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·防治实践·

Sweet综合征口腔黏膜表现1例报道及文献回顾

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【摘要】 目的 探讨Sweet综合征的口腔黏膜病损表现，为临床早发现并正确诊断该病提供参考。**方法** 报道1例60岁女性Sweet综合征患者的口腔黏膜病损表现，并结合相关文献对Sweet综合征进行分析。**结果** 患者双下肢皮肤红斑伴口腔黏膜破溃疼痛3 d，患者皮损症状较轻，但口腔黏膜多发性大面积糜烂，疼痛明显，故首诊于口腔科。患者发病过程中伴有发烧，体温38.5 ℃；实验室检查示C反应蛋白升高（35.2 mg/L），血沉加快（77.00 mm/h）；患者两侧膝盖及下肢可见散在分布红色斑块，轻度压痛，皮损组织病理学检查示：真皮全层见散在不成熟中性粒细胞聚集灶浸润。根据患者临床体征和实验室检查，皮损组织病理结果的镜下符合Sweet综合征的表现，诊断为Sweet综合征。给予患者1 mL复方倍他米松注射液肌肉注射仅1次；患者对糖皮质激素治疗效果反应良好；口腔采用复方氯己定溶液含漱，病损黏膜处重组牛碱性成纤维细胞生长因子溶液外用，3次/d，疗程为1周；用药4 d后复诊，体温恢复正常，口腔病损明显减轻；2周后复诊，小腿及膝盖处红斑几乎全部消退，口腔黏膜病损基本消失；半年后随访，结果显示皮损未复发；2年后随访，病情稳定，病损未见复发。回顾相关文献表明，Sweet综合征是一种少见的病因不明的炎性反应性皮病，临床上可分为3种类型：特发型、肿瘤相关型以及药物诱导型，男女患病比为1∶4，典型临床表现为急性出现的疼痛性红色斑块或结节，病损多位于四肢，常伴发热，外周血中性粒细胞数目增多，血沉加快，C反应蛋白阳性。系统应用糖皮质激素是本病最重要的治疗方法，大多数患者可在短期内改善皮损，但可能会存在潜在感染或停药后复发的情况。部分Sweet综合征患者可伴有口腔病损，但目前有关Sweet综合征在口腔黏膜表现的病例报道却很少，使得临床容易误诊。**结论** 口腔黏膜病损可能为Sweet综合征的皮肤外表现，应综合考虑患者的全身情况，尽快完善皮肤活检以明确诊断，以免延误病情。

【关键词】 Sweet综合征；急性发热性嗜中性皮病；口腔糜烂；红斑；口腔黏膜；C反应蛋白；糖皮质激素；鉴别诊断

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Oral mucosal manifestations of Sweet's syndrome: a case report and literature review

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【Abstract】 Objective To explore the oral mucosal manifestations of Sweet's syndrome and provide a reference for its early detection and correct diagnosis. **Methods** The oral mucosal manifestations of a 60-year-old female patient with Sweet's syndrome are described in detail, followed by a discussion of the related literature. **Results** The patient had skin erythema of both lower extremities, which was accompanied by oral mucosal ulceration and pain for 3 days. The patient presented with mild cutaneous lesions and diffuse large-scale erosion in the oral mucosa with obvious pain. During the onset of the disease, the patient was accompanied by fever with a temperature of 38.5°C. After visiting the Department of Stomatology, laboratory tests showed an increase in C-reactive protein (35.2 mg/L) and an accelerated

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erythrocyte sedimentation rate (77.00 mm/h). Scattered red plaques and mild tenderness were observed in the knees and lower limbs. Histopathological examination of the skin lesions revealed scattered infiltration of immature neutrophils across the entire dermis. The patient responded well to glucocorticoid therapy. According to the clinical signs and laboratory examination, combined with the lesion histopathological results, a diagnosis of Sweet's syndrome was given. The patient was administered 1 mL compound Betamethasone injection only once intramuscularly. In the meantime, the patient was asked to gargle with compound chlorhexidine solution and topically apply recombinant bovine basic fibroblast growth factor solution to the damaged mucosa three times a day for 1 week. After 4 days of medication, the patient's body temperature had returned to normal and the oral lesions were significantly reduced. After 2 weeks, the erythema in the leg and knee had almost all subsided, and the oral mucosal lesions had disappeared. The patient was followed up 6 months after treatment, with no recurrence of skin lesions. After 2 years of follow-up, the disease was stable with no recurrence. A review of the relevant literature shows that Sweet's syndrome is a rare inflammatory reactive dermatosis with unknown etiology, which can be divided into three clinical types: specific, tumor-related, and drug-induced. The male/female prevalence ratio is 1:4. The salient clinical manifestations are abrupt onset of painful erythematous plaques or nodules most commonly involving the extremities, often accompanied by pyrexia, elevated neutrophil count, elevation of the erythrocyte sedimentation rate, and positive C-reactive protein. The use of glucocorticoids is the most common treatment for this disease, and most patients see a rapid improvement in skin lesions; however, some may experience infection or recurrence after withdrawal. Some patients with Sweet's syndrome are accompanied by oral lesions, but cases of oral mucosal damage have been rarely reported, and this condition is easily misdiagnosed. **Conclusion**　Oral mucosal lesions may be extraterritorial manifestations of Sweet's syndrome, and the patient's systemic condition should be comprehensively considered. Skin biopsy should be completed as soon as possible to make a clear diagnosis, so as not to delay the disease.

