Pityriasis rubra pilaris heralding diagnosis of urothelial carcinoma: a case report

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Abstract

Pityriasis rubra pilaris is a papulosquamous inflammatory dermatosis that can be associated with HIV, autoimmunity, infections, certain medications, and neoplasms. Paraneoplastic pityriasis rubra pilaris has previously been reported in association with solid organ malignancies and once with leukemia. Herein, we present an elderly man with paraneoplastic pityriasis rubra pilaris, heralding the diagnosis of low-grade papillary urothelial carcinoma. Our patient's pityriasis rubra pilaris resolved after surgical resection of the tumor.

Keywords: erythroderma, papillary, paraneoplastic dermatoses, pityriasis rubra pilaris, PRP, urothelial carcinoma

Introduction

Pityriasis rubra pilaris (PRP) is an often idiopathic papulosquamous inflammatory dermatosis characterized by hyperkeratotic follicular papules coalescing in orange-red scaly plaques, distinctive islands of sparing, and palmoplantar keratoderma. Associations include HIV, autoimmunity, infections, neoplasias, and certain medications [1]. Paraneoplastic PRP has previously been reported 15 times in association with solid organ malignancies and once with leukemia [2-17]. Herein, we present a patient with paraneoplastic PRP that resolved after tumor resection of low-grade papillary urothelial carcinoma.

Case Synopsis

A 72-year-old man presented to dermatology for a 6-week history of an intensely itchy bright red rash which began on the trunk and proximal extremities, progressing distally. He denied any new medications. Physical examination revealed innumerable erythematous thin plaques with copious fine scale in a symmetric generalized distribution with islands of sparing on the trunk and extremities (**Figure 1A**, **B**). The face, scalp, and ears were involved; the palms were erythematous to subtly orange with fissures and mild hyperkeratosis (**Figure 1C**).

Two punch biopsies showed a combination of spongiotic inflammation and superimposed vacuolar interface dermatitis (**Figure 2**). Evidence for a lymphoproliferative process, such as lymphocyte atypia or lymphocyte exocytosis into a non-spongiotic epidermis, was not seen. Complete blood count, C-reactive protein, erythrocyte sedimentation rate, alanine aminotransferase, aspartate aminotransferase, serum IgE, creatinine, and glomerular filtration rate were normal. The patient was diagnosed with PRP due to clinicopathologic correlation; he was started on topical clobetasol for the body and tacrolimus for the face.

Three days later he presented to the primary care department with acute-onset of painless, grossly red urine, confirmed by urinalysis and culture as hematuria without bacterial growth. Abdominal CT showed a 2.5cm soft tissue mass of the urinary

