and long-term outcomes.

We report the case of a 73-year-old woman who presented to her dermatologist with a 4-month history of bilateral pruritic and painful nodules on the palmar hands that had been diagnosed at an outside hospital as deep granuloma annulare (DGA) unresponsive to corticosteroids. Nodules of DGA are often asymptomatic and painless and resolve either spontaneously or improve with application of topical corticosteroids [8]. Biopsy is done in the case of symptomatic lesions, atypical presentations, or if the diagnosis is under question. A skin biopsy from our patient demonstrated interstitial mucin in the dermis and subcutis, changes consistent with DGA (Fig. 1); however, the unresponsiveness to treatment and constellation of physical exam findings enumerated below led to a diagnosis of ovarian cancer-related PFPAS.

Our patient reported severe functional limitations of her hands and intense pain without relief despite high doses of oxycodone. On exam, she had bilateral flexion contractures of all the digits (Fig. 2). The dorsal aspects of her PIPs and MCPs were erythematous, edematous, and tender to direct palpation. There was blotchy bilateral erythema that seemed to follow the track of the flexor tendons. She also had limited internal rotation at the left shoulder and slight limitation of internal rotation about both hips. The remainder of the examination of the peripheral and root joints of the arms and legs showed no tenderness, swelling, limitation of range of motion, or instability. Bimanual pelvic examination revealed omental fullness and a palpable pelvic mass, which was found on ultrasound to be consistent with ovarian carcinoma. Magnetic resonance imaging (MRI) of her hands revealed palmar fasciitis (Fig. 3). Anti-nuclear antibodies (ANA) serology was negative and her rheumatoid factor (RF) factor was within normal limits (9 IU/mL; normal range, 0–13 IU/mL). Her past medical history was significant for bilateral total knee arthroplasty and osteoarthritis.

At this time, the patient's diagnosis was revisited. Her unresponsiveness to corticosteroids for treatment of DGA, progressively worsening functional limitation of her hands, intense bilateral pain in her hands, and findings of a pelvic mass better correlated with the diagnosis of PFPAS.

She underwent surgical debulking of stage III papillary serous cystadenocarcinoma of the ovaries and received adjuvant chemotherapy. At 21 months follow-up, the patient reported drastically increased functional restoration of her hands and markedly decreased pain. On exam, she had persistent flexion contractures at the digits with little active flexion. Extension and flexion at the right wrist were

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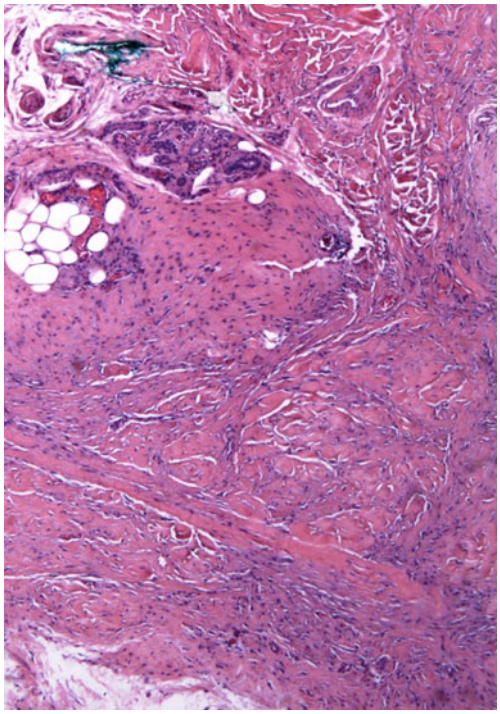

Fig. 1 Right hand skin biopsy demonstrating mild dermal fibrosis and marked thickening of deep dermal and subcutaneous connective tissue with hyalinization of collagen and fibrohistiocytic cells arranged interstitially and in short fascicles. A colloidal iron stain revealed a mild increase in interstitial mucin in the dermis and subcutis, which were consistent with a fibrohistiocytic process like DGA but not rheumatoid nodule or gout

45° and 30° and extension and flexion at the left wrist were 60° and 60°. She continued to have limited internal rotation at the left shoulder.

The diagnostic challenge of PFPAS arises from the heterogeneity of patient presentations, findings on skin biopsy, and radiography of the hands. There are, however, clinically salient features that are common in patients with PFPAS. Patients present with varying levels of arthralgia of the hands with or without involvement of other joints like the shoulders and knees. Examination of the hands reveals firm, painful nodules, digital swelling with flexion contractures, and palmar erythema. These findings are considered to be PFPAS only alongside demonstration of a neoplasm. In the case of ovarian cancer-related PFPAS, ovarian neoplasms have been found before and after the characteristic hand findings of PFPAS [5, 6].

