Cutaneous Mastocytosis as a Rare Differential Diagnosis for Unilateral Chronic Facial Pain and Erythema: A Case Report

Matthias Troeltzsch, MD, DMD
Resident
Department of Oral and Maxillofacial Surgery
Ludwig-Maximilians-University
Munich, Germany

Ronald Berndt, MD
Pathologist
Institute of Pathology
Ansbach, Germany

Timothy Woodlock, MD
Medical Oncologist
Department of Medicine
Unity Health System
and Department of Medicine
University of Rochester School of Medicine and Dentistry
Rochester, New York, USA

Karl Messlinger, MD, PhD
Associate Professor
Department of Physiology and Pathophysiology
University of Erlangen-Nuremberg
Erlangen, Germany

Markus Troeltzsch, MD, DMD
Resident
Department of Oral and Maxillofacial Surgery
University of Göttingen
Göttingen, Germany

Correspondence to:
Dr Matthias Troeltzsch
Department of Oral and Maxillofacial Surgery
Ludwig-Maximilians-University
Lindwurmstrasse 2a
80337 Munich, Germany
Fax: +49 89 5160 2917
Email: matthias_troeltzsch@hotmail.com

Cutaneous mastocytosis (CM) has been associated with urticaria, itching, and pain of the affected regions. Although the occurrence of CM in the facial skin is rare, it may be a cause of chronic facial pain, and pain characteristics may mistakenly be interpreted as trigeminal nerve pathology. However, the dermatological appearance of the different variants of cutaneous mastocytosis is distinct and should be considered as an uncommon differential diagnosis in an orofacial pain diagnostic algorithm. This article presents a case of telangiectasia macularis eruptiva perstans, a rare type of cutaneous mastocytosis, as the underlying cause of chronic facial pain, erythema, and swelling. J OROFAC PAIN 2013;27:367–371. doi: 10.11607/jop.1164

Key words: chronic facial pain, cutaneous mastocytosis, erythema, ketofifen, telangiectasia

Mastocytosis is defined as local or systemic aggregation and proliferation of clonal mast cells.[1,2] Local and systemic types of mastocytosis can be differentiated.[1,3]

Local forms of mastocytosis usually present on the skin as macular, papular, or telangiectatic lesions or urticaria.[1,4] The affected areas may exhibit intermittent or permanent itching, flushing, edema, pain, or blistering.[4,5] Cutaneous mastocytosis (CM) comprises several diseases: urticaria pigmentosa, mastocytoma, diffuse cutaneous mastocytosis, and telangiectasia macularis eruptiva perstans (TMEP).[4,6] The trunk and limbs are CM predilection sites[6,7] and involvement of the facial skin by CM is extremely uncommon.[6,8,9] The course of the disease until final diagnosis is long.[2,5,8–11] The long-term prognosis of CM is favorable,[6] although to date no curative treatment approach has been scientifically proven.[5,6]

Systemic mastocytosis involves the presence of extracutaneous clonal mast cell manifestations, such as organ or skeletal infiltrates.[1,2,12] Systemic mastocytosis may exhibit an aggressive course and requires close monitoring.[4,12] An association between mastocytosis and myeloid disorders has been reported.[2,4,11]

The clinical symptoms of mastocytosis are caused by mast cell mediator release, which has the potential to induce anaphylactic reactions.[1,11,12] Symptomatic treatment options include pharmacologic mast cell stabilization, antihistaminic drugs, anti-inflammatory drugs, and immunomodulators.[4,6,12] In severe cases, laser therapy and photodynamic therapy after topical or systemic administration of psoralen (psoralen and ultraviolet A light [UVA]; PUVA) therapy have been applied successfully.[13–15]

In the following case report, an extremely rare variant of CM is described as the underlying cause of chronic facial pain. This is only the third report of its kind in the literature.[8,9]