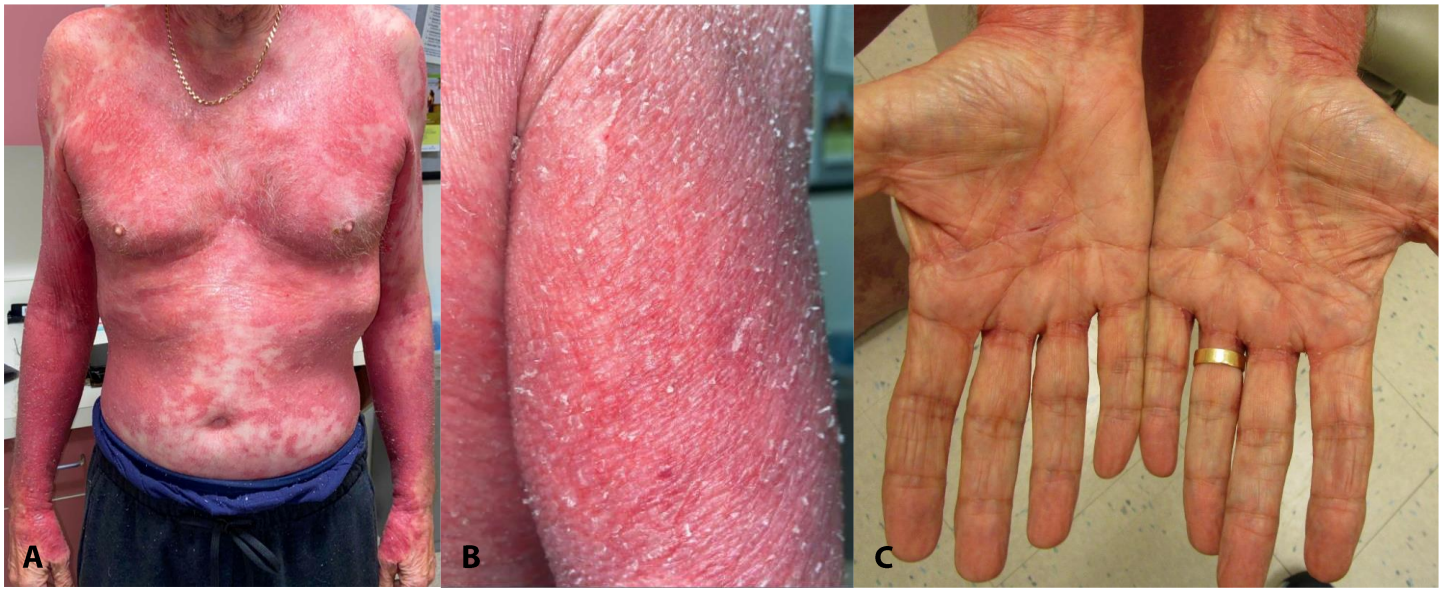

Figure 1. ***A)*** *Innumerable erythematous thin plaques with copious shedding scale in a symmetric generalized distribution with islands of sparing on the trunk and extremities.* ***B)*** *Involvement of the proximal posterior right arm.* ***C)*** *Orange hue, hyperkeratosis, and fissuring of the palms.*

bladder (**Figure 3**), which was resected and confirmed by pathology as a low-grade papillary urothelial carcinoma. Cutaneous PRP symptoms resolved within two weeks and did not recur over four months of follow-up.

Case Discussion

Pityriasis rubra pilaris is a rare papulosquamous inflammatory dermatosis. It can be categorized into six clinical subtypes according to Griffiths classification based on age, disease extent, prognosis, and other features. Type I (classic adult) is the most common form, accounting for over half of cases. It is characterized by acute onset beginning on the upper body with caudal spread over weeks-to-months; erythroderma and fine powdery scales of the face and scalp may be seen [1].

Paraneoplastic PRP is very rare: in one series of 168 PRP patients, only one had an associated malignancy

