Sweet’s syndrome in a patient with acute Crohn’s colitis and longstanding ankylosing spondylitis

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Case report

A 53-year-old woman presented to the University Hospital because of progradient abdominal spasms beginning three weeks earlier and diarrhea during the last week. General malaise, loss of appetite and reduction of body weight from 91 to 84 kg. In parallel, painless, only slight itching vesicules and papules on the back and the left thigh had developed during the last week. AS had been diagnosed in this patient 12 years ago based on a history of recurrent inflammatory back pain in the buttocks and lower lumbar spine but also pain and swelling of both knees for 22 years. Other joints, such as the ankles, wrists and fingers, never showed inflammatory signs. X-rays of the skeleton showing partial ankylosis of the sacroiliac joints and lumbar spine with two enormous synostoses supported the diagnosis of AS. The patient also reported having developed psoriatic skin lesions occasionally. There was a strong family history of psoriasis and AS, with the father and brother also suffering from both diseases.

The patient had taken 20 mg piroxicam daily continuously for some years. Sometimes intra-articular steroid injections in the knee joints had been performed.

On physical examination, the patient was found to be obese and in a reduced general state of health, but with normal vital signs. Remarkable were a diffuse tenderness of the belly on physical examination, and swelling and tenderness in both ankle joints. On the upper parts of the back and on the left thigh several

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succulent erythematous plaques with a diameter of up to 5 cm and signs of beginning bullous transformation were found (Fig. 1). The examination of the head and neck was unremarkable except for episcleritis as diagnosed by two independent ophthalmologists.

The white blood cell count was 12100/ml (normal 4000 - 10000/ml) with a left shift of 16% stabs, 55% neutrophils, 11% lymphocytes, 17% monocytes and 1% eosinophils. A blood smear was otherwise normal. Slight normochrome and normocytic anemia with a haemoglobin count of 11.8 g/dl (normal 12 - 16 g/dl) was found. Both the ESR with 80 mm/1st hour (normal < 18 mm) and the C-reactive protein with 300 mg/l (normal < 6 mg/l) were increased. HLA-B27 was positive. In repeatedly performed stool cultures no enteropathogenic bacteria, eggs or parasites were detected. Blood cultures were also negative.

Histopathological examination revealed floride cryptitis with cryptical abscesses and granulomas supporting the diagnosis of Crohn’s disease.

Immunosuppressive therapy with prednisolone 60 mg daily for one week and 40 mg in the second week was started. Thereafter the dose was reduced weekly by 10 mg, and later by 5 mg. In parallel peroral sulfasalazine was started and mesalazin clysmas were given. With the initiation of steroid therapy for the treatment of CD the skin lesions diagnosed as Sweet’s syndrome showed rapid improvement. Within one day the progression of the skin changes had stopped and 2 days later it started to decrease. After one week a marked reduction in size was noted and after 2 weeks there was nearly a complete palliation of the erythema. Furthermore, upon tapering of the steroid dose with improving CD, no regression occurred.

A chest-X-ray, an ultrasound of the belly and a gynecological examination were normal. Colonoscopy of the distal 50 cm of the gut showed diffuse red spotting of the mucosa with multiple fissural ulcerations but without pseudopolypes.

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Discussion
The association of ankylosing spondylitis and Crohn’s disease is well recognized (5). Arthritis in patients with CD and ulcerative colitis, the two major chronic inflammatory bowel diseases, are considered as part of the spectrum of spondylarthropathies (6) which also covers AS as the SpA prototype, reactive arthritis, undifferentiated SpA and a major percentage of patients with psoriatic arthritis (7).

Sweet’s syndrome or acute febrile neutrophilic dermatosis was first described by this author in 1964 (1). Since this time more than 500 patients have been reported in the literature. The criteria for a diagnosis of Sweet’s syndrome have been proposed elsewhere (3, 4). Initially this acute inflammatory skin disease was considered to be idiopathic. Then reports began to appear of acute febrile neutrophilic dermatosis in connection with a number of other rheumatological diseases such as rheumatoid arthritis, Sjögren’s syndrome, systemic lupus erythematosus and mixed connective tissue disease (Table I) (2).

However, the association of Sweet’s syndrome with spondylarthropathy is new. In this regard, it is of special importance - especially in a patient reporting a history of psoriasis - to differentiate between the skin lesions of Sweet’s syndrome, psoriatic skin lesions and erythema nodosum, all of which can be seen together with spondylarthropathy. Additionally, both erythema nodosum and Sweet’s syndrome have been reported in Crohn’s disease (8).

