

Clinical Communications

Telangiectasia macularis eruptiva perstans or highly vascularized urticaria pigmentosa?

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Clinical Implication

- Telangiectasia macularis eruptiva perstans is a rare form of mastocytosis in the skin characterized by flat dermal telangiectatic macules. Our analysis indicates it is being overdiagnosed in patients when a more accurate diagnosis would be urticaria pigmentosa.

TO THE EDITOR:

Telangiectasia macularis eruptiva perstans (TMPEP) was first described by Weber and Hellenschmied¹ in 1930 based on a single case report of a 60-year-old woman with slightly raised, reddish telangiectatic macules of general distribution, although it was noted that individual telangiectasia could not be visualized.

This original report did not include histologic findings.¹ Weber² subsequently evaluated a second case of a patient with urticaria pigmentosa (UP) that closely resembled the index patient with TMPEP and, based on these 2 cases, concluded that TMPEP was a pigmentless variant of UP that presents primarily in adulthood.^{1,2} In subsequent reports, mast cell infiltration was noted histologically in both UP and TMPEP; however, the gross appearance and perivascular distribution of mast cells and association with dilated vessels was said to distinguish TMPEP from UP. Thus, TMPEP now is usually referred to as a rare form of cutaneous mastocytosis in which the skin has flat telangiectatic macules in a generalized distribution.³⁻⁶ The relative lack of information on the consequences of a diagnosis of TMPEP has led to confusion in clinical management. Based on these observations, we conducted a survey of patients who were evaluated for mastocytosis and who carried a diagnosis of TMPEP to determine how the diagnosis of TMPEP was being applied and if there were any consistent features to report.

By using the National Institutes of Health Biomedical Translational Research Information System, we conducted a retrospective chart review of 299 subjects who were referred to the National Institute of Allergy and Infectious Diseases, with institutional review board approved mastocytosis protocols. All the subjects

TABLE I. Demographic and clinical characteristics of the patients referred with TMPEP

Patient no.	Age (y)	Sex	Referral diagnosis	TMPEP diagnosis	Skin biopsy characteristics					NIH diagnosis
					Telangiectasia	Infiltrate	Increased mast cells	Perivascular	Dilated vessels	
1	34	F	TMPEP	Bx	N	MC, MN	Y	Y	N	UP, ISM
2	45	F	TMPEP	Both	Y	MC, E	Y	Y	—	UP
3	28	F	TMPEP	Bx	—	MC, E	—	Y	—	UP, ISM
4	51	M	TMPEP	Bx	—	MC, E	N	Y	—	UP
5	42	F	TMPEP	Bx	—	MC	Y	Y	Y	UP
6	62	F	TMPEP/UP	Clinical	NR	NR	NR	NR	NR	UP, ISM
7	43	F	UP	Bx*	NR	NR	NR	NR	NR	UP, ISM
8	22	F	CM	Bx	NR	NR	NR	NR	NR	UP, ISM
9	48	F	CM	Bx	Y	MC, E	Y	Y	Y	UP, ISM
10	20	F	CM	Bx	—	MC, MN	Y	Y	—	UP
11	46	F	SM	Both	—	MC	—	Y	—	UP, ISM
12	22	F	SM	Bx	NR	NR	NR	NR	NR	UP, ISM
13	29	F	SM	Bx	NR	NR	NR	NR	NR	UP, ISM
14	28	F	SM	Bx	—	MC	—	—	—	UP, ISM
15	28	M	SM	Bx	Y	MC	Y	—	—	UP, ISM
16	40	F	SM	Both	Y	MC, MN	Y	Y	NR	UP, ISM
17	43	M	SM	Bx	—	MC, MN	Y	Y	NR	UP, ISM
18	32	F	SM	Bx	—	MC, L	Y	Y	Y	UP, ISM
19	42	M	SM	Bx	NR	NR	NR	NR	NR	UP, ISM
20	20	M	SM	Bx	Y	MC, E, L	Y	Y	—	UP
21	48	M	SM	Both	Y	MC, E, L	—	Y	Y	UP
22	2	M	M	Bx	—	L	Y	Y	—	No M
23	58	M	M	Both	—	MC, E, L	Y	Y	—	UP, ISM
24	54	F	None	Both	Y	MC, MN	Y	Y	—	UP

—, No comment; *Both*, by both skin biopsy and clinical observation; *Bx*, skin biopsy; *Clinical*, clinical observation on physical examination; *CM*, cutaneous mastocytosis; *E*, eosinophils; *ISM*, indolent systemic mastocytosis; *L*, lymphocytic; *M*, mastocytosis; *MC*, mast cells; *MN*, mononuclear; *N*, no; *NIH*, National Institutes of Health; *NR*, not reported; *SM*, systemic mastocytosis; *Y*, yes.

