A teenage girl with recurrent fever, abdominal pain and diarrhea

A teenage girl was hospitalized with a fever, diarrhea and abdominal pain. The cause of the symptoms should prove to be a disease that receives little attention in our time. The incidence has decreased significantly in recent decades, but the condition remains.

A girl in her teens was reported to the pediatric and adolescent ward from an emergency room after two days of fever, diarrhea and abdominal pain. No one else in the family was sick. She had had something similar twice before that fall, where one episode was perceived as scarlet fever and treated like it. When examining the emergency room, the patient seemed dehydrated, she was dizzy and had pain throughout her body. 

CRP was measured at > 200 mg / L (<5 mg / L). The medical doctor chose to put the patient in a hospital with acute infectious gastroenteritis as a tentative diagnosis. She was transported by ambulance, and during transport, the ambulance staff contacted the on-call pediatrician and reported concerns about the patient’s condition due to tachycardia of 160 beats / minute and low blood pressure (90/50 mm Hg). The level of consciousness was unaffected.

Abdominal pain with acute diarrhea, fever and dehydration in children and adolescents is a common problem. Initially, infectious gastroenteritis is suspected, with virus causing 70%, bacteria 10-20% and parasites <10% (1). Differential diagnoses include appendicitis, invagination, urinary tract infection, pneumonia, hemolytic uremic syndrome, congenital metabolic conditions and sepsis.

Upon arrival at the emergency room, the patient was alert and ready. She was afebrile, breathed rapidly at a frequency of 24 per minute, had pale and cold skin with weak peripheral pulses, sinus tachycardia of 160 beats / min, blood pressure 85/62 mm Hg and capillary filling time of 5 seconds (<2 s). She was palpation seam in the lower abdomen with no peritonitis suspected. There were normal findings of auscultation of the heart and lungs. The mucous membranes of the mouth and eyes were striking red.

At this time, septic shock was suspected with a possible starting point in the abdomen. Blood cultures were taken and samples were taken to grow bacteria from the throat and urine. 20 ml / kg of NaCl 9 mg / ml was given in a new fluid shock, and empirical intravenous antibiotic treatment was prescribed based on the patient’s weight with ampicillin 3 g x 4, gentamicin 350 mg x 1 and metronidazole 1.5 g x 1. Since she until now had responded poorly to the fluid treatment, hydrocortisone 200 mg x 1 was given intravenously, as adrenal failure is an important differential diagnosis. This had no effect. The patient was transferred to the intensive care unit for further treatment and evaluation.

Septic shock in children is defined as sepsis with cardiovascular dysfunction (hypotension or need for vasopressor to maintain normal blood pressure or at least two of the following: prolonged capillary filling time, oliguria, metabolic acidosis, elevated arterial lactate) (2). The condition has high mortality (3).

An important factor in improving the prognosis of septic shock is early detection of the diagnosis. One can expect a rapid multiorgan failure if you do not start treatment early and reverse the development (4). Our patient received volume therapy already in the ambulance, and at the first assessment in the emergency room the suspicion was reinforced. Furthermore, it is crucial to start early, preferably within one hour, with empiric antibiotic therapy.

Income blood samples showed C-reactive protein (CRP) 325 mg / l (<5 mg / l), normal findings on hematological specimens, including leukocytes 13.9 · 10⁹ / l (4.5–14 · 10⁹ / l), and normal liver tests. The values of creatinine were 111 µmol / l (45-90 µmol / l), urea 11.4 mmol / l (2.6-6.4 mmol / l) and albumin 32 g / l (36-48 g / l).

Capillary acid-base status showed pH 7.39 (7.36-7.44), pCO₂ 4.2 kPa (4.7-6.0 kPa), base excess -5.3 mmol / l (-3, 0–3.0 mmol / l), bicarbonate 18.7 mmol / l (22.0–26.0 mmol / l) and lactate 3.9 mmol / l (0.5–2.2 mmol / l).

Urinary incontinence showed leukocytes 3+, albumin 2+, blood 2+ and negative nitrite.
The blood samples with elevated CRP were interpreted as a powerful inflammatory process, probably infection. Elevated creatinine is matched with prerenal renal failure due to dehydration and low albumin levels with leakage through the body's capillaries. Acid-base status showed a compensated metabolic acidosis, partly caused by hypoperfusion with elevated lactate as a consequence, as well as respiratory compensation with hypocapnia. Urinary tract showed leukosuria, which made urinary tract infection a differential diagnosis, as well as leakage of albumin from the kidneys. Hematuria was an uncertain finding due to concomitant menstruation.

Over the first 2–3 hours, the patient had received NaCl 9 mg / ml fluid corresponding to 80 ml / kg without adequate circulation effect. In addition to volume therapy, a pressor in the form of noradrenaline was given 0.04 μg / kg / min. This combined to reverse the patient's circulatory shock.

In connection with the primary assessment in the emergency room, it emerged that the patient had had a tampon for more than 12 hours. This she was asked to remove. It turned out that all three episodes with similar symptoms had occurred during menstruation.

