



# Eight-year old male patient with painful swelling and eruptions in the legs

Bahar Büyükkaragöz<sup>1</sup>, Mesut Koçak<sup>2</sup>, Emine Hafize Erdeniz<sup>2</sup>, Aysun Çaltık Yılmaz<sup>1</sup>, Uğur Ufuk Işın<sup>2</sup>, Zennure Takcı<sup>3</sup>, Servet Güreşçi<sup>4</sup>, Sacit Günbey<sup>2</sup>

<sup>1</sup>Unit of Pediatric Nephrology, Keçiören Training and Research Hospital, Ankara, Turkey

<sup>2</sup>Clinic of Pediatrics, Keçiören Training and Research Hospital, Ankara, Turkey

<sup>3</sup>Unit of Dermatology, Keçiören Training and Research Hospital, Ankara, Turkey

<sup>4</sup>Unit of Pathology, Keçiören Training and Research Hospital, Ankara, Turkey

## Case

An eight-year old boy who was healthy previously had a history of use of trimethoprim-sulphamethoxazole (TPM-SMX) because of diarrhea ten days before presentation. He was hospitalized because painful swelling occurred in the legs under this treatment, he had fever and joint pain for the last five days. In his personal history, there was no pathology except for frequent aphthous ulcers in the mouth and it was learned that he had no familial history of any hereditary or rheumatic disease.

Physical examination findings were as follows: body weight: 27 kg (50-75p), height: 125 cm (25-50p), arterial blood pressure: 100/60 mmHg, one painful aphthous ulcer in the buccal mucosa, abdominal tenderness, painful erythematous nodules on the extensor surfaces of the lower extremities and arthritis in the left ankle (Figure 1). Pustular lesions were observed on the skin areas where blood samples were taken.

Laboratory tests revealed leukocytosis (WBC:24 000/mm<sup>3</sup>) and mild anemia (hemoglobin: 11.5 g/dL) in complete blood count, platelet count was normal (370 000/mm<sup>3</sup>). Neutrophil predominance (89.7%) was found on peripheral blood smear, but no atypical cell was observed. Acute phase reactants were markedly high (C-reactive protein: 10.9 mg/dL (0-0.8), erythrocyte sedimentation rate: 48 mm/h, fibrinogen: 908 mg/dL). Blood biochemistry and complete urinalysis were found to be normal. Throat culture revealed normal flora. Stool microscopic examination performed for acute gastroenteritis was found to be normal, rotavirus antigen was found to be negative and no pathogenic microorganism grew in stool culture. The tests directed to the possible underlying causes performed in the patient whose skin lesions were evaluated as erythema nodosum, who had a previous history of diarrhea, prolonged fever and arthritis findings were as follows: salmonella and brucella serology (-), viral tests: HBs Ag (-), antiHBs (+), cytomegalovirus (CMV) IgM (+), CMV IgG (+), CMV PCR (-), high positive CMV avidity, normal serum immunoglobulins and complements levels, p-ANCA (-), HLAB5 (-), antinuclear antibody (-), antidsDNA (-) and rheumatoid factor (-). Purified Protein Derivative-PPD test (-), ophthalmological examination, whole abdominal ultrasonography and echocardiography were found to be normal.

In the follow-up, it was observed that the patient's fever did not drop below 38.5°C, arthritis findings developed in the left elbow and the lesions extended towards the upper extremities (Figure 2). At this stage, skin biopsy was performed.

**Address for Correspondence:** Bahar Büyükkaragöz, Unit of Pediatric Nephrology, Keçiören Training and Research Hospital, Ankara, Turkey.  
E-mail: karamanbahar@yahoo.com

**Received:** 11.11.2013 **Accepted:** 10.01.2014

©Copyright 2014 by Turkish Pediatric Association - Available online at [www.turkpediatricsivi.com](http://www.turkpediatricsivi.com)

