Rethinking pityriasis rubra pilaris as a paraneoplastic syndrome: Two cases of pityriasis rubra pilaris with concomitant underlying malignancy

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INTRODUCTION

Pityriasis rubra pilaris (PRP) is a chronic papulosquamous dermatosis characterized by orange-salmon–colored plaques with scales, islands of sparing, palmoplantar keratoderma, and keratotic follicular papules.[1,2] There are 6 categories of PRP as follows: (1) classic adult type, (2) atypical adult type, (3) classic juvenile type, (4) circumscribed juvenile type, (5) atypical juvenile type, and (6) HIV-associated PRP.[1,2] Currently, PRP is not considered to be a paraneoplastic syndrome due to limited case numbers. We present 2 cases of paraneoplastic PRP, review the literature, and reevaluate the discussion of PRP as a paraneoplastic syndrome.

Abbreviation used:

PRP: pityriasis rubra pilaris

CASE REPORTS

Case 1

A 75-year-old woman presented with a 3-month history of a widespread, red, pruritic rash. Examination revealed flat-topped erythematous papules coalescing into plaques on the upper portion of the left extremity. Punch biopsy sample revealed subacute spongiotic dermatitis compatible with contact dermatitis or atopic dermatitis. She was maintained on topical steroids and started on prednisone. One year before, she had undergone a thoracic needle biopsy for pulmonary nodules, revealing a possible diagnosis of hypersensitivity pneumonitis. Serial imaging showed stable nodules throughout this time.

The rash spread to her palms, soles, trunk, and arms, with prominent hyperkeratotic follicular papules on the upper portion of extremities coalescing over the trunk (Fig 1). Various therapies trialed over 3 months included mycophenolate, acitretin, and topical and intramuscular steroids. A repeat biopsy sample demonstrated superficial perivascular dermatitis with patchy epidermal acanthosis, predominant CD3 T-cells, a singular hair follicle with adjacent hyperkeratosis, and a hint of retained parakeratotic nuclei (Fig 2). A second opinion from the University of Michigan suggested histopathology consistent with PRP, correlating to the clinical appearance and refractory treatment.

A month later, despite decreased plaque elevation, the rash worsened with increased confluence and onycholysis. She was started on methotrexate. The patient noted new onset muscle weakness, leg swelling, mood swings, joint pain, unintentional

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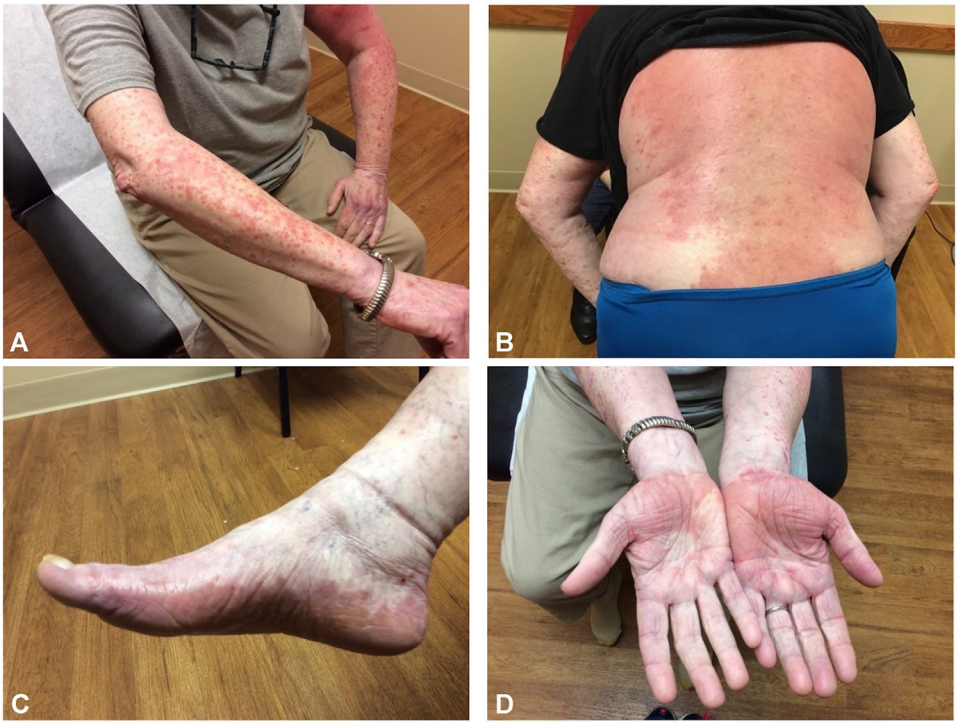

Fig 1. Case 1: Pityriasis rubra pilaris**. A,** Forearms, (**B**) back, (**C**) medial view of right foot, and (**D**) bilateral palmar surface of hands demonstrating orange-salmon–colored follicular papules with scales coalescing into plaques with islands of sparing and palmoplantar keratoderma.