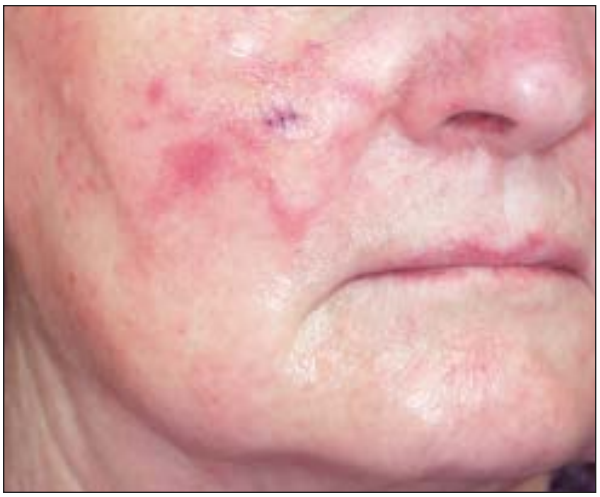


Fig 1 Clinical appearance of telangiectasia macularis eruptiva perstans in the facial skin. Sutures are still in place at the biopsy site.

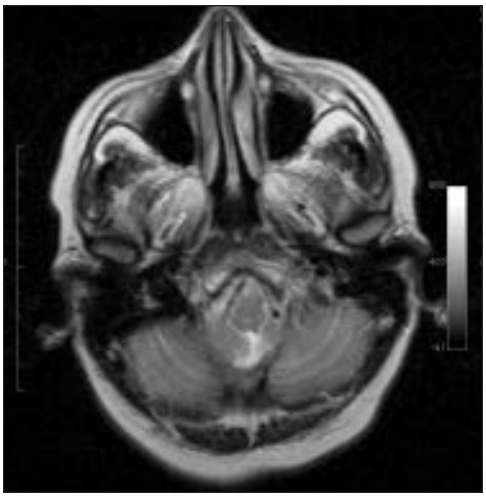


Fig 2 T2-weighted axial magnet resonance imaging (MRI) with contrast agent showing the level of the affected skin area without enhancement of contrast agent and without signs of acute maxillary sinusitis.

Case Report

A 69-year-old woman was referred to the oral and maxillofacial surgery department by her family physician for evaluation of chronic recurrent, unilateral, right-sided facial pain with recurrent edema and erythema for 4 years (Fig 1). She described the pain as intermittent, pricking, and pruritic, lasting for several minutes with an intensity of up to 7 on a visual analog scale (VAS). The referring family physician suspected odontogenic pathology as the reason for the patient's medical condition. She reported that heat aggravated her symptoms. Her medical history included hypertension, surgically treated colorectal cancer, replacement of the left knee joint by an endoprosthesis due to osteoarthritis, lumbar spondylarthrosis, and carpal tunnel syndrome. The patient was allergic to brown plasters. She denied abuse of cosmetics or facial ointments. Her daily prescriptions were 160 mg valsartan and 25 mg hydrochlorothiazide once daily for each and 500 mg metamizole three times daily. Prior examination by otorhinolaryngology specialists had ruled out the initial diagnosis of acute exacerbation of maxillary sinusitis. At a previous consultation with a neurologist, central nervous pathology was ruled out. Magnetic resonance imaging (MRI) with contrast agent rendered 5 months prior to initial presentation to the department showed signs of mild chronic sinusitis but no facial soft tissue abnormalities (Fig 2). The pain had been classified as atypical trigeminal neuralgia, and treatment with 200 mg carbamazepine twice daily was initiated. This approach had not improved the symptoms and was discontinued. Endoscopic paranasal surgery was also ineffective.

At the initial presentation, the patient was oriented in time and space; there were no signs of dizziness, impaired vision, or restricted ocular movement. Crawling sensations of the limbs or trunk were not noted, which was interpreted as the absence of paresthesia.[16] The patient exhibited no signs of allodynia, hyperalgesia, or numbness, as assessed with the sharp and blunt end of a dental probe, a painter's brush, and a cotton swab.[16] The character of the pain ruled out trigeminal neuralgia, and the absence of somatosensory dysfunction excluded continuous neuropathic pain.[16] However, the pain was limited to areas innervated by the maxillary branch of the trigeminal nerve. She denied episodes of facial paralysis and angioedema of the upper lip. The right facial side was exclusively affected.

Clinical examination revealed erythematous macules that were localized in the infraorbital portion of the right cheek (Fig 1) and scattered telangiectasias (Fig 3). A palpable induration existed above the right nasolabial fold. No other signs of pain upon palpation for each of the other trigeminal sensory branches were noted. Facial nerve function was normal. Darier's sign (urtication upon rubbing) was negative (Fig 4). No tenderness upon palpation of the masticatory and cervical muscles was observed. There were no temporomandibular joint sounds. No dental or oral pathologies were found by intraoral examination and radiographs.