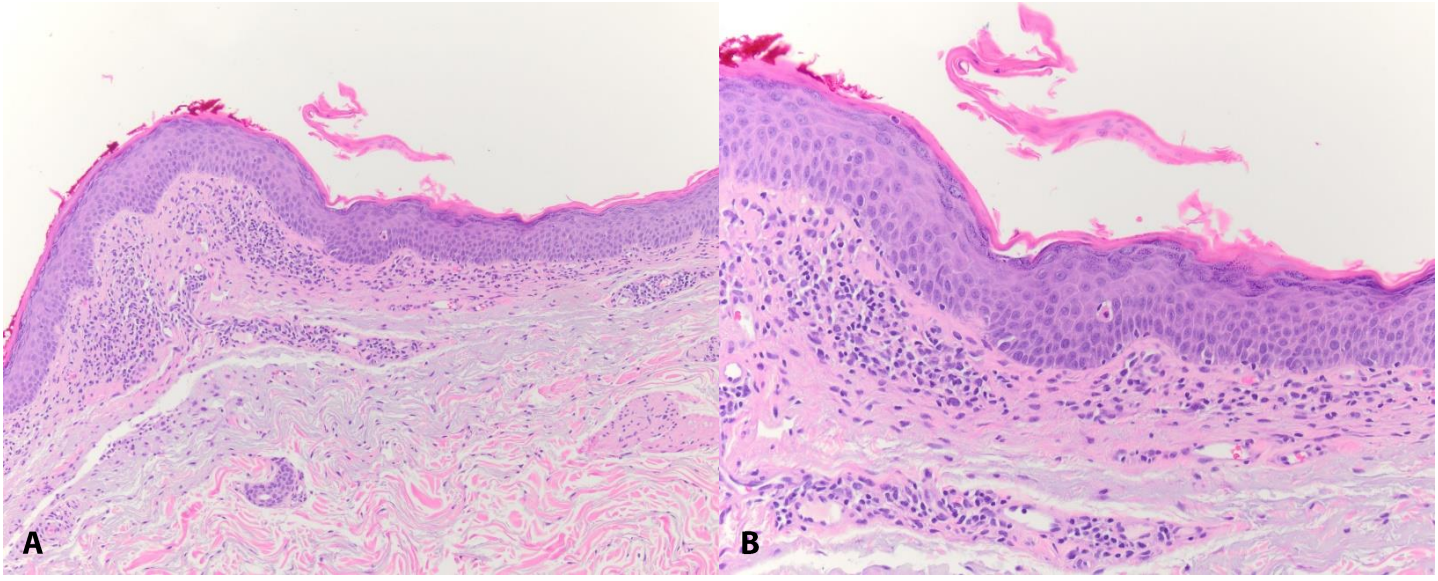

Figure 2. *Right posterior arm biopsy sections showed a combination of inflammatory patterns including spongiotic inflammation and superimposed vacuolar interface dermatitis. H&E,* ***A)*** *100×;* ***B)*** *200×.*

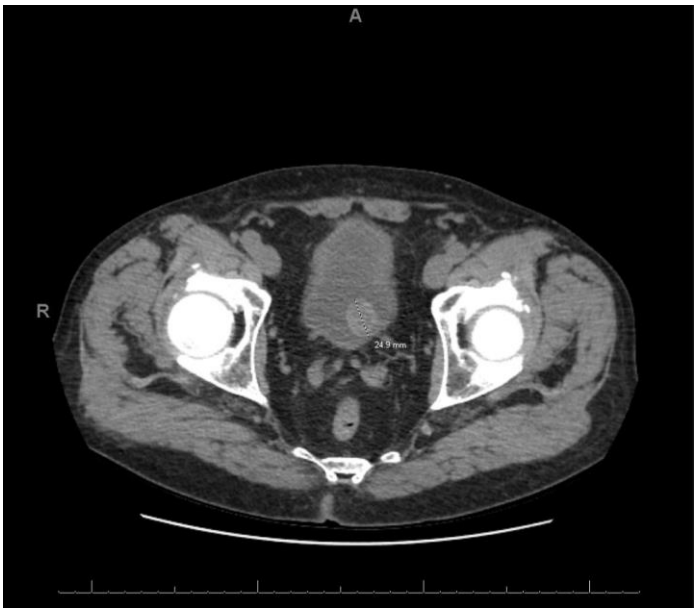

Figure 3. *Abdominal CT revealed a 2.5cm urinary bladder soft-tissue mass, confirmed after resection to be low-grade papillary urothelial carcinoma.*

[18]. Most cases of paraneoplastic PRP are consistent with Griffiths Type I [2-10,12-17], with one being Type II (atypical adult) due to atypical mucocutaneous findings [11]. Both sexes are equally affected by PRP [19], but 70.6% of paraneoplastic cases are male [2-17]. Type I idiopathic PRP has an excellent prognosis: over 80% experience remission, often spontaneously, within three years [20].

Histologically, PRP classically shows alternating vertical and horizontal orthokeratosis and parakeratosis (checkerboard pattern), hypergranulosis, irregular acanthosis (short and broad Rete ridges), thick suprapapillary plates, sparse superficial perivascular lymphohistiocytic infiltrate, and follicular plugging with parakeratosis at follicular orifice edges (shoulder parakeratosis), [1]. In practice these classic findings are not always present, and the histopathology may be nonspecific.