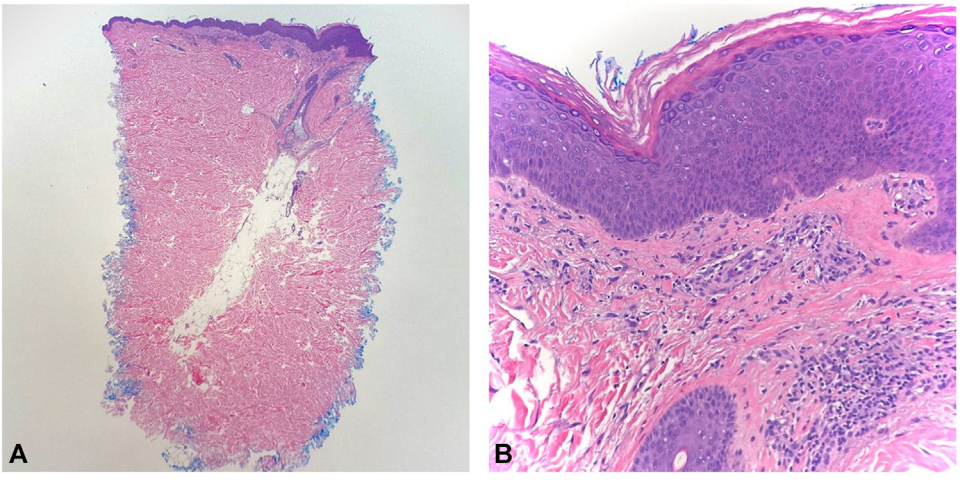

Fig. 2. Case 1: Histopathology. **A,** Irregular epidermal acanthosis is present to either side of a hair follicle. There is modest superficial dermal perivascular inflammation present, but no deeper inflammation. **B,** Compact hyperkeratosis is present adjacent to a follicular opening. A few retained parakeratotic nuclei are present. There is no significant basement membrane alteration or vacuolar interface damage. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A,** ×20; **B,** ×100.)

weight loss, and worsening shortness of breath, and was admitted to the hospital; CT-scan of the chest imaging revealed an increase in the size of her pulmonary nodules. She was diagnosed with stage IV non-small cell carcinoma with metastasis to the liver and bones. Significant improvement of the rash was noted 2 months following methotrexate therapy, but this was discontinued in anticipation of chemotherapy. Unfortunately, the patient succumbed to her disease shortly thereafter.