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【Key words】 Sweet syndrome; acute febrile neutrophilic dermatosis; oral erosion; erythema; oral mucosa; C-reactive protein; glucocorticoid; differential diagnosis

【Competing interests】 The authors declare no competing interests.

Sweet综合征(急性发热性嗜中性皮病)是一种较少见的反应性炎性皮病,最近研究报道该病男女患病比为1∶4,好发年龄为60岁,与种族无关[1-2],皮损多位于四肢及头颈部,也可累及眼、神经系统及内脏器官,由于发病率较低,临床表现多样,使得临床医生容易误诊[3-4]。本文报告了一例Sweet综合征的口腔黏膜病损表现,并结合相关文献进行了探讨,为临床及早发现并正确诊断该病提供借鉴。

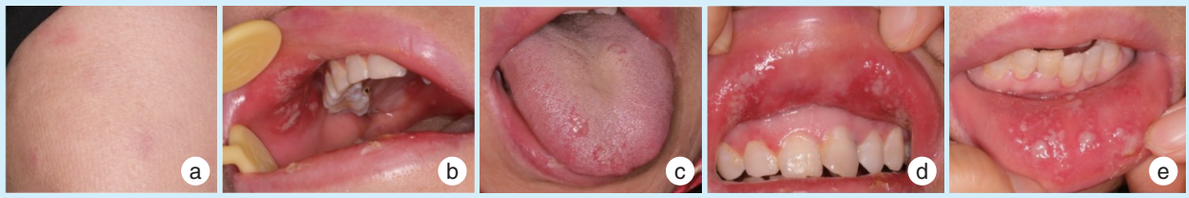
1　临床资料

1.1　病史

患者,女,60岁。主诉:双下肢皮肤红斑伴口腔黏膜破溃疼痛3 d。现病史:患者7 d前无明显诱因于双下肢出现红斑,未予治疗;3 d前口腔黏膜多处破溃,疼痛明显,伴发热,体温最高达38.5 ℃,患者自行服用四季抗病毒胶囊及退烧药(具体不详),症状未见缓解;于2021年10月5日就诊于青岛市市立医院口腔科。既往史:过敏性鼻炎,否认药物过敏史,否认全身系统性疾病及传染病史,个人史及家族史无特殊。

1.2　临床检查及实验室检查

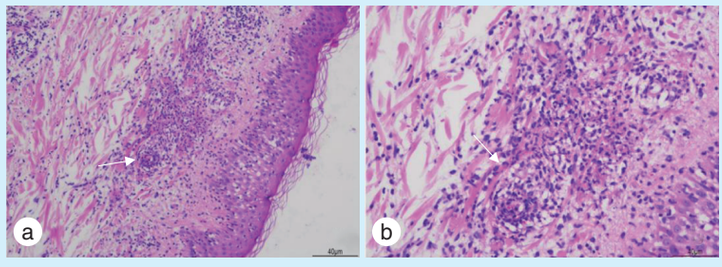
两侧膝盖及下肢可见散在分布红色斑块,大小不等,皮损边缘略隆起于皮面,呈结节状,轻度压痛,未见水疱及破溃面;两侧颊黏膜近前庭沟处、上下唇黏膜内侧以及舌尖可见多处糜烂,表面覆盖黄白色假膜,周围黏膜充血水肿,疼痛明显(图1),颈部未扪及明显肿大淋巴结。实验室检查:单核细胞计数0.75 × 10^9/L,单核细胞百分率14.60%,超敏C反应蛋白35.2 mg/L,红细胞沉降率77.00 mm/h,白细胞、红细胞及血红蛋白均正常,生化常规、风湿指标等未见异常。请本院皮肤科会诊,行皮肤病理活检,皮损组织病理示:(下肢)皮肤表皮基底细胞灶状液化变性,局部棘细胞间水肿,表皮淋巴细胞浸润,真皮全层见散在不成熟中性粒细胞聚集灶,并可见核碎屑及小血管壁纤维素性坏死(图2)。



