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Streptococcal toxic shock syndrome in a patient with rheumatoid arthritis

Sirs,

Streptococcal toxic shock syndrome (STSS) attributed to group A Streptococcus (GAS) is a disease that presents suddenly with circulatory failure followed with rapid failure of multiple organs. Cases of STSS were reported by Adams *et al*. (1) in 1985 and by Cone *et al.* (2) in 1987. In Japan 198 cases of STSS have been reported between 1993 and 1999, after the first report by Shimizu *et al*. (3) in 1993. Recently, many cases (4) involving perinatal women who developed STSS triggered by uterine contraction caused by purulent myometritis have been reported. In this paper, we report our encounter with fulminant STSS caused by GAS in a patient with rheumatoid arthritis (RA).

A 67-year-old male was admitted to the hospital with edema and pain in the left lower extremity that had developed 2 days before and quickly worsened. He had no obvious injury or preceding infection. The patient was diagnosed as having stage IV RA based on the criteria proposed by the American College of Rheumatology in 1987. The patient's condition was controlled with prednisolone at 10 mg/day.

At admission, the patient's blood pressure was 100/62 mmHg, pulse rate 90/min and body temperature 36.2°C. Edema with severe pain was evident in the entire left lower extremity; changes in skin color suggestive of necrotizing fasciitis were not observed. Blood test results are shown in Table I.

The results of the physical examination and laboratory tests were indicative of septicemia. Blood samples were cultured to isolate the pathogenic organism and the patient was treated with piperacillin sodium at 4 g/day, imipenem 1 g/day and -globulin 2500 mg/day. Although the serum concentration of CPK was abnormally high, the serum CPKMB level of 3% was normal. There was no abnormal ST segment changes observed in the electrocardiogram. The CPK isozyme patterns showed 0% BB and 97% MM.

On physical examination, a 10 cm epidermolytic lesion was present on the lateral side of the left lower extremity, with a large amount of serosanguineous, low viscous effusion. Afterward, the patient's confusional state worsened. He suddenly lost consciousness and was in cardiopulmonary arrest. Cardiopulmonary resuscitation was immediately performed, but the patient died approximately 12 hr after admission. GAS was isolated from the blood specimens. The bacteria was later typed as T22/M22 and was found to be producing streptococcal pyogenic exotoxin (SPE) B and C *in vitro*.

Diagnostic criteria (5) for STSS have been proposed by the Centers for Disease Control and Prevention (Atlanta, USA). In the present case, AI section: GAS was isolated from peripheral blood; B1 section: Renal impairment; creatinine ≥ 2 mg/dl for adults or ≥ twice the upper limit of normal for age. In patients with preexisting renal disease, a ≥ 2-fold elevation over the baseline level; B3 section: Liver involvement; SGOT, SGPT, or total bilirubin levels ≥ twice the upper limit of normal for age. In patients with pre-existing liver disease, a ≥ 2-fold elevation over the baseline level. Unfortunately, an autopsy could not be performed for ethical reasons.

STSS is a disease that presents suddenly with circulatory failure followed by rapid failure of multiple organs. In Japan, approximately 70% of the reported STSS cases are preceded by some form of infection such as respiratory (e.g. upper and lower airways) or urinary tract infection. However, only an accurate diagnosis and prompt treatment at an early stage may save patients with septicemia caused by GAS (6). The recommended therapy includes administration of a large dose of penicillin, -globulin preparation, supportive treatment for shock which often occurs with septicemia, and aggressive debridement of necrotic tissues (7). Despite these aggressive treatments,the mortality rate in cases of STSS with septicemia remains high at 30% to 40% (8).

Most SPEs belong to the large family of superantigens that are potent stimulators of lymphocytes from mice, rabbits and humans (9). SPE-stimulated lymphocytes may contribute significantly to the development of STSS through the massive release of cytokines (9). On the other hand, GAS also produces many extracellular products such as streptolysine-O, streptolysine-S, streptokinase and hyaluronidase, and these may also play a role in the development of STSS.

Our patient suffered from edema and pain of the left lower extremity associated with epidermolysis and leakage of effusion. We did not perform aggressive debridement because of the lack of skin color changes suggestive of necrotizing fasciitis. However, given the increased levels of serum CPK and Mb, it is legitimate to assume the presence of necrotizing fasciitis and myolysis involving the left lower extremity.

In only 30% to 35% of reported STSS cases was there a clear underlying disease, such as tumor, diabetes mellitus and liver disorder and drug abuse (6). Only one case of STSS as a complication of RA has been confirmed by the research group in the Ministry of Health and Welfare of Japan. The patient in our case had a history of RA complicated by the long term administration of steroids and NSAIDs. It is most likely that the patient's immune function was

Table I. Laboratory findings after admission.