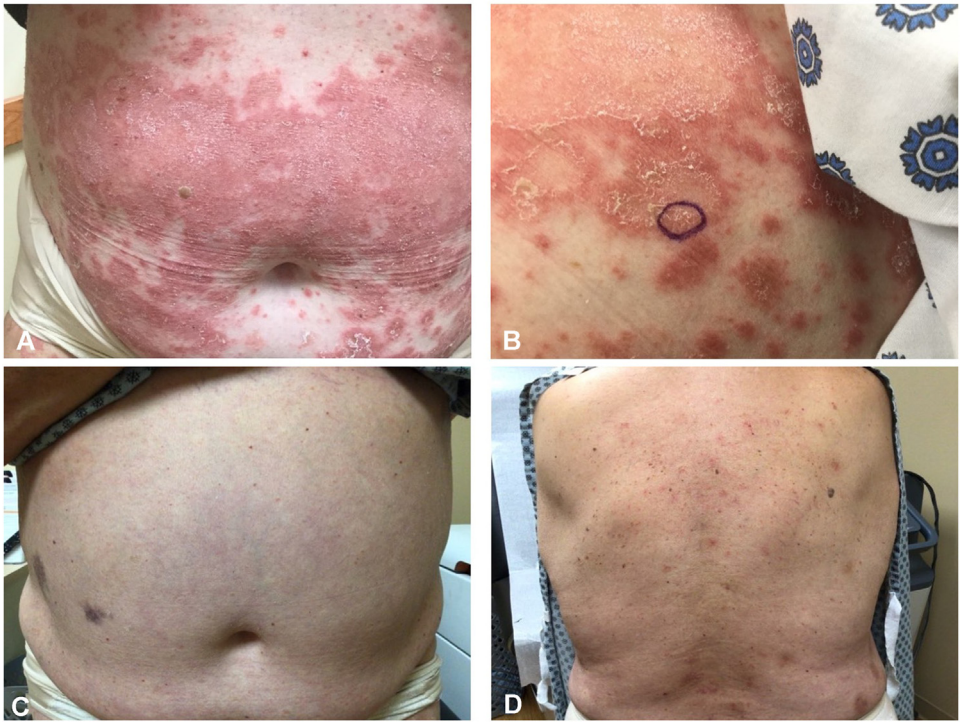

Fig. 3. Case 2: Pityriasis rubra pilaris**. A,** Abdomen demonstrating orange-salmon–colored follicular papules coalescing into plaques with scales and islands of sparing. **B,** The outlined punch biopsy site. The (**C**) abdomen and (**D**) back with total resolution of the rash 14 months after lumpectomy and excimer laser treatments.

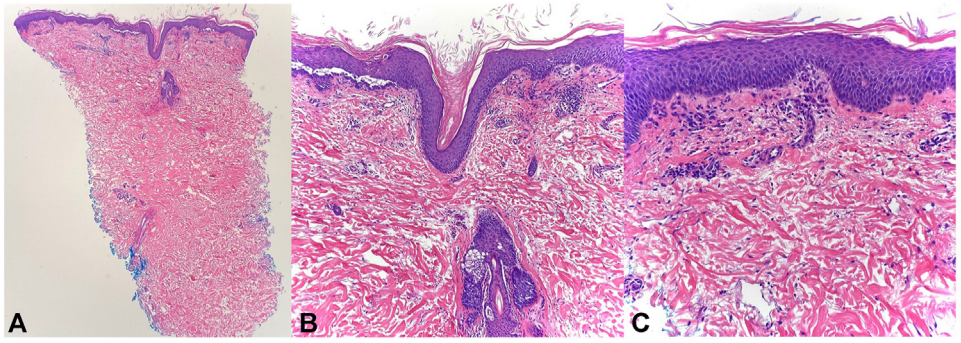

Fig. 4. Case 2: Histopathology. **A,** The epidermis is thickened across the biopsy. Zones of acantholysis are visible centrally and there is irregular hyperkeratosis. Sparse perivascular inflammation is limited to the superficial dermis. **B,** Hyperkeratosis is seen around a hair follicle and overlies a zone of acantholytic dyskeratosis. The follicle has early plugging. **C,** The irregular, somewhat psoriasiform, acanthosis is accompanied by alternating zones of parakeratosis and orthokeratosis. (**A, B,** and **C,** Hematoxylin-eosin stain; original magnifications: **A,** ×20; **B,** ×100; **C,** ×200.)

Case 2

A 67-year-old woman presented after 1 month of a flaking, pruritic, and erythematous rash located on the extremities and trunk. She was diagnosed with pityriasis rosea via biopsy analysis at an outside facility before her presentation. Examination revealed pink, oval patches with a collarette of scales.

Her condition worsened with increased burning, scales, and pruritus 1 month after treatment. The eruption developed into orange-salmon–colored plaques with scales and islands of sparing with outlying perifollicular hyperkeratotic papules (Fig 3). Biopsy result showed epidermal acanthosis, hyperkeratosis, acantholytic dyskeratosis, parakeratosis surrounding

Table I. Summary of demographics, associated malignancy, treatments, and outcomes