The differential diagnosis of erythrodermic PRP includes atopic dermatitis, psoriasis, seborrheic dermatitis, keratodermas, erythroderma progressiva symmetrica, erythrokeratoderma variabilis, follicular eczema, acquired ichthyosis, generalized hypersensitivity reactions, lichen planopilaris, and cutaneous T-cell lymphomas [1]; these can be distinguished by clinicohistologic elements.

The etiology and pathogenesis of PRP are unclear, with postulated mechanisms involving gain-of-function mutations in the caspase recruitment domain 14 (*CARD14*) gene [21] and disrupted keratinocyte differentiation caused by autoimmune interference with epidermal retinoid signaling pathways [22]. Paraneoplastic PRP may involve secretion of functional peptides or hormones from the malignancy, or immune cross reaction between normal host cells and initially-targeted tumor cells [7,23]. Epidermal cell kinetics show increased cell proliferation rates in PRP patients [24]. In the setting of actinic damage this may precipitate cutaneous malignancies [15], (skin was the cancer-affected organ in three reports of paraneoplastic PRP), [13-15].

Our patient was fortunate to have gross hematuria which prompted rapid identification of his malignancy; most paraneoplastic PRP patients undergo prolonged testing before cancer is found [2-17]. We cannot say what course his PRP may have taken if the tumor diagnosis had been delayed. The tendency of PRP to spontaneously remit calls into question whether it is truly paraneoplastic on occasion [1]. Malignancies in general are common and it is feasible that some PRP patients could have coincidental cancers diagnosed during their clinical course simply by receiving more in-depth evaluation than in a typical primary care checkup. Three of the five postulates of Curth are left unsatisfied by paraneoplastic PRP reports: no specific tumor is prevailingly co-occurring, no case-control studies show a statistically significant association with malignancies, and no shared gene loci explain a connection between PRP and cancers [25]. Still, compelling reports show PRP resolving after treatment of malignancies.

Our case and several reports of paraneoplastic PRP satisfy two postulates of Curth: concurrent onset and parallel clinical course with malignancy [25]. Of the 17 reported cases, 10 patients had resolution of PRP during, or soon after malignancy treatment. Three died before the malignancy could be managed; three articles did not describe effects of malignancy treatment on PRP. An additional report–did not describe any treatment of the malignancy. For the 5

cancers managed with surgical resection alone, resolution time of PRP ranged from one to four weeks. Resolution times of PRP were reported less consistently and described less precisely when malignancies were treated with radiotherapy or chemotherapy, perhaps because these patients were being managed intensively in oncology. Most paraneoplastic PRP patients had some improvement with topical corticosteroids, emollients, oral retinoids, or a combination (**Table 1**).

Conclusion

Although more research is needed to determine whether Type I PRP may occur as a truly paraneoplastic entity, our case supports age-appropriate cancer screening in these patients. Suspicion for an underlying malignancy should be higher for males and those with specific risk factors. These patients may require an in-depth work-up that includes urinalysis, and there should be a low threshold for CT scans of the chest, abdomen, and pelvis.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 1. *The 17 reported cases of paraneoplastic pityriasis rubra pilaris (PRP). In all cases, skin eruption preceded diagnosis of malignancy, and clinicopathologic findings were compatible with PRP. Twelve patients (70.6%) were male, and the average age was 68.4 years old (when excluding one outlier, who was 26 years old). The organs affected by malignancy included the lungs (4 cases), skin, liver (3 cases), bladder, blood, breast, colon, kidney, larynx, and prostate (1 case each).*