*UP seen on skin biopsy specimen.

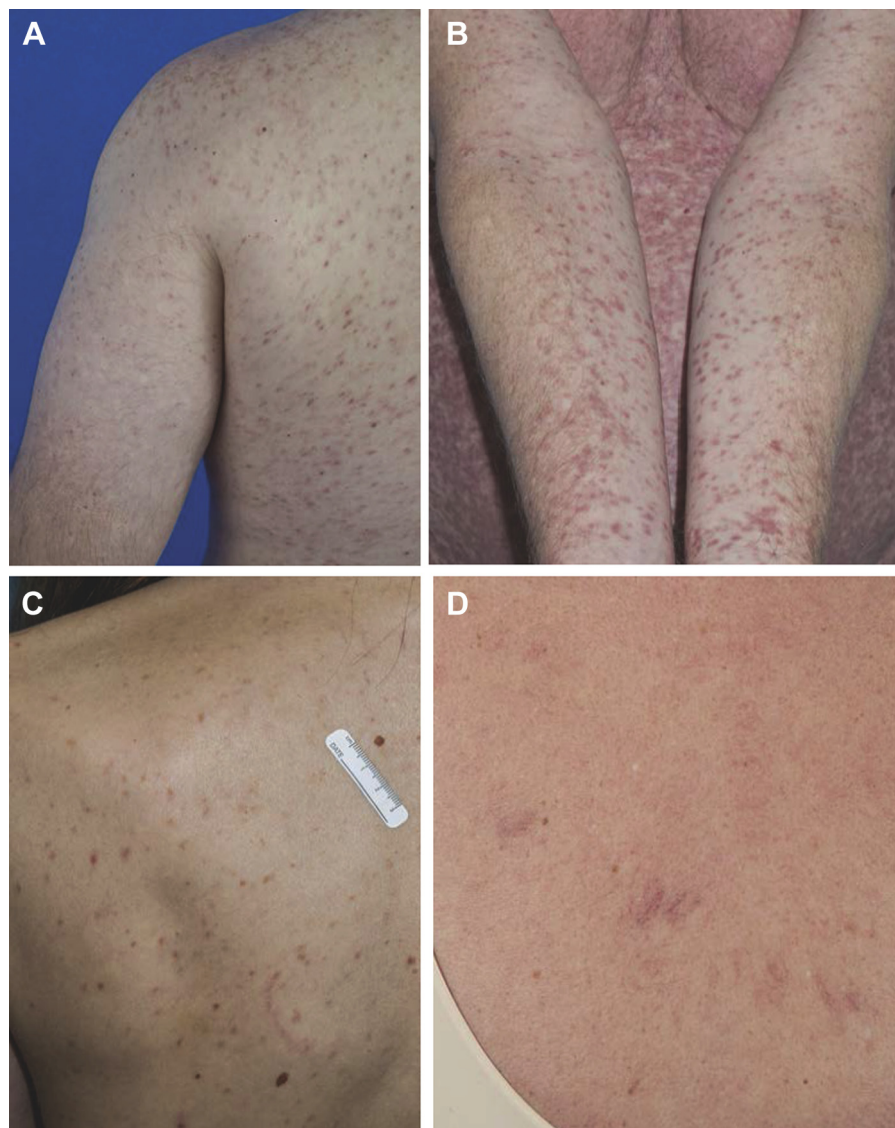


FIGURE 1. TMEP or UP? Three pictures of patients referred with a diagnosis of TMEP but have cutaneous lesions consistent with UP. A, A 48-year-old man diagnosed with UP and no evidence of systemic mastocytosis. B, A 58-year-old man with UP and indolent systemic mastocytosis. C, A 42-year-old woman with UP and no evidence of systemic mastocytosis. D, A 52-year-old woman with TMEP, and an elevated tryptase level of 36.0 ng/mL. Her bone marrow biopsy shows increased mast cells with >25% appearing spindle-shaped but no mast cell aggregates. Macular telangiectasia are present.

signed informed consent. We identified 24 subjects whose records included the diagnosis of TMEP (Table 1). We then analyzed clinical and laboratory data, including skin and bone marrow biopsy specimens, as relevant to the diagnosis of mastocytosis in the skin, including TMEP and UP, and systemic mastocytosis.

Of the 24 subjects identified with a diagnosis of TMEP, 8 were men (33%) and 16 were women (67%). The median age at initial visit to the National Institutes of Health was 41 years (interquartile range, 28.0–47.5 years). Six subjects had “TMEP” specified in the referring diagnosis, whereas the remaining 18 subjects were referred for “cutaneous or systemic mastocytosis,” with TMEP reported by skin biopsy or clinical observation.