DOI:10.5152/tpa.2014.1707



**Figure 1. Bilateral ankle arthritis and erythematous nodules in the lower extremity**

#### Diagnosis : Sweet syndrome

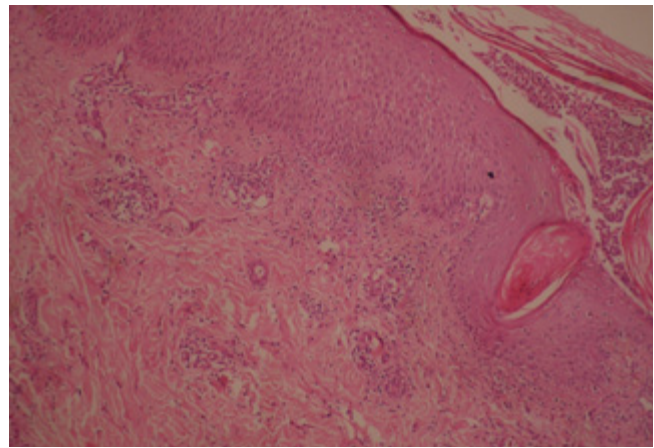
Skin biopsy revealed lymphohistiocytic infiltration accompanied by polymorphonuclear leukocytes in the perivascular area in the dermis (Figure 3). Repeated peripheral blood smear was found to be normal in the patient who was diagnosed with Sweet syndrome. Bone marrow examination could not be done, since the family did not give consent. 0.05 mg/kg/day colchicine was started primarily, but it was observed that no response was obtained in the follow-up. Therefore, 2 mg/kg/day oral prednisolone was started and it was observed that fever subsided completely after the second day of treatment and the lesions regressed. The patient whose clinical findings rapidly improved and acute phase reactants became normal was discharged. In the outpatient follow-up, the dose of prednisolone was tapered gradually and prednisolone was discontinued at the end of the 8th week. At the end of the first year, it was observed that the patient had normal clinical and laboratory findings.

#### Discussion

Sweet syndrome is an acute febrile neutrophilic dermatosis described by Robert Douglas Sweet (1) in 1964 for the first time. This syndrome is characterized with fever, neutrophilia and inflammatory skin lesions and is observed rarely in children (2-4). Only 5-8% of the cases occur in the childhood (3, 5, 6). Although it is mostly idiopathic, infections (especially acute gastroenteritis and upper respiratory tract infections), vaccines, drugs, immune deficiency syndromes, connective tissue diseases including systemic lupus erythematosus and dermatomyositis and neoplastic diseases (most commonly acute myelocytic leukemia in the childhood) are involved in the etiology (6-11). Although the pathogenesis is not known exactly, it has been proposed that triggering factors (bacteriae, viruses, tumor antigens or drugs) increase the release of proinflammatory cytokine release in target organs by leading to hypersensitivity and thus cause to neutrophilic and histiocytic infiltration (2, 8). Intensive infiltration with mature neutrophils is observed in the middle and upper dermis on histopathological examination of the skin lesion (12, 13).



**Figure 2. Arthritis in the left elbow and erythematous nodules in the upper extremity**



**Figure 3. Perivascular lymphohistiocytic infiltration below the stratified squamous epithelium (HE x100)**

The rash of the syndrome is specific and pathognomonic for the disease. As observed in our patient, the lesions have an acute onset and are in the form of painful, sharply circumscribed erythematous plaques or nodules. They show an asymmetrical distribution. There may be a single lesion or multiple lesions and they may have different shapes and sizes. Malignancy should be considered primarily especially in patients with typical lesions including bullous lesions (14).

It is known that acute gastroenteritis and drugs can trigger Sweet syndrome. It was known that our patient had a history of gastroenteritis which started 10 days before presentation to our hospital and use of TMP-SMX for gastroenteritis. In the literature, Sweet syndrome related with use of TMP-SMX has been reported in children (15). Therefore, we think that both states might have triggered the clinical picture in our patient.

CMV IgM and IgG were positive in our patient. Thereupon, CMV avidity was found to be highly positive and CMV PCR was found to be (-). Thus, it was thought that the patient had no active CMV infection, but a recent CMV infection. In the literature, there are publications which show the relation of Sweet syndrome with CMV infection (16). Therefore, it was concluded that CMV infection might be another triggering factor in our patient.

It is known that patients may have a sterile neutrophilic inflammatory process in all other organs in addition to neutrophilic infiltration in the skin. Therefore, a sterile arthritis picture may be observed in all patients with Sweet syndrome as observed in our patient (2, 17). Mucosal involvement is a finding which is not observed rarely. Generally, apthous lesions are found in the upper respiratory tract and gastrointestinal tract as observed in our patient (2, 18). Skin findings of Sweet syndrome should be differentiated from the other neutrophilic dermatoses (erythema multiforme, erythema nodosum, pyoderma gangrenosum, leukocytoclastic vasculitis and infections) (8, 19). Hence, skin lesions were evaluated as erythema nodosum at the first presentation in our patient. Our patient additionally had a history of recurrent oral apthous lesions. At the time of presentation, one painful apthous ulcer was observed on the buccal mucosa. Behçet's disease was considered in the patient who also had arthritis and a positive pathergy test. However, uveitis and genital apthous lesions which are important criteria for Behçet's disease was absent in our patient and HLAB5 was found to be (-). It is known that pathergy test may also be positive in Sweet syndrome (5). The skin biopsy of our patient made the diagnosis of Sweet syndrome. However, it has been reported in the literature that Behçet's disease may be one of the underlying causes of Sweet syndrome (20). Therefore, it was concluded that this patient should be also followed up in terms of Behçet's disease in the long-term, though infectious causes and drug usage were thought to be triggering factors.