a: scattered erythema of both knees and lower extremities could be seen with varying size, and the edges of lesions were slightly raised on the skin surface; b-e: multiple erosions were observed on both sides of the buccal mucosa near the vestibular groove, the medial mucosa of the upper and lower lip, and the tip of the tongue. The surface was covered with a yellowish white false membrane, and the surrounding mucosa showed hyperemia and edema

Figure 1　A 60-year-old female with Sweet's syndrome presented with lesions of the lower extremity and mucosal lesions at the initial visit

图1　60岁女性Sweet综合征患者初诊时下肢皮损表现及口腔黏膜病损表现



a&b: epidermal squamous epithelium with hyperkeratosis, local interspinous edema, focal liquefaction degeneration of basal cells, epidermal lymphocyte infiltration, scattered aggregation of immature neutrophils throughout the dermis, nuclear debris, and fibrinous necrosis of small blood vessel walls were observed (white arrow). (HE, a: ×100, b: ×200)

Figure 2　Histopathological images of lower extremity lesions of a 60-year-old female with Sweet's syndrome

图2　60岁女性Sweet综合征患者下肢皮损组织病理像

1.3　诊断

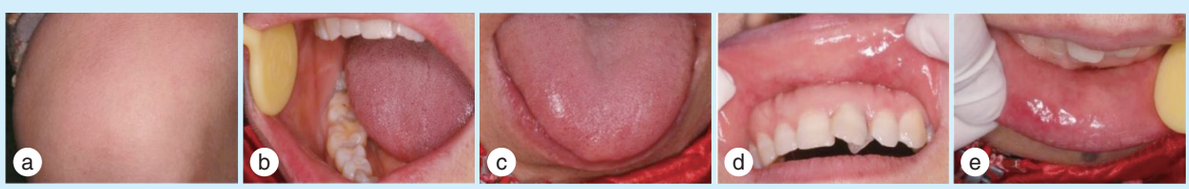
根据患者临床体征、实验室检查及组织病理结果，诊断：Sweet综合征。

1.4　治疗

给予患者1 mL复方倍他米松注射液肌肉注射仅1次；口腔采用复方氯己定溶液含漱，病损黏膜处重组牛碱性成纤维细胞生长因子溶液外用，3次/d，疗程为1周。用药4 d后复诊，体温正常，口腔病损明显减轻。2周后复诊，小腿及膝盖处红斑几乎全部消退，口腔黏膜病损基本消失（图3）。半年后随访，皮损未见复发。2年后随访，病情稳定，病损未复发。

2　讨　论

Sweet综合征是一种少见的可伴有全身症状的皮肤病，是由外界化学或物理刺激因素、宿主免疫失调、遗传易感性共同作用的结果[3]。Sweet综合征可分为3种类型：特发型、肿瘤相关型以及药物



a: after 2 weeks of treatment, the erythema on both knees and lower extremities almost completely subsided, the color became lighter, and the scope narrowed; b-e: the lesions of the buccal mucosa near the vestibular groove, the medial mucosa of the upper and lower lip, and the tip of the tongue basically disappeared, the erosion healed, and the oral mucosa tended to be normal

Figure 3　Manifestations of lower extremity lesions and oral mucosal lesions in a 60-year-old female with Sweet's syndrome after 2 weeks of treatment

图3　60岁女性Sweet综合征患者治疗2周后下肢皮损及口腔黏膜病损表现

诱导型[5]。其中大多数Sweet综合征是特发型的，该型通常与上呼吸道或胃肠道感染、自身免疫性疾病、以及怀孕等相关，易反复发作[6-7]；部分Sweet综合征可能与恶性肿瘤相关[8-10]，尤其是血液系统的肿瘤，推测Sweet综合征可能是肿瘤的临床表现，也可能是肿瘤复发的标志之一，回顾性研究发现恶性肿瘤患者的血红蛋白和血小板水平相对较低[7, 11]；此外，药物可以诱发Sweet综合征[12]，主要表现为药物摄入与临床表现之间的时间依赖关系，且停药后病损可消退[13-14]。本研究患者排除了肿瘤和药物诱导相关的因素，患者在发病前有过敏性鼻炎病史，因而考虑本病例属于特发型，过敏性鼻炎可能为诱发因素。