Malignancy organ	Malignancy type	Age, sex	Treatments & response	Outcome, follow-up	Ref
Bladder	Low-grade urothelial carcinoma	72, M	Topical clobetasol & tacrolimus: moderate improvement Tumor resection: PRP resolved within 2 weeks of surgery	No recurrence after 4 months of follow-up	This case
Blood	Acute stem cell leukemia	74, M	Topical steroids, high-dose vitamin A, & oral prednisone: moderate alleviation of PRP	Died of hepatitis & sepsis	[2]
Breast (right)	Poorly-differentiated adenocarcinoma with widespread metastases	75, F	Acitretin & prednisolone: PRP receded temporarily	Died of paraneoplastic pulmonary embolism	[3]
Colon (ascending & sigmoid)	Well-differentiated adenocarcinoma	89, F	Acitretin, hydrocortisone, emollients Right hemicolectomy: PRP resolved within 1 month	Long-term follow-up not described	[4]
Kidney (left)	Papillary renal cell carcinoma	76, M	Acitretin: slow temporary improvement x2 months Acitretin increased, cyclosporine added: temporary improvement Radical nephrectomy: PRP resolved within 1 month, acitretin & cyclosporine stopped	No recurrence after 1 year Died of bone metastases	[5]
Larynx (left vocal cord)	SCCis	46, M	Acitretin, emollients: slow partial improvement Cordectomy: rapid PRP resolution; acitretin decreased, then stopped	PRP resolved at 7.5 months No recurrence after 1 year	[6]
Liver (hepatic hilum)	Cholangioadenocarcinoma	59, F	1st episode: acitretin, emollients: temporary PRP remission x3 months 2nd episode: mtx & folic acid: PRP resolved after 7.5 months Chemotherapy started	No recurrence after 2 years of chemotherapy	[7]
Liver (right lobe)	Hepatocellular carcinoma	26, M	Vitamin A in Aquaphor ointment Intrahepatic doxorubicin: PRP significantly improved at 2 months	Long-term follow-up not described	[8]
Lung	Adenocarcinoma	66, M	Oral steroids, acitretin, emollients, & UVB: refractory Lobectomy: PRP resolved within 1 week	Long-term follow-up not described	[9]
Lung	Adenocarcinoma	69, M	Acitretin: PRP cleared for 4 years, then relapsed 1 year later, diagnosed with adenocarcinoma	Long-term follow-up not described	[10]

			Partial resection, radio & chemotherapy: effect on PRP not described		
Lung	Primary large cell bronchogenic carcinoma (right hilum)	61, F	Acitretin, then mtx: limited responses Radiotherapy: PRP much improved within 2 months & resolved by 6 months	No recurrence after 5 years	[11]
Prostate	Early stage prostate carcinoma Abdominal ultrasound & PSA	58, M	Acitretin, emollients, photoprotection, & keratolytics: much improved at 1 month	Long-term follow-up not described	[12]
Skin	BCC (face, anus, perianal)	73, M	Oral vitamin A, topical urea ointment: minimal response Excisions, radiotherapy, topical chemotherapy: effect on PRP not described	Long-term follow-up not described	[13]
Skin	KS (feet, extremities, penis), focally invasive LM (occipital scalp), & BCC (auricular)	73, M	Isotretinoin: worsened Etretinate: partial response after 1 month Surgical removal of LM & BCC, etretinate continued: PRP resolved at 8 months	No recurrence after 2 years	[14]
Skin	MCC of left arm with multiple metastases, multiple SCCs	79, F	Etretinate: no improvement Palliative dose of fractionated radiotherapy: effect on PRP not described	Long-term outcome of PRP not described	[15]
Unknown primary	Undifferentiated metastatic SCC in lung & paratracheal	83, M	Topical triamcinolone & clobetasol (several months): refractory Radiation & paclitaxel: PRP resolved without topicals	Long-term follow-up not described	[16]
Unknown primary	Undifferentiated metastases in liver	42, M	Topical steroids: marked improvement of PRP within 6 weeks	Died of diffuse abdominal carcinomatosis	[17]

BCC, basal cell carcinoma; KS, Kaposi sarcoma; LM, lentigo maligna; MCC, Merkel cell carcinoma; Ref, reference; SCC(is), squamous cell carcinoma (in-situ).