In the diagnosis of the disease, two significant criteria including typical skin lesions and biopsy finding and at least two of the criteria including fever and presence of triggering factors (infection, malignancy, inflammatory disease), abnormal laboratory findings (increased acute phase reactants, leukocytosis and neutrophilia) and rapid response to steroid treatment should be present (12). Our patient had all these criteria. The prominent finding on histopathological examination of the skin lesions is intensive neutrophil infiltration in the upper-middle dermis (1, 21). A predominantly histiocyte-rich infiltration was observed together with neutrophils on skin biopsy of our patient. In the recent literature, histiocyte-rich form of the disease has been reported with a gradually increasing rate and thus it is thought that this is a developmental stage of the disease rather than being a different type (22).

The first line treatment is corticosteroids. The recommended therapeutic dose is 1 mg/kg/day for 10 days (23). It is known that exacerbations occur more commonly when the steroid dose is reduced rapidly especially in children (8). Therefore, slow tapering of the steroid dose is recommended. Since it is known that Sweet syndrome may be more resistant to steroid treatment in children compared to adults, it has been reported that treatment may be continued up to 5 months (23). It has been reported that use of colchicine or potassium iodide alone or in combination with steroids may give satis-

factory results (24). It was planned to perform bone marrow examination to exclude the possibility of an underlying malignancy in our patient after the diagnosis of Sweet syndrome was made. However, the family did not give consent for this investigation. Cervical, thoracic and abdominal computerized tomography examinations performed to exclude other solid organ malignancies were found to be normal. Colchicine was given to the patient as the first-line therapy instead of steroids. When it was observed that the patient's clinical picture did not improve at all, oral prednisolone treatment was administered and a marked response was obtained from the second day.

Sweet syndrome may recur once or more times in 30% of the patients (8). It is known that recurrences mostly occur in patients with Sweet syndrome related with malignancies (25). However, no development of exacerbation or malignancy was found during the one-year follow-up period in our patient.

Conclusively, this case is remindful in terms of the requirement of considering Sweet syndrome in the differential diagnosis in patients with prolonged fever and skin rash. It should be kept in mind that painful apthous lesions and arthritis may be found related with neutrophilic inflammatory process which can also involve other organs in addition to fever, leukocytosis, neutrophilia and prominent skin lesions which are typical in Sweet syndrome. Our case is interesting and didactic because it indicates the possibility that many etiological factors including CMV infection, acute gastroenteritis and use of TMP-SMX may be involved in development of Sweet syndrome. In addition, this patient was presented to emphasize the importance of long-term follow-up in terms of development of recurrence, malignancy and Behçet's disease in Sweet syndrome which is observed rarely in the childhood.

**Informed Consent:** Written informed consent was obtained from the parents of the patient who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - B.B.; Design - B.B., A.Ç.Y.; Supervision - M.K., S.G.; Funding - E.H.E., U.U.I.; Materials - Z.T., S.G.; Data Collection and/or Processing - B.B.; Analysis and/or Interpretation - B.B., M.K., A.Ç.Y., Z.T., S.G.; Literature Review - B.B., E.H.E., U.U.I.; Writer - B.B., M.K.; / Critical Review - S.G., A.Ç.Y.; Other - E.H.E., S.G., S.G., Z.T., U.U.I.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

