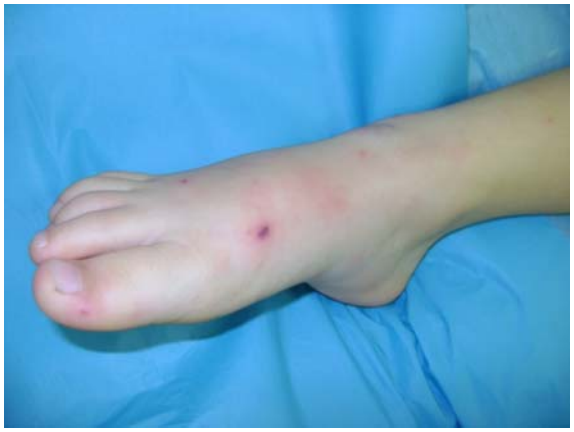
A child with fever and hemorrhagic rash

A 4-year-old boy was taken to medical admission unit of the Scientific Center of Children's Health (Federal State Budgetary Research Institution) on the parents' arms. Complaints at admission: pyretic fever, limb skin eruptions, leg pain, asthenia, atony and anorexia. The child had been ailing for two days. The disease onset was acute and characterized by body temperature rise up to 40 ^{o}C. Body temperature rises were observed four times within one day; the parents had been giving the boy ibuprofen. Maculopapular rash appeared on hands and feet a few hours after the fever onset; emesis had been observed once. The number of rash elements had been gradually increasing proximally spreading across the limbs; the first papules had started to take hemorrhagic form. Intoxication had been building up; the child had been confined to bed due to asthenia and pain in lower limbs.

At examination: the child is conscious; condition – severe (due to intoxication); symptoms of meningism; no focal neurological symptoms. Abundant rash has appeared on the skin of arms and legs, irregularly shaped hemorrhagic elements of various sizes with a tendency to merge – on hands and feet. Eruptions in more proximal positions appear as red nonpruritic macules and papules (pic.).



Pic. Hemorrhagic rash appearing as stars on hands and feet of a child with pyretic fever

Probable diagnosis:

1. Acute toxicoallergic reaction.
2. Thrombocytopenic purpura (Werlhof's disease).
3. Meningococcemia.
4. Juvenile arthritis with systemic onset.

Correct answer: 3. Meningococcemia.

Toxicoallergic reaction is characterized by acute onset; general malaise (adynamia, food refusal, myalgiae, arthralgiae etc.) precedes skin eruptions. Rash takes form of roundish erythematous macules with cyanotic fringe. The elements are characterized by radial growth and depression of the central part (due to edematous swelling). Eruptions appear primarily symmetrically on extensor surfaces. In 80-90% of cases, eruptions are observed on mucosae and characterized by ulceration. In this patient, pyretic fever and intoxication also preceded eruptions; however, hemorrhagic rash, its localization and development were not characteristic of toxicoallergic reaction.

Werlhof's disease (immunopathological thrombocytopenic purpura) is a chronic intermittent disease, which essentially is the primary hemorrhagic diathesis. Acute forms develop in most children (80-90%) at an early age; symptoms develop 2-3 weeks after onset of a viral infection or vaccination. Clinical manifestations of the disease are specific: sudden development of purpura – a generalized microcirculatory hemorrhagic syndrome. Hemorrhagic syndrome is usually represented by intradermal (petechiae and/or ecchymosis), mucosal and scleral hemorrhage; bleed, especially nose and gum bleed; visceral bleed. Characteristic features of purpura in patients are polymorphism of hemorrhages, polychromia, asymmetry and spontaneity of appearance and inconsistence with the extent of exposure. Condition of the children with acute forms of the disease, especially in the event of untimely diagnosis, becomes extremely severe due to progression of thrombocytopenia.

Juvenile arthritis is a systemic disease of connective tissue with predominant affection of small joints. It is characterized by pyretic fever and body temperature rises, especially in the morning. Rash is usually macular, linear and non-persistent; it appears and disappears at the height of fever and localizes primarily in the area of joints, on the face and lateral body surfaces. Appearance of hemorrhagic rash is associated with development of hemophagocytic syndrome. However, articular syndrome represented by joint movement restriction, edema and pain syndrome remains the leading one in the clinical pattern of juvenile arthritis. In most cases, the disease does not progress this fast.

Specificity of the rash (hemorrhagic elements appearing as stars), which appeared and progressed in the setting of pyretic fever and intoxication, progressive deterioration in the child's condition and meningeal symptoms contribute to diagnosing meningococcemia in this patient.

Meningococcemia is a relatively rare generalized form of meningococcal infection, which usually develops in under-3 children. Meningococci are usually carried in nasopharynx. Carriage may be complicated by a focal inflammatory process – meningococcal nasopharyngitis – a local form of a clinically significant meningococcal infection. According to different authors, nasopharyngitis constitutes up to 10% of all the infection cases. Bacterial entry to the blood stream results in development of meningococcemia and initiation of a generalized septic process.

Meningococcemia is characterized by acute onset with body temperature rise up to febrility. Fever is usually accompanied by pronounced intoxication. Rash is a characteristic symptom of the disease. Roseola or roseola-papular elements varying in diameter and not characterized by definite localization appear in the onset of the disease. Hemorrhagic elements, especially irregularly shaped elements, with a tendency to enlarge and merge spread in 2-24 hours (the progression rate depends on the course pattern). The first elements of hemorrhagic rash are usually located on the lower body. Development of hemorrhagic rash at an early stage of the disease on the upper body and the face serves as an adverse prognostic factor, as well as development of primary hemorrhagic elements on the skin. Hemorrhage to small joints (metacarpal, wrist joints), as well as to oropharyngeal mucosae, sclerae, conjunctivae and parenchymatous organs, may occur in children.

Meningococcemia treatment effectiveness depends on the time of diagnosis establishment and beginning of etiotropic therapy. Before prescribing an antibiotic, it is advisable to intravenously administer glucocorticosteroids (prednisolone or dexamethasone) to children, as meningococcal

destruction by a bactericidal antibiotic results in release of a large amount of endotoxin, which leads to the development of toxic shock syndrome and multiple organ failure. Chloramphenicol as the starting antibacterial drug may serve as an alternative. Study results demonstrated that *in vitro* use of chloramphenicol does not result in increase in the amount of free endotoxin.

According to the Russian national protocols, the drug of choice for meningococcemia is benzylpenicillin in the dose of 200-300,000 U/kg per day (usually in 6 intramuscular or intravenous intakes). However, the 3rd generation cephalosporins are nowadays viewed as the standard of etiotropic therapy in both adults and children around the world. The treatment requires prescription of ceftriaxone in the dose of 80-100 mg/kg in 1 or 2 intakes per day for 10-14 days. Meropenem is considered an alternative drug.

Prevention consists in early and timely detection, isolation and treatment of ill persons / carriers. The site of infection is subjected to disinfection, linen boiling, dishwashing, ultraviolet irradiation and air change. All persons who have closely contacted the patient are prescribed rifampicin in the dose of 600 mg for 2 days or ciprofloxacin in the dose of 500 mg once.

The earliest possible diagnosis establishment and antibacterial therapy prescription, toxic shock syndrome prevention, early diagnosis and fast beginning of correction of critical conditions on the way to an inpatient hospital contribute to a favorable outcome of the disease.

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