Author (publication year)	Sex	Age (y)	Diagnosed malignancy	All documented topical and systemic treatments	Rash outcome and treatment(s) which provided improvement/ resolution
Davis et al, (2022)	F	75	Stage IV metastatic non-small cell carcinoma	Acitretin, methotrexate, topical steroids	Improvement after 2 months of methotrexate. Patient died shortly after diagnosis.
Davis et al, (2022)	F	67	Infiltrating ductal carcinoma and DCIS of the left breast	Topical steroids, prednisone, methotrexate, excimer laser	Improvement with surgical resection of the malignancy and 18 treatments of excimer laser.
Vance[5] (2022)	M	49	Chronic lymphocytic leukemia	Acitretin, topical steroids	The rash persisted as the malignancy was not treated.
Lamberg[6] (2021)	M	72	Pulmonary adenocarcinoma	Acitretin	Complete resolution with acitretin, surgical resection, and chemoradiation. In the setting of the PRP and malignancy recurrence, the rash persisted as the malignancy was not treated.
Kwak[7] (2021)	F	72	Myelodysplastic syndrome	Topical steroids, topical urea	Near full resolution after 2 cycles of decitabine, topical steroids, and topical urea.
Fekete[1] (2019)	M	58	Prostate carcinoma	Acitretin, keratolytic emollients	Improved with acitretin and keratolytic emollients.
Bar-Ilan[8] (2017)	F	59	Metastatic cholangiocarcinoma	Acitretin, methotrexate	Resolution after 30 weeks of methotrexate.
Remedios[9] (2014)	M	83	Metastatic squamous cell carcinoma of unknown origin	Topical steroids	PRP resolved nearly completely after radiation and paclitaxel chemotherapy.
Vitiello[10] (2013)	F	89	Adenocarcinoma of the colon	Acitretin, topical steroids, emollients	Near complete resolution 1 month after tumor resection.
Garretson[11] (2011)	M	66	Primary pulmonary adenocarcinoma	Acitretin, topical steroids	Complete resolution 1 week after tumor resection.
Batinac[4] (2009)	M	46	Laryngeal carcinoma	Acitretin	Complete resolution after tumor resection.
Batchelor[12] (2005)	M	76	Renal cell carcinoma	Acitretin, methotrexate	Complete resolution 1 month after tumor resection.
Kurzydio[13] (2004)	F	61	Primary large cell bronchogenic carcinoma	Acitretin, methotrexate	Improvement within 1-2 months of starting radiotherapy; complete resolution within 6 months. Nails improved over 12 months.
Kloos[14] (2002)	F	75	Poorly differentiated metastatic adenocarcinoma of unknown origin	Acitretin, prednisolone	Erythroderma temporarily receded with acitretin and steroids. No resolution of PRP. Patient died from a paraneoplastic pulmonary embolism soon after diagnosis.
Huynh[15] (2002)	F	79	Merkel cell and squamous cell carcinomas	Etretinate	Rash persisted despite etretinate and radiotherapy. At final follow up, the patient had evidence of malignancy recurrence.
Sharma[16] (1997)	M	26	Hepatocellular carcinoma	Oral retinoid, topical vitamin A, emollients	Improvement in the rash after 2 months of doxorubicin therapy and topical vitamin A.
Tannenbaum[17] (1996)	M	73	Kaposi sarcoma, lentigo malignant melanoma, basal cell carcinoma	Isotretinoin, etretinate	Complete resolution of rash and Kaposi sarcoma after surgical excision of melanoma and basal cell carcinoma and 10 months of etretinate.

Continued

Table I. Cont'd

Author (publication year)	Sex	Age (y)	Diagnosed malignancy	All documented topical and systemic treatments	Rash outcome and treatment(s) which provided improvement/ resolution
Sánchez-Regaña[18] (1995)	M	42	Diffuse abdominal carcinomatosis with hepatic metastases	Topical steroids and emollients	Complete resolution after 6 weeks with topical steroids and emollients.
Reinhardt[19] (1983)	M	74	Acute undifferentiated leukemia	Topical steroids, prednisone, oral vitamin A	Improvement with topical steroids and prednisone. Patient died shortly afterwards due to associated complications during a secondary procedure and from the malignancy.

DCIS, ductal carcinoma in situ; *PRP*, Pityriasis rubra pilaris.

the follicle, and early follicular plugging, which was suggestive of PRP (Fig 4). The rash continued to progress despite trials of antihistamines, pramoxine hydrochloride lotion, acitretin, methotrexate, prednisone, and topical steroids.

Concurrently, routine mammography imaging with an ultrasound-guided biopsy sample revealed infiltrating ductal carcinoma and ductal carcinoma in situ of the left breast. The patient underwent a lumpectomy with an improvement of her rash several months later. She continued methotrexate and topical steroids due to rash persistence. Additionally, we evaluated the efficacy of a 308-nm excimer laser (XTRAC, Strata) as an adjunct therapy. Excimer laser was started at 150 mJ/cm^2 and gradually increased to 422 mJ/cm^2 over 18 treatments with dosage adjustments between 5% to 25%. Every treatment resulted in noticeable plaque improvement.