The on-duty gynecologist took a bacterial sample from the patient's vagina and confirmed that there were no foreign bodies there. The patient reported that during menstruation she often slept with a tampon, and the size she used turned out to be large for her age. In addition, she used a tampon throughout the menstrual period of approx. seven days, and sometimes 1-2 days extra.

Antibiotic treatment was extended with clindamycin 10 mg / kg × 4 intravenously, as it was suspected that the patient's illness now, and possibly during the two previous menstrual-related episodes, could be due to infection with toxin-producing yellow staphylococci. In such a situation, clindamycin will inhibit the toxin production of the bacteria.

Some strains of *Staphylococcus aureus* produce toxins which are superantigens that trigger a potent cytokine response. The starting point may be the colonization of, for example, the abdomen, where a tampon promotes the growth of these colonies. Other possibilities are otherwise banal wound infections where the pathogenic microbe has the ability to produce toxins. Thus, the infection itself does not need to be severe, but the bacterium's ability to produce certain toxins stimulates a strong immune response with a sepsis-like course (5).

The day after admission, the patient was better circulatory, and the pressor could be discontinued. She had normal diuresis and blood tests showed normalization of creatinine levels. The patient had no rash, but she had conjunctival injection with conjunctival injection and “raspberry tongue” appropriate for a general hyperemia.

She met several criteria for toxic shock syndrome: fever, hypotension, and multiple organ involvement (renal failure, myalgia, vomiting and diarrhea, and mucosal hyperemia) (6).

There was no growth in blood culture, but there was the growth of *S. aureus* in the cervix specimen. Cloxasacillin 2 g × 4 was added to clindamycin 10 mg / kg × 4 intravenously.

Five days after hospitalization, the patient's general condition was good and switched from intravenous to oral treatment with antibiotics after resistance determination (sulfamethoxazole / trimethoprim 80 mg / 400 mg 2 tablets × 2). Total treatment time with antibiotics was 14 days. She was told to be careful about using tampons and that she should rather use bandages because, increased risk of recurrence.

The bacterial isolate with yellow staphylococci was sent to the State Serum Institute in Copenhagen for toxin detection, and toxic shock syndrome toxin-1 (TSST-1) was detected.

### Discussion

Our patient went to the emergency room with the usual symptoms of a banal gastrointestinal infection, but she was more circulatively affected than would be expected in such a condition.

The state of toxic shock syndrome is characterized by rapid onset of fever and general impairment, circulatory action with low blood pressure, skin and mucosal involvement with diffuse macular erythroderma and hyperemia as well as involvement of multiple organ systems. The disease process is mediated by specific toxins produced by *S. aureus*, with toxic shock syndrome toxin-1 accounting for the vast majority. The toxin spreads hematogenically and produces symptoms local and distant from where the bacterium is located, which explains why blood culture most often does not show the growth of the pathogenic microbe. Early control of primary focus is therefore an important part of treatment. The toxin acts as a superantigen capable of potent activation of cytokine-producing cells in the immune system (7).

The diagnosis is made clinically and there are diagnostic criteria published by the Centers for Disease Control and Prevention (6). It is pointed out that isolation of *S. aureus* is not obligatory but still common and is found in mucosal samples in 80-90% of patients with
toxic shock syndrome. Isolates can be investigated for the ability of staphylococcal toxin production in research laboratories. Growth in blood culture is found in only 5% of cases, reflecting the ability of toxin production and its effects, and not the microbe itself, that is the most important factor in disease progression (8).

About half of the cases of toxic shock syndrome are related to menstruation and tampon use (9). In menstruation-related cases, the risk increases with the degree of absorbency, duration of tampon use during a period, and the length of time a single tampon is in the vagina (10). The condition was first described in 1978, and increased attention among other things in the 1980s led to a reduction (11). Cases not associated with menstruation are seen in a number of other conditions involving S. aureus, such as postoperative infections, mastitis, arthritis, skin infections, etc. (9). Over the past two years, seven children and adolescents have been diagnosed and treated for toxic shock syndrome at the Department of Children and Youth, Sørlandet Hospital Kristiansand. Five of these were associated with tampon use. All patients had used one single vial for more than eight hours (12).

Treatment of toxic shock syndrome is based on shock reversal, removal of any foreign matter by suspected focus (tampon, pessary, piercing, osteosynthetic material, etc.), possible abscess drainage, and empirical antibiotic treatment such as sepsis with the addition of protein synthesis inhibitors (clindamycin) (9). Further supportive treatment of other failing organ systems may also be necessary. In menstruating women, we recommend that the patient be examined by a gynecologist to verify that there are no tampons or other foreign bodies.

Of menstruating women, 70-80% have developed antibodies to toxic shock syndrome toxin-1 when late in their teens, and in the 40s this has risen to 90-95%. People with toxic shock syndrome more often have lower antibody levels than others and also have an impaired ability to form antibodies after an illness episode. This explains why some people are at risk of relapse (13).

Toxic shock syndrome related to tampon use is still relevant as differential diagnosis of abdominal pain, fever and diarrhea in adolescents and young adults. Early diagnosis and treatment are important for the course.

The patient and both her parents have consented to the publication of the article.
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12. Unpublished figures from the Department of Children and Youth, Sørlandet Hospital Kristiansand.