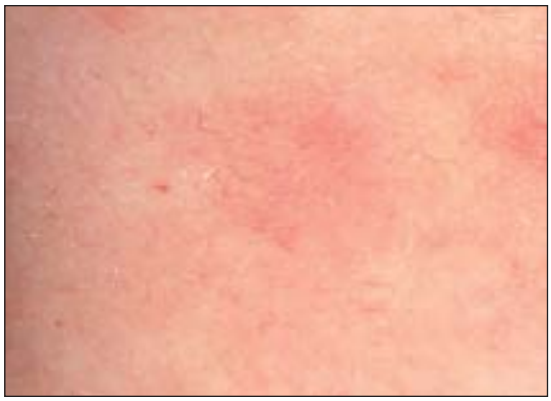


Fig 3 Scattered telangiectasias present within and around the erythematous macules.

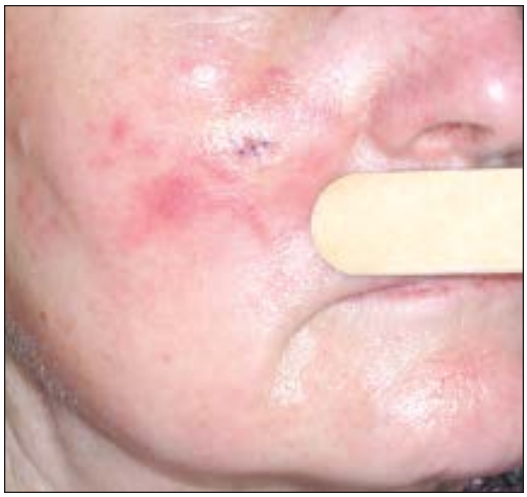


Fig 4 Negative Darier's sign of the affected skin area.

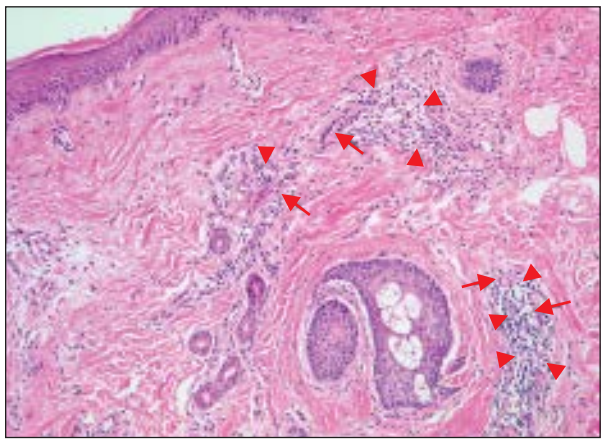
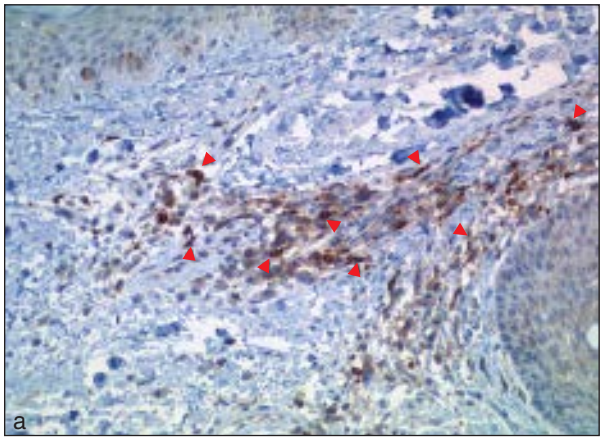
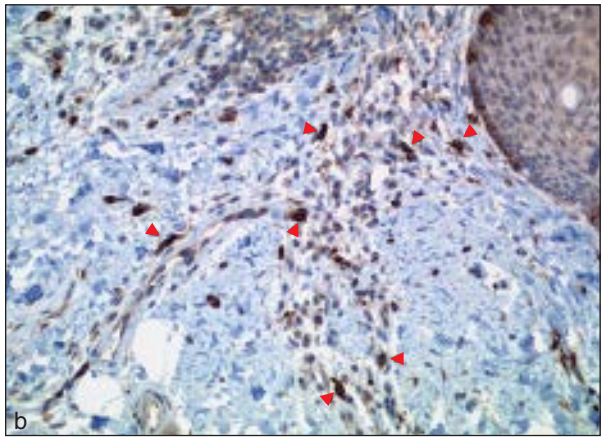


Fig 5 *(right)* Hematoxylin-eosin staining showing infiltrate of lymphoyctes and atypical mast cells *(arrowheads)* around partly ectatic blood vessels *(arrows)*.