DISCUSSION

The Genetic and Rare Diseases Information Center estimates that there are between 300 to 3000 active cases of PRP in the United States.[3] It is unclear how many cases are associated with an underlying malignancy. Risk factors for PRP include family history, medications, immune dysfunction, infections, and environmental triggers.[1,4] Combining the cases of paraneoplastic PRP in the literature and our cases, 11 of 19 (58%) were men and 9 of 19 (42%) were women (Table I).[1,4-19] The average age of diagnosis is 65 years, ranging from 26 to 89 years. On the basis of the findings in the literature, PRP is associated with a wide variety of neoplasms, including, but not limited to malignancies affecting the pulmonary, gastrointestinal, and hematologic systems (Table I).[1,4-19]

Differential consideration of other paraneoplastic skin eruptions is important during clinical evaluation. Wong-type dermatomyositis is an exceedingly rare malignancy-associated dermatomyositis with significant clinical and histologic overlap with PRP,[20] and should be considered in case 1 due to the late onset of symptoms. Wong-type dermatomyositis presents with red-orange–colored papules coalescing into plaques and palmoplantar keratoderma, along with the hallmark features of dermatomyositis, including Gottron papules, heliotropic rash, and poikiloderma. Histopathology often shows follicular plugging, orthokeratotic invaginations, dermal mucin deposition, and vacuolar interface dermatitis. As the histopathology in case 1 is nonspecific, it would be prudent to consider Wong-type dermatomyositis on the basis of clinical symptoms. However, the lack of cutaneous dermatomyositis features on physical examination favors the diagnosis of PRP.[20]

The primary therapy for paraneoplastic PRP is the treatment of malignancy.[1,4,7-10,12,13,16-19] One of our cases demonstrated notable improvement of cutaneous symptoms after surgical resection of the breast tumor, although residual flares of PRP were noted afterward. Excimer laser therapy was used due to its documented advantages in clearing persistent psoriatic plaques with improvement after each treatment.[21]

A review of most cases associated with neoplasms has begun to explore whether the diagnosis of PRP could be attributed to a true paraneoplastic cutaneous syndrome.[8] Although rare, establishing PRP as a paraneoplastic process could aid clinicians in diagnosing underlying tumors when fulminant PRP exists.

The diagnosis of PRP is rare, particularly as a paraneoplastic process. Diagnosis is based on clinical presentation and histopathology. When PRP is recalcitrant to treatment, a paraneoplastic process should be considered with additional based on the basis of the patient's history and physical examination. Furthermore, we recommend that patients with adult onset PRP undergo age-appropriate cancer screenings and obtain thorough skin examinations. Management of paraneoplastic PRP includes treatment of the malignancy and topical or systemic therapies if needed. Due to the significant symptomatology and chronicity, it is vital to recognize the need for further research in this field and delineate specific management protocols.

Conflicts of interest

Dr Nazareth is a paid consultant for STRATA Skin Sciences, 2020-present. Dr Bogner and Authors Davis, Raine, and Swartzman have no conflicts of interest to declare.