## References

1. Sweet RD. An acute febrile neutrophilic dermatosis. *Br J Dermatol* 1964; 74: 349-56. [\[CrossRef\]](#)

2. Makis A, Stavrou S, Chaliasos N, et al. Acute febrile neutrophilic dermatosis (Sweet's syndrome) in a child, associated with a rotavirus infection: a case report. *J Med Case Rep* 2010; 4: 281. [\[CrossRef\]](#)
3. Hospach T, von den Driesch P, Dannecker GE. Acute febrile neutrophilic dermatosis (Sweet's syndrome) in childhood and adolescence: two new patients and review of the literature on associated diseases. *Eur J Pediatr* 2009; 168: 1-9. [\[CrossRef\]](#)
4. Kasapçopur Ö, Sever L, Çalışkan S, ve ark. Sweet sendromu. *Türk Ped Arş* 1996; 31: 285-8.
5. Halpern J, Salim A. Pediatric sweet syndrome: case report and literature review. *Pediatr Dermatol* 2009; 26: 452-7. [\[CrossRef\]](#)
6. Gray PE, Bock V, Ziegler DS, Wargon O. Neonatal Sweet syndrome: a potential marker of serious systemic illness. *Pediatrics* 2012; 129: e1353-9. [\[CrossRef\]](#)
7. Cohen PR. Sweet's syndrome--a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis* 2007; 26: 2-34.
8. Karaman S, Celkan T. Sweet Sendromunun eşlik ettiği juvenil myelositer lösemili bir olgu. *Türk Onkoloji Dergisi* 2005; 20: 37-9.
9. Tsuji H, Yoshifuji H, Nakashima R, et al. Sweet's syndrome associated with systemic lupus erythematosus: a case report and review of the literature. *J Dermatol* 2013; 40: 641-8. [\[CrossRef\]](#)
10. Hatch ME, Farber SS, Superfon NP, Ligorsky RD, Williams HE. Sweet's syndrome associated with chronic myelogenous leukemia. *J Am Osteopath Assoc* 1989; 89: 363-70.
11. Heer-Sonderhoff AH, Arning M, Wehmeier A, Südhoff T, Zumdick M. Neutrophilic dermal infiltrates in granulocytopenic patients with acute leukemia. *Ann Hematol* 1995; 71: 257-61. [\[CrossRef\]](#)
12. Su WPD, Liu HH. Diagnostic criteria for Sweet's syndrome. *Cutis* 1986; 37: 167-74.
13. Von der Driesch P. Sweet's syndrome (acute febrile neutrophilic dermatosis). *J Am Acad Dermatol* 1994; 31: 535-56. [\[CrossRef\]](#)
14. Akı T, Karıncaoğlu Y, Özcan H, Eşrefoğlu Seyhan M, Kalaycı B, Karadağ N. Büllöz lezyonların eşlik ettiği idiyopatik Sweet sendromu olgu tartışması. *İnönü Üniversitesi Tıp Fakültesi Dergisi* 2004; 11: 255-8.
15. Khaled A, Kharfi M, Fazaa B, et al. A first case of trimethoprim-sulfamethoxazole induced Sweet's syndrome in a child. *Pediatr Dermatol* 2009; 26: 744-6. [\[CrossRef\]](#)
16. Oskay T, Karademir A, Kutluay L. Sweet's syndrome associated with cytomegalovirus infection. *Int J Dermatol* 2004; 43: 57-9. [\[CrossRef\]](#)
17. Watanabe T, Nakashima K, Shindo M, Yoshida Y, Yamamoto O. Multiorgan involvement in Sweet's syndrome. *Clin Exp Dermatol* 2009; 34: e343-4. [\[CrossRef\]](#)
18. Bouw J, Kater AP, van Tongeren J, Schultz MJ. Upper-airway obstruction instigated by Sweet's syndrome. *Med Sci Monit* 2007; 13: CS53-5.
19. Vance E, Granter S, Skarin A. Sweet's syndrome. *J Clin Oncol* 1997; 15: 860-1.
20. Hassikou H, Tabache F, Baaj M, Safi S, Hadri L. Sweet's syndrome in Behçet's disease. *Joint Bone Spine* 2007; 74: 495-6. [\[CrossRef\]](#)
21. Farhi D, Wallach D. The neutrophilic dermatoses. *Dermatol Nurs* 2008; 20: 274-82. 22.
22. Liu CI, Hsiao CH, Wu JT, Tsai TF. Sweet syndrome with histiocytoid infiltrate and neutropenia: a rare combination. *J Am Acad Dermatol* 2009; 61: 882-4. [\[CrossRef\]](#)
23. Cohen PR. Neutrophilic dermatoses: a review of current treatment options. *Am J Clin Dermatol* 2009; 10: 301-12. [\[CrossRef\]](#)
24. Yi S, Bhate C, Schwartz RA. Sweet's syndrome: an update and review. *G Ital Dermatol Venereol* 2009; 144: 603-12.
25. Rochael MC, Pantaleão L, Vilar EA, et al. Sweet's syndrome: study of 73 cases, emphasizing histopathological findings. *An Bras Dermatol* 2011; 86: 702-7. [\[CrossRef\]](#)