Figs 6a and 6b *(below)* Immunohistochemical staining for *(a)* cluster of differentiation (CD) 25 and *(b)* CD 117 demonstrates the presence of atypical mast cells *(arrowheads)* in the perivascular infiltrates.





The patient history and clinical examination suggested that a localized skin-related pathology was the causative agent of pain, so a skin biopsy was performed. For pathologic examination, hematoxylin-eosin staining (Fig 5), Giemsa staining, as well as immunohistochemical staining of the specimen for cluster of differentiation (CD) 25, CD 117, and tryptase were performed (Figs 6a and 6b). Histopathologic examination revealed local accumulation of CD 25/CD 117-positive mast cells with

atypical, spindle cell–like morphology. Furthermore, ectatic blood vessels, lymphocytic infiltrates, and an adjacent edema were present (Figs 5 and 6). The surrounding skin displayed signs of chronic sun injury in the form of actinic elastosis. These findings led to the final diagnosis of telangiectasia eruptiva perstans (TMEP), a rare variant of CM. The patient was referred to a dermatology department and received treatment with 1 mg ketofifen twice daily. The patient's symptoms resolved over 3 months.

Discussion

The present case report presents CM in the form of TMEP as a rare differential diagnosis for chronic facial pain, erythema, and edema. Facial manifestation of mastocytosis is rare.[17,18] However, the clinical appearance of mastocytosis is diverse.[18–24] It can present as brown or red macular lesions (urticaria pigmentosa),[18,23] nodules (mastocytoma),[18,23] flushing skin areas,[17,20] or erythroderma.[19] There are reports about morphological facial changes caused by mastocytosis.[22,24]

Symptoms of CM include macular and papular rashes, flushing, edema, and blistering.[1,4,25] It may be difficult to differentiate these lesions from clinical differential diagnoses.[3] CM can mimic allergic reactions, viral or bacterial infections, bruises, café-au-lait spots, or nevi.[3,19,20,26] The patient history and additional clinical findings, such as rhinitis, may help the examiner to detect allergic reactions.[20] However, the systemic signs of anaphylaxis, such as hypotension, abdominal pain, diarrhea, nausea, and flushing, can also appear in mastocytosis patients.[19,20] CM can induce blistering and pain similar to herpetic or bacterial infections.[4,26] CM blisters are not usually limited to dermatomes and can appear throughout the entire integument.[26] Clinical findings, such as fever and laboratory testing for C-reactive protein, white blood cell count, or procalcitonin, may help to identify cases of bacterial infection.[19,20] Furthermore, Darier's sign is usually positive in CM lesions and absent in herpetic blisters or erysipelas.[3] In summary, skin biopsies and laboratory findings (serum tryptase, urine n-methylhistamine) may be the decisive steps in the confirmation of mastoytosis.[3,19,20]

TMEP is a rare variant of CM that typically involves lesions on the skin of the limbs and the trunk.[5] Literature searches revealed only two previously published cases of facial TMEP.[8,9] While both urticaria pigmentosa and TMEP may cause erythematous macules on the skin,[4,10] the presence of telangiectasias is the defining characteristic of TMEP.[3,6,7] Furthermore, Darier's sign is negative in TMEP, whereas it is positive in all other CM variants.[1,4] Telangiectasias can result from several conditions, including rosacea, Rendu-Osler syndrome, nevus flammeus, basal cell carcinoma, or mycosis fungoides.[8,27] Recurrent pain and swelling are not regularly associated with these diagnoses.[8] However, only pathohistologic examination of biopsy specimens can provide definitive diagnosis.[4] In both previously described cases of unilateral facial TMEP as well as the present case, the patients described chronic itching and episodic urticaria.[8,9] CM involvement regularly causes local pruritus, pain, erythema, and swelling.[1,10,12]

Aside from cutaneous problems, neurologic pathology can be associated with mastocytosis.[28,29] Mastocytosis patients are prone to develop different forms of primary headache and back pain.[28,29] An increased incidence of multiple sclerosis has been reported for mastocytosis patients.[28] Therefore, neurologic evaluation is vital in the diagnostic algorithm for mastocytosis.[28,29] As the patient's facial pain sensations in the presented case were mistakenly interpreted as trigeminal nerve pathology, the primary referral led the patient to a neurologist.