TMEP generally is described with onset in adulthood, distribution on the chest and extremities, and association with a negative Darier sign.^{4–7} In contrast, UP is often found in a

generalized and random distribution, has the highest concentration of lesions on the trunk, is associated with a positive Darier sign, and is commonly reported in both children and adults.^{4,5} In our TMEP group, the rash was most frequently distributed on the chest and the extremities, and resembled in appearance that of classic UP (Figure 1, A to C). TMEP is shown in Figure 1, D.

The Darier sign was positive in 6 of 15 patients (40%). Of the 24 patients identified with TMEP, 9 reported a history of anaphylaxis (24%) and 4 had syncope (17%). All the patients (100%) reported cutaneous manifestations, such as urticaria, pruritus, or flushing. Eighteen patients reported gastrointestinal symptoms (75%), such as abdominal pain, cramping, nausea, vomiting, or diarrhea. Cardiovascular symptoms, such as tachycardia or palpitations, were reported with 9 patients (38%). Two patients had palpable hepatosplenomegaly (8%). Dual-energy x-ray

absorptiometry had been performed at outside facilities on 12 patients and yielded 5 with osteopenia (42%) and 1 with osteoporosis (8%), based on the World Health Organization definitions.⁸ Thus, the majority of patients identified with TMEP had extracutaneous findings.

All 24 patients underwent a laboratory evaluation. The white blood cell counts, hemoglobin, platelets, prothrombin time, partial thromboplastin time, C-reactive protein, and serum B₁₂ levels were normal. The median serum tryptase and serum IgE levels in the TMEP group were 24.2 ng/mL (interquartile range, 14.7–48.6 ng/mL) and 8.85 IU/mL (interquartile range, 5.0–17.1 IU/mL), respectively. Serum tryptase and IgE levels were comparable among the patients ultimately diagnosed with mastocytosis in the skin (all UP) and those with indolent systemic mastocytosis (tryptase level, 22.6 vs 32.4 ng/mL; $P = .18$; IgE level, 8.7 vs 6.8 IU/mL; $P = .67$, respectively).

TMEP is said to be histopathologically identified by the presence of mast cell infiltrates around venules, with dermal-dilated capillaries of the superficial venous plexus.⁴ Upon review of 18 TMEP skin biopsy specimen reports, all noted mast cell infiltration, of which 89% were distributed perivascularly. Dilated vessels were noted in 4 patients (22%). The presence of telangiectasias is an important defining characteristic of TMEP and a distinguishing feature from UP, yet few of our patients had evidence of telangiectasias on observation (Table 1). Thus, in this group of patients, a definite diagnosis of TMEP was not substantiated by the presence of characteristic skin lesions and distinctive histopathology.

Twenty-one patients underwent bone marrow biopsy for evaluation of possible systemic mastocytosis. Sixteen patients (67%) met the World Health Organization diagnostic criteria for indolent systemic mastocytosis, 7 (29%) had mastocytosis limited to the skin (mastocytosis in the skin, all UP), and 1 patient (4%) did not meet criteria for mastocytosis in the skin or systemic disease.⁹ Although the diagnosis of TMEP was not clinically substantiated in any of these patients, the majority of our cohort was ultimately diagnosed with indolent systemic mastocytosis. The high correlation in our cohort with systemic mastocytosis (typically found in adults with UP) indicates that it is more appropriate to reclassify TMEP as a highly vascularized form of UP. For symptomatic relief, both patients with TMEP and those with UP may benefit from treatment with oral antihistamines, montelukast, and/or psoralen with UV A.^{10,11}

Although both cutaneous forms of mastocytosis can be limited to the skin, bone marrow evaluation should be pursued if clinical history and findings indicate systemic involvement. Prognosis depends on whether the patient meets World Health Organization criteria for systemic mastocytosis. Based on our findings,

the diagnosis of TMEP appears to be overused, has little clinical utility, and is confusing to physicians and patients. Highly vascularized UP more accurately describes these pigmented macular lesions that localize with observable telangiectasia. We suggest that, in the majority of instances in which the diagnosis of TMEP is used, the lesions are more accurately described as UP.

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This work was supported by the Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health (ZIA AI000249-32).

Conflicts of interest: C. Prussin is on the American Board of Allergy and Immunology. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication May 27, 2014; revised June 27, 2014; accepted for publication July 1, 2014.

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2213-2198

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<http://dx.doi.org/10.1016/j.jaip.2014.07.002>

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