Sweet’s syndrome and psoriasis usually show clear differences, both macroscopically and microscopically. While the skin lesions in Sweet’s syndrome have a succulent-purulent aspect, plaques are predominant in psoriasis. Histologically, Sweet’s syndrome is characterized by an edema of the dermis with leucocyte infiltrations, while psoriatic lesions are confined to the epidermis without involvement of the dermis (9). The differentiation between Sweet’s syndrome and erythema nodosum also normally does not present any problems. Clinically painful pre-tibial nodes are characteristic of erythema nodosum. Microscopically, infiltrations of the leucocytes are limited to the borderline area between the dermis and subcutis (9). Erythema elevatum diutinum, which is also marked by neutrophilic infiltration, clearly differs from Sweet’s syndrome in its clinical course.

Some cases reported in the literature describe the syndrome during recidive of chronic Crohn’s disease, but there is only one other case of the acute onset of Crohn’s disease and Sweet’s syndrome in parallel and contemporaneously (10). However, it is possible that Crohn-like gut lesions may be present for a long time in AS patients without being detected. Thus, the association described in our patient might be due to a manifestation of Crohn’s disease which lies beyond the spectrum of SpA. An independent contribution of AS is less probable, but cannot be excluded. No increased frequency of HLA-B27 has been described in patients with Sweet’s syndrome. In one series with Japanese patients an increased frequency of HLA-Bw54 was reported (8). A study on Caucasian patients did not show any significant deviation in the frequency of HLA-A, HLA-B or HLA-C antigens; only a trend towards a negative association with HLA-A19 and HLA-B40 was found (11).

No definite pathogenetic conclusions on the connection between Sweet’s syndrome and Crohn’s disease can be drawn at the moment, since the respective pathogeneses of the two diseases have not been clarified to date. Both diseases have in common the clustering of leucocytes either in the dermis or as microabscesses in the submucosa of the intestinal wall. Hypotheses have been raised regarding the deposition of immune complexes and complement on the vessel walls, similar to the type III hypersensitivity reactions causing immune complex-mediated vasculitis. Other authors have suggested T cell-dependent cellular immune reactions or altered neutrophil functions to be more important (4). Taking into consideration all the data presently available, the pathogenesis of Sweet’s syndrome remains unclear.

To provide a short overview, Sweet’s syndrome can be subdivided into four groups - a classical idiopathic form, a para-inflammatory form, a paraneoplastic form, and the occurrence during pregnancy. The idiopathic form is most frequent, covering 60-70% of the cases. In about 20 to 30% of the patients an infection of the upper respiratory or the gastrointestinal tract is reported (4). In 10% of cases of Sweet’s syndrome, an association with a bacterial, viral or fungal infection has been described, but the related antigens have never been detected in the skin lesions. Sterile lung involvement has been often reported (12). Renal involvement, including acute renal failure, has been described. More rarely, heart involvement and sterile osteomyelitis may occur (4). In rare cases of Sweet’s syndrome organ involvement, especially involvement of the lungs or the central nervous system, have been life-threatening (12).

A connection between acute febrile neutrophilic dermatosis and malignancy has been reported in 10-20% of cases (13). In more than 75% of cases with malignancy a hematological disorder has been seen, with acute myeloid leukemia being the most common (13). Of the solid tumors about 35% are seen in the urogenital tract, 20% in the breast and 20% in the urogenital tract (13). On rare occasions Sweet’s syndrome has been reported in patients with lung cancer, melanoma or thyroid carcinoma. The typical skin manifestations of Sweet’s syndrome are seen within one month of the tumor manifestation and often show a close connection to regression and tumor recurrence (13).

In only about 2% of cases has Sweet's syndrome been described in pregnancy (14). An association of Sweet’s syndrome with different drugs such as all-

Table I. Sweet’s syndrome and its association with various rheumatic diseases (7).

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<tr>
<th>Condition</th>
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<tr>
<td>Rheumatoid arthritis</td>
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<td>Mixed connective tissue disease</td>
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<td>Sjögren’s syndrome</td>
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<td>Crohn’s disease</td>
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<tr>
<td>Colitis ulcerosa</td>
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<tr>
<td>Sarcoidosis</td>
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<td>Erythema nodosum</td>
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trans-retinol acid, G-CSF, minocycline, trimethoprim-sulfa-methoxazole and hydralazine must also be mentioned (15). None of these medications was used in our patient. Neither on physical examination nor on chest-X-ray or ultrasound could any tumor masses be seen. Pregnancy was not possible.

The treatment of choice for Sweet’s syndrome is the systemic application of steroids. Alternatively dapsone, colchicine, potassium iodide and cyclosporine A have been used (4). In most cases steroids lead to an improvement within 1 to 2 days and complete healing within 1 to 2 weeks, but recurrences are possible. In our patient Sweet’s syndrome completely disappeared and did not return in a one-year period.

In conclusion, SpA may be added to the list of joint and muscle disorders associated with Sweet’s syndrome. In the case of SpA, the differentiation of the nature of the skin lesions is important, since the treatment is clearly different.

References