Given the unremarkable neurologic examination, the absence of somatosensory disturbances, the unsuccessful prior treatment with anticonvulsants, and the presence of visible clinical signs, a neuropathic origin of pain was eliminated from the diagnosis.[30] Previous diagnostic measures involving radiographs and MRI without significant pathologic findings, clinical examination by specialists, and failed therapeutic approaches did not include a biopsy of the affected skin sites as a diagnostic step. The symptoms of swelling, erythema, and pain sensations resembled allergic reactions[1,4] and may have involved the release in the skin of mast-cell mediators.[1] Therefore, mastocytosis was among the differential diagnoses and was confirmed histologically.

The histologic image of TMEP is characterized by dilated vessels, an inflammatory infiltrate, and an accumulation of atypical mast cells with spindle-like morphology and metachromatic granules.[5,10] Special immunohistochemical staining (CD 25/CD 117) can demonstrate the presence of atypical, clonal mast cells pertinent to the diagnosis.[4] Although the etiology of TMEP is unclear,[4] it can be speculated that chronic sunlight exposure might play a role, as adjacent skin may show signs of concomitant sun injury as in the present case.

As mentioned above, the treatment of CM is symptomatic and involves mast-cell stabilization, antihistaminic drugs, immunomodulators and anti-inflammatory drugs.[4,6] Laser therapy and PUVA

therapy may relieve the symptoms in treatment resistant cases.[1,4,13] In the present case, treatment with ketofifen, a mast-cell stabilizer and H1-antagonist,[31] alleviated the symptoms after 3 months. Although systemic involvement by mastocytosis in TMEP cases is rare,[4] it has been associated with hematologic neoplasms.[2,11] Therefore, thorough examination of CM patients with respect to visceral organs and the skeletal and central nervous system is reasonable.[4] No evidence for systemic mastocytosis in the present patient was observed.

Conclusions

TMEP as the cause of chronic facial pain, swelling, and erythema is rare. However, if the clinical image of mastocytosis is well defined, its diagnosis can be confirmed histologically and simple treatment can provide relief. Therefore, a skin biopsy should be considered in the diagnostic algorithm of chronic facial pain in combination with the typical clinical symptoms of CM.