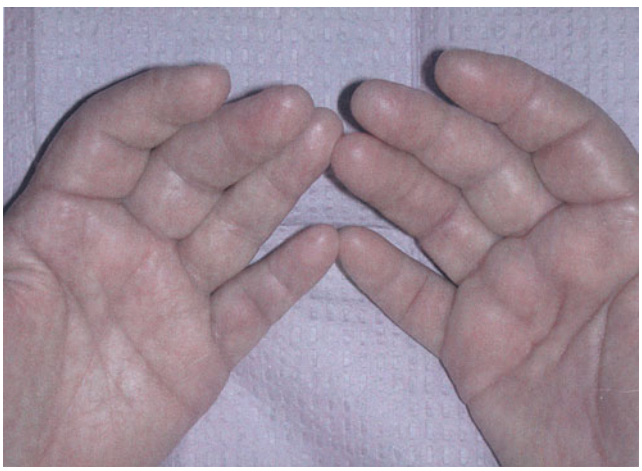

Fig. 2 Photograph of patient's hands at initial evaluation

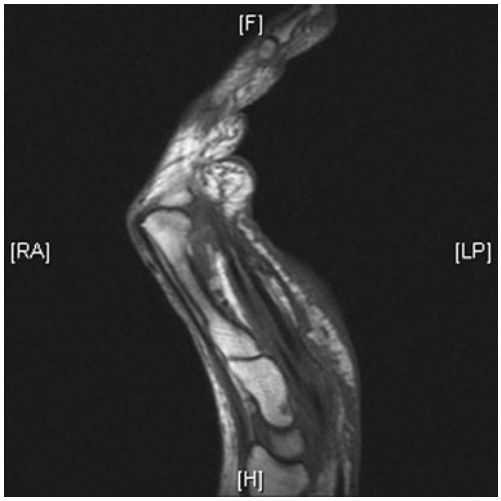

Fig. 3 Increased T2 prolongation confined to the deep fascial plane in the palm and the subcutaneous tissue along the dorsal wrist extending into the dorsal fingers without any abnormal signal noted within the muscle. These areas of T2 prolongation enhanced on the fat suppressed T1 sequence and are consistent with fasciitis. Radiography of the left hand was not done because the patient reported discomfort

The diagnostic value of skin biopsy is variable; it can demonstrate features of fibrosis and inflammatory infiltrate that can lead to inclusion of PFPAS along with DGA in the differential, but such findings are not specific for either disease. Reports have noted the presence of C3, IgM, and IgG in biopsied patients but without consistency or significant predictive value [10, 13]. Our case highlights the presence of increased mucin deposition in PFPAS, which is histopathologically indistinguishable from the mucin deposition found in DGA. The cumulative findings from skin biopsy may suggest an immunologic role in the causation of this paraneoplastic syndrome.

In the case we report, MRI of the hand demonstrated findings consistent with a fibrohistiocytic process, which would include both PFPAS and DGA; however, the use of MRI and other hand radiography is insufficient to lead to a diagnosis of PFPAS.

The role of testing for ANA and RF in the diagnosis of PFPAS is yet to be determined. In Bremer's 1950 report of what is thought to be the first case of PFPAS, the patient was ANA and RF negative [1]. Since then, there have been reports of patients negative for both, positive for either, and positive for both [5, 7]. The patient we report was negative for both, which raised clinical suspicion for a paraneoplastic syndrome rather than one of rheumatic etiology.

While the exact pathogenesis of PFPAS is unclear, Medger et al. suggested that fibroblast proliferative factor may play a critical role in the development of PFPAS, but were unable to establish a causative link between the two [6]. Recently, Yogarajah et al. reported a 74-year-old woman with ovarian cancer-related PFPAS who had significantly elevated levels of CTGF (139 U) when compared to the normal range established by using healthy controls (24.1±5.5 U; mean, ±SEM) [15].

The average age of the previously 15 reported cases of ovarian carcinoma-related PFPAS is 59.3 years (range, 25–75) while the patient we report is significantly older than this at 73. Inclusion of our patient raises the average age of ovarian cancer-related PFPAS patients to 60, which is also the median age for women with ovarian cancer [2]. Our patient had a 4-month duration between presenting symptoms of PFPAS and diagnosis of ovarian cancer, bringing the current time to diagnosis from initial PFPAS symptoms of 14 of the 16 cases to 6.9 months (data not available for two cases). Of the 16 cases, ten died at an average age of 13.3 months following diagnosis (range, 2–66 months), five underwent clinical remission of ovarian cancer, and one patient was lost to follow-up.

Patients successfully treated for ovarian carcinoma have variable improvement of presenting hand symptoms. Of the five patients that went into ovarian cancer remission, only one patient had unilateral resolution of flexion contractures despite bilateral presentation. Most patients, including those that did not undergo clinical remission, had variable but persistent flexion contractures. The patient we report has had the longest follow-up time (21 months) of any patient in remission for ovarian cancer and PFPAS. Her case demonstrates that clinical remission of underlying neoplasm in patients with PFPAS while improving pain in the hands does not predictably lead to significant improvement of flexion contractures of the digits even at long-term follow-up.

The role of surgery in the management of PFPAS contractures is unknown. Only one patient diagnosed with PFPAS has a history of hand surgery. She underwent exploratory surgery of the hands prior to her diagnosis of ovarian cancer and PFPAS. At surgery, she was found to have thickening of the skin, subcutaneous edema, and tenosynovitis of tendons with palmar fasciitis. She also underwent synovectomy of thumb, index, and long finger flexors with K-wire fixation of the DIP of the index finger [5]. Whether a patient like ours, who has persistent digital flexion contractures but clinical remission of underlying neoplasm, could have improved quality of life with release of flexion contractures remains unknown.

When taken together, all 16 reported cases of ovarian cancer-related PFPAS demonstrate important clinical features, including the presence of palmar fibrosis and inflammatory fasciitis with varying degrees of flexion contractures. The diagnosis can be challenging, but the decreased time to diagnosis of PFPAS as in our case demonstrate that patient's with underlying ovarian carcinoma can successfully undergo remission of their cancer and lead healthy lives, despite being limited by their digital flexion contractures.

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Conflicts of Interest None to disclose

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