REFERENCES

1. Fekete GL, Boda D, Căruntu C, Fekete L. Paraneoplastic pityriasis rubra pilaris in association with prostate carcinoma: a case report and literature review. *Exp Ther Med*. 2019;18:5052-5055. https://doi.org/10.3892/etm.2019.8169
2. Griffiths WA. Pityriasis rubra pilaris. *Clin Exp Dermatol*. 1980;5:105-112. https://doi.org/10.1111/j.1365-2230.1980.tb01676.x
3. U.S. Department of Health and Human Services. Pityriasis rubra pilaris - about the disease. Genetic and Rare Diseases Information Center. Accessed August 8, 2022. https://rarediseases.info.nih.gov/diseases/7401/pityriasis-rubra-pilaris
4. Batinac T, Kujundzić M, Peternel S, Cabrijan L, Troselj-Vukić B, Petranović D. Pityriasis rubra pilaris in association with laryngeal carcinoma. *Clin Exp Dermatol*. 2009;34:e917-e919. https://doi.org/10.1111/j.1365-2230.2009.03701.x
5. Vance P, Wyles S, Alavi A. Paraneoplastic pityriasis rubra pilaris preceding leukemia. *Adv Skin Wound Care*. 2022;35:1-4. https://doi.org/10.1097/01.ASW.0000826828.53117.8c
6. Lamberg O, Cao S, Sabater-Geib S, Lowe L, Elder J. A case of recurrent and paraneoplastic pityriasis rubra pilaris. *JAAD Case Rep*. 2021;12:74-76. https://doi.org/10.1016/j.jdcr.2021.04.025
7. Kwak RB, Hafeez F, Lian C, Nambudiri VE. Paraneoplastic pityriasis rubra pilaris heralding onset of new hematologic malignancy. *Am J Hematol*. 2021;96:272-274. https://doi.org/10.1002/ajh.25897
8. Bar-Ilan E, Gat A, Sprecher E, Zeeli T. Paraneoplastic pityriasis rubra pilaris: case report and literature review. *Clin Exp Dermatol*. 2017;42:54-57. https://doi.org/10.1111/ced.13009
9. Remedios IM, Jensen JD, Beckum K, McKay K, Kissel R. Paraneoplastic pityriasis rubra pilaris as the presenting manifestation of metastatic squamous cell carcinoma. *J Drugs Dermatol*. 2014;13:610-612.
10. Vitiello M, Miteva M, Romanelli P, et al. Pityriasis rubra pilaris: was it the first manifestation of colon cancer in a patient with pre-existing psoriasis? *J Am Acad Dermatol*. 2013;68:e43-e44. https://doi.org/10.1016/j.jaad.2010.05.013
11. Garretson CB, Machan ML, Krejci-Manwaring J, Aires D, Tonkovic-Capin V. Letter: Adenocarcinoma of the lung associated with pityriasis rubra pilaris. *Dermatol Online J*. 2011;17:14. https://doi.org/10.5070/D36VR5R017
12. Batchelor RJ, Yung A, Merchant W, Goodfield MJ. Pityriasis rubra pilaris as the initial presentation of renal cell carcinoma? *Clin Exp Dermatol*. 2005;30:442-443. https://doi.org/10.1111/j.1365-2230.2005.01781.x
13. Kurzydlo AM, Gillespie R. Paraneoplastic pityriasis rubra pilaris in association with bronchogenic carcinoma. *Australas J Dermatol*. 2004;45:130-132. https://doi.org/10.1111/j.1440-0960.2004.00061.x
14. Kloos C, Müller UA, Höffken K, et al. Paraneoplastic pityriasis rubra pilaris in metastatic adenocarcinoma without diagnosable primary. Article in German. *Dtsch Med Wochenschr*. 2002;127:437-440. https://doi.org/10.1055/s-2002-20423
15. Huynh NT, Hunt MJ, Cachia AR, Veness MJ. Merkel cell carcinoma and multiple cutaneous squamous cell carcinomas in a patient with pityriasis rubra pilaris. *Australas J Dermatol*. 2002;43:48-51. https://doi.org/10.1046/j.1440-0960.2002.00552.x
16. Sharma S, Weiss GR, Paulger B. Pityriasis rubra pilaris as an initial presentation of hepatocellular carcinoma. *Dermatology*. 1997;194:166-167. https://doi.org/10.1159/000246088
17. Tannenbaum CB, Billick RC, Srolovitz H. Multiple cutaneous malignancies in a patient with pityriasis rubra pilaris and focal acantholytic dyskeratosis. *J Am Acad Dermatol*. 1996;35:781-782. https://doi.org/10.1016/S0190-9622(96)90753-7
18. Sánchez-Regaña M, López-Gil F, Salleras M, Umbert P. Pityriasis rubra pilaris as the initial manifestation of internal neoplasia. *Clin Exp Dermatol*. 1995;20:436-438. https://doi.org/10.1111/j.1365-2230.1995.tb01368.x
19. Reinhardt LA, Rosen T. Pityriasis rubra pilaris as the initial manifestation of leukemia. *Cutis*. 1983;31:100-102.
20. Castillo RL, Femia AN. Covert clues: the non-hallmark cutaneous manifestations of dermatomyositis. *Ann Transl Med*. 2021;9:436. https://doi.org/10.21037/atm-20-5252
21. Ardeleanu V, Sabina Radaschin D, Tatu AL. Excimer laser for psoriasis treatment: a case report and short review. *Exp Ther Med*. 2020;20:52-55. https://doi.org/10.3892/etm.2020.8529