References

1. Rama TA, Corte-Real I, Gomes PS, Escribano L, Fernandes MH. Mastocytosis: Oral implications of a rare disease. J Oral Pathol Med 2011;40:441–450.
2. Bachmeyer C, Guillemette J, Blum L, et al. Telangiectasia macularis eruptiva perstans and multiple myeloma. J Am Acad Dermatol 2000;43:972–974.
3. Horny HP, Sotlar K, Valent P, Hartmann K. Mastocytosis: A disease of the hematopoietic stem cell. Dtsch Arztebl Int 2008;105:686–692.
4. Valent P, Horny HP, Escribano L, et al. Diagnostic criteria and classification of mastocytosis: A consensus proposal. Leuk Res 2001;25:603–625.
5. Gibbs NF, Friedlander SF, Harpster EF. Telangiectasia macularis eruptiva perstans. Pediatr Dermatol 2000;17:194–197.
6. Cengizlier R, Hucumenoglu S, Ozen A, Tulin Sayli R. Treatment of telangiectasia macularis eruptiva perstans with montelukast. Allergol Immunopathol (Madr) 2009;37:334–336.
7. Betti R, Vergani R, Tolomio E, Martino P, Crosti C. Guess what! Telangiectasia macularis eruptiva perstans involving the upper arms in an adult male. Eur J Dermatol 2000; 10: 563–564.
8. Gonzalez-Castro U, Luelmo-Aguilar J, Castells-Rodellas A. Unilateral facial telangiectasia macularis eruptiva perstans. Int J Dermatol 1993;32:123–124.
9. Fried SZ, Lynfield YL. Unilateral facial telangiectasia macularis eruptiva perstans. J Am Acad Dermatol 1987;16: 250–252.
10. Sarkany RP, Monk BE, Handfield-Jones SE. Telangiectasia macularis eruptiva perstans: A case report and review of the literature. Clin Exp Dermatol 1998;23:38–39.
11. Martin LK, Romanelli P, Ahn YS, Kirsner RS. Telangiectasia macularis eruptiva perstans with an associated myeloproliferative disorder. Int J Dermatol 2004;43:922–924.
12. Castling B, Smith AT, Myers B. Involvement of the jaw bones in systemic mastocytosis. Br J Oral Maxillofac Surg 2006; 44:87–88.
13. Rishpon A, Matz H, Gat A, Brenner S. Telangiectasia macularis eruptiva perstans: Unusual presentation and treatment. Skinmed 2006;5:300–302.
14. Tebbe B, Stavropoulos PG, Krasagakis K, Orfanos CE. Cutaneous mastocytosis in adults. Evaluation of 14 patients with respect to systemic disease manifestations. Dermatology 1998;197:101–108.
15. Ellis DL. Treatment of telangiectasia macularis eruptiva perstans with the 585-nm flashlamp-pumped dye laser. Dermatol Surg 1996;22:33–37.
16. Baron R, Binder A, Wasner G. Neuropathic pain: Diagnosis, pathophysiological mechanisms, and treatment. Lancet Neurol 2010;9:807–819.
17. Horan RF, Austen KF. Systemic mastocytosis: Retrospective review of a decade's clinical experience at the Brigham and Women's Hospital. J Invest Dermatol 1991;96:5S–13S; discussion 14S, 60S–65S.
18. Akoglu G, Erkin G, Cakir B, et al. Cutaneous mastocytosis: Demographic aspects and clinical features of 55 patients. J Eur Acad Dermatol Venereol 2006;20:969–973.
19. Hoeger PH, Harper JI. Neonatal erythroderma: Differential diagnosis and management of the "red baby". Arch Dis Child 1998;79:186–191.
20. Izikson L, English JC, 3rd, Zirwas MJ. The flushing patient: Differential diagnosis, workup, and treatment. J Am Acad Dermatol 2006;55:193–208.
21. Bulat V, Mihic LL, Situm M, Buljan M, Blajic I, Pusic J. Most common clinical presentations of cutaneous mastocytosis. Acta Clin Croat 2009;48:59–64.
22. Chodkiewicz HM, Cohen PR. Systemic mastocytosis-associated leonine facies and eyebrow loss. South Med J 2011; 104:236–238.
23. Barker A, Stewart RW. Case report of mastocytosis in an adult. South Med J 2009;102:91–93.
24. Mutreja D, Purohit A, Singh PK, Pati HP. A 60-year-old lady with leonine facies: A rare diagnosis. Indian J Pathol Microbiol 2012;55:566–568.
25. Horny HP, Sotlar K, Valent P. Mastocytosis: State of the art. Pathobiology 2007;74:121–132.
26. Hannaford R, Rogers M. Presentation of cutaneous mastocytosis in 173 children. Australas J Dermatol 2001;42:15–21.
27. Bloom B, Marchbein S, Fischer M, Kamino H, Patel R, Latkowski JA. Poikilodermatous mycosis fungoides. Dermatol Online J 2012;18:4.
28. Smith JH, Butterfield JH, Pardanani A, DeLuca GC, Cutrer FM. Neurologic symptoms and diagnosis in adults with mast cell disease. Clin Neurol Neurosurg 2011;113:570–574.
29. Smith JH, Butterfield JH, Cutrer FM. Primary headache syndromes in systemic mastocytosis. Cephalalgia 2011; 31: 1522–1531.
30. Dworkin RH, Backonja M, Rowbotham MC, et al. Advances in neuropathic pain: Diagnosis, mechanisms, and treatment recommendations. Arch Neurol 2003;60:1524–1534.
31. Gruber R, Vassilaki I, Zelger B. Concomitant juvenile xanthogranuloma and cutaneous mastocytosis in a 3-year-old Swedish girl: Case report and review of the literature. Int J Dermatol 2011;50:611–614.