	Values		Normal ranges
WBC	1700		4000 - 8000/ l
RBC	322 x 10^4		450 - 550 x 10^4/ l
Hb	10.7		14 - 18 g/dl
PLT	8.2		20 - 40 x 10^4/ l
GOT	257	≠	10 - 28 IU/l
GPT	98	≠	5 - 33 IU/l
CPK	9,189	≠	35 - 200 IU/l
Mb	29,953	≠	0 - 65 ng/ml
Na	139		135 - 150 mEq/l
K	4.8		3.5 - 5.3 mEq/l
Cl	96		96 - 107 mEq/l
BUN	69.4	≠	7 - 22 mg/dl
Cre	4.73	≠	0.6 - 1.2 mg/dl
TP	5.4		6.7 - 8.5 g/dl
Alb	2.8		3.8 - 5.5 g/dl
CRP	35.4	≠	0.4 mg/dl >
IgG	1,171		680 - 1620 mg/dl
IgA	303		84 - 438 mg/dl
IgM	66		57 - 288 mg/dl

thereby compromised (10). Accordingly, he developed a sudden shock from septicemia and died without exhibiting conventional signs such as soft tissue necrosis or necrotizing fasciitis. Septicemia without fever is not rare, as illustrated by this case. Some reports state that fever was not observed in 30% of STSS cases (6).

Septicemia tends to occur in patients with underlying diseases such as hypertension and diabetes mellitus (6). The possibility of STSS should be considered in patients with severe pain in the extremities which is suggestive of necrosis, even in the absence of skin color changes. Therefore, it is necessary to have a high index of suspicion for an infectious etiology and to begin treatment immediately before the diagnosis of disease is confirmed.

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Spondyloarthropathy and Turner's syndrome

Sirs,

Chromosomal abnormalities have lately been shown to lead to a predisposition for autoimmune diseases. Case reports exist in the literature demonstrating the association of Turner's syndrome (TS) with polyarticular or oligoarticular type of juvenile chronic arthritis (JCA) (1, 2). We present an unusual case of a TS patient who suffered from buttock and low back pain and oligoarticular arthritis, concluding with a delayed diagnosis of arthritis resembling ankylosing spondylitis.

A 30-year-old female presented to our clinic suffering from occasional pain and swelling in both knees and the right ankle, as well as pain in the buttock area since her childhood. Her back pain had an insidious onset and showed progression over the years with no response to simple analgesics anymore. Examination revealed an atypical facial appearance, growth retardation, the absence of secondary sex characteristics along with primary amenorrhoea. She had a short stature, short webbed neck with a low hairline, wide chest with atrophic nipples and juvenile female external genitalia. Neck rotation was limited. She had painful and limited trunk flexion with forward bending mainly performed via hip flexion. Sacroiliac provocation tests were painless but limitation of bilateral hip rotation, shortened hamstring muscles and pain in the right knee on performing passive range of motion were observed. No neurological deficit was detected. Radiological investigation revealed bilateral grade III sacroiliitis and signs of inflammation in both hip joints (Fig. 1), as well as generalized osteopenia.

Routine haemanalysis indicated a normal blood count, slightly elevated liver function tests and high alkaline phosphatase levels. Serologic investigation was negative for C reactive protein, rheumatoid factor, ANA and markers for Hepatitis B, Brucella and Salmonella infections. The erythrocyte sedimentation rate was 34 mm/h. HLA typing was negative for HLA B27. She had low serum estradiol and elevated FSH and LH levels and normal thyroid function tests. Pelvic ultrasonography demonstrated a hypoplasic uterus and fibrotic gonads. Caryotype analysis was performed and a 45 XO configuration revealed Turner's syndrome. Bone mineral density measurement by the DEXA technique revealed severe osteoporosis of the lumbar vertebrae (t = -5.58 SD). A diagnosis of spondylarthropathy co-existing with TS was reached and anti-inflammatory medication along with vitamin D and calcium supplementation was started, as well as advising a home exercise program to the patient.

The relationship of TS with arthritis had only been demonstrated through case reports in the literature until Zulian *et al.* (3) published a large series of patients with JCA associated with TS. The prevalence of the two conditions together was shown to be at least 6 times greater than would be expected if they were only randomly associated. Two different patterns of arthritis were present in their series and also in the literature; polyarticular and oligoarticular. Our case is of interest due to the form of presentation of the arthritis. To our knowledge, this is the first description of TS-related arthropathy involving the axial joints along with the peripheral joints.

It has been suggested that chromosomal breakage and rearrangement can induce the specific immunological alterations which are responsible for the onset of arthritis and other autoimmune conditions seen in patients with TS (3). Another possible link

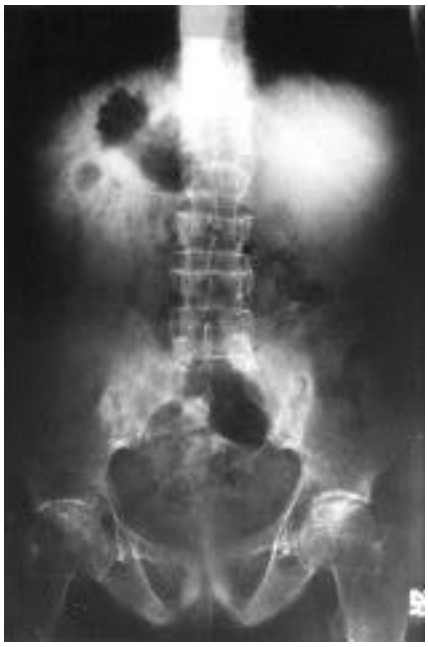

Fig. 1. Anteroposterior lumbosacral radiogram demonstrating bilateral Grade III sacroiliitis, hip involvement and generalized osteopenia.