Sweet综合征的典型临床表现为急性出现的疼痛性红色斑块或结节，常伴发热，血清炎症标志物（如红细胞沉降率、C反应蛋白）增高，真皮内密集中性粒细胞浸润[6, 15, 16]，皮损多累及四肢及头颈部，此外，部分Sweet综合征患者可伴有口腔病变，如口腔糜烂、溃疡或水疱[17-18]。本研究患者发病期间皮肤表现为轻微压痛的结节性红斑，皮损较轻，但伴有严重的口腔黏膜病损，口腔黏膜多处大面积糜烂，表面覆盖黄白色假膜，疼痛明显，故就诊于口腔科。此时首诊医生应综合考虑患者的全身情况，结合患者皮肤表现，做出鉴别诊断，同时，口腔科医生也应充分了解Sweet综合征的临床特征，考虑到其可能为Sweet综合征的皮肤外表现，请皮肤科会诊并尽快完善皮肤活检以明确诊断。

确诊Sweet综合征应满足诊断主要标准两条，以及4条次要标准中的任意两条[19-20]。主要标准：①突然发生的疼痛性红色斑块或结节，偶有水疱或脓疱；②组织学见真皮内致密的中性粒细胞浸润，无白细胞碎裂性血管炎表现。次要标准：①有全身不适或发热大于38 ℃；②发病前有预防接种、感染或相关疾病，包括炎症性疾病、血液系统增生性疾病、实体恶性肿瘤及妊娠；③发病时实验室检查结果符合以下其中的3条：红细胞沉降率超过20 mm/h、C反应蛋白阳性、白细胞计数大于8×10^9/L、中性粒细胞比例大于70%；④系统应用糖皮质激素疗效显著。本例患者两侧膝盖及下肢可见散在分布红色斑块，轻度压痛；皮损组织病理学检查示：真皮全层见散在不成熟中性粒细胞聚集灶浸润，符合2条主要诊断标准条件。该患者发病过程中伴有发烧，体温38.5 ℃；对糖皮质激素治疗效果反应良好，符合次要标准中的2条，该患者诊断为Sweet综合征。

本例患者全身症状较轻，以口腔大面积糜烂为主要表现，对于累及四肢的特征性皮损并伴有口腔黏膜病损的患者，常需与以下几种疾病相鉴别：①白塞病，表现包括复发性口腔溃疡、眼炎、生殖器溃疡以及结节性红斑等，口腔溃疡多为其首发症状，上皮层溶解破溃脱落形成凹陷，边缘规则，表面覆盖黄色假膜，周围有红晕带，疼痛明显[21-23]；②多形性红斑口腔黏膜，可发生广泛充血水肿，大面积糜烂，渗出较多，形成厚的假膜，疼痛明显，但发病较急，病损常呈对称分布，典型表现为皮肤的虹膜状红斑，又称靶形红斑[24-26]；③结节性红斑，临床表现为小腿伸侧对称分布的深在性触痛结节，表面不发生溃疡，可伴有发热，组织病理见皮下脂肪层和脂肪小叶间隔中炎症细胞浸润[27-29]。此外，Sweet综合征还是炎症性肠病（溃疡性结肠炎、克罗恩病）常见的肠外表现[30-31]，应结合患者临床表现及相关检查进行排查，本研究患者无腹痛腹泻等全身症状，故排除炎症性肠病。

特发性Sweet综合征患者若无治疗干预，通常在6～8周内可自愈。其中系统应用糖皮质激素是本病最重要的治疗方法，患者可在短期内改善皮损，但可能会存在潜在感染或停药后复发的情况[19]。碘化钾和秋水仙碱也是治疗本病的药物，有介导免疫抑制及抑制白细胞趋化的功能，还有研究报道了生物制剂对Sweet综合征的疗效[1, 13]。本例患者应用复方倍他米松肌肉注射1次，口腔采用复方氯己定溶液含漱，病损黏膜处重组牛碱性成纤维细胞生长因子溶液外用，4 d后体温正常，2周后皮损消退，口腔黏膜病损也消失，治疗效果良好，2年后随访皮损尚未复发。Sweet综合征临床表现差异较大，口腔黏膜表现无明显特异性，因此口腔医师应全面认识该病以免延误病情。

【Author contributions】 Niu YF designed the study and wrote the article. Yang F, Dong L and Fan JC processed the research, collected, analyzed the data. Zhang CY designed the study, guided and critically reviewed the article structures. All authors read and approved the final manuscript as submitted.

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