VERTEBRAL COMPLICATIONS OF LATE-ONSET NEONATAL SEPSIS

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Objective. To analyze characteristic features of spinal lesions as a manifestation of late-onset neonatal sepsis.
Material and Methods. Medical histories, clinical, and instrumental data of 9 children operated on for consequences of spinal lesions associated with late-onset neonatal sepsis were studied. Design: retrospective clinical study. Level of evidence – IV.
Results. Neonatal sepsis occurred at the age of 5 days to 2.5 months after birth. Main clinical manifestations of the disease were caused by pneumonia observed in 7 of 9 children. Spinal lesion was diagnosed within 3–12 months after the disease onset. Its main manifestation was kyphotic deformity caused by the T4–T11 vertebral body destruction. Average age of children at surgery was 13.4 months (range: 7 to 21 months). All patients underwent two-stage surgical treatment including anterior fusion and posterior instrumentation of the spine. Long-term results were followed for up to 5 years.
Conclusion. Spinal lesions as a manifestation of late-onset neonatal sepsis are rare disorders, and are characterized by vast destruction of vertebral bodies and development of paravertebral and epidural abscesses in neurologically intact patients. However, they are diagnosed only after the onset of kyphosis. Verification of spondylitis etiology fails due to the prior massive antibiotic therapy and insufficient examination in the acute phase of sepsis. Surgical treatment of spondylitis caused by late-onset neonatal sepsis is carried out when the infection is under control, and aims at the anterior column reconstruction and the correction of kyphotic deformity.
Key Words: neonatal sepsis, spinal lesion.

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Despite the progress in obstetrics and neonatology, infections are common and important cause of neonatal and infantile diseases and mortality. According to Stoll and Shane [25], 2 % of fetuses are infected in utero and up to 10 % of children are infected during the first month of life.

Neonatal infections are unique for several reasons:

– fetus and newborn can be infected from various sources (mother, relatives, medical personnel) and in various ways (transplacental, contact, oral, intravenous). The source of infection is often unknown;

– various etiologic agents (bacteria, viruses, fungi, protozoa, mycoplasma);

– wide variety of clinical manifestation, from subclinical to severe systemic forms of the disease. Diseases expression is determined by the massiveness of infection (amount of microbial cells), exposure time, and virulence of the infectious agent, clinical and immune status of the newborn;

– complexity of diagnosis and treatment, especially in premature children with concomitant congenital disorders.

Nursing measures for premature fetuses, which are inevitably associated with increased terms of hospital stay after birth, also increase the risk of acquired infections [10, 25].

Neonatal sepsis is a pathological process, which is based on generalized acyclic infection, usually caused by activation of pathogenic bacterial microbiota with underlying dysfunction of immune, especially phagocytic, protection system followed by the development of inadequate systemic inflammatory response, infectious inflammation focus (foci), or bacteremia and multiple organ failure [4, 5].

In the international literature starting from the 1990s, there are concepts of early-onset neonatal sepsis (EONS) and late-onset neonatal sepsis (LONS), which correspond to early and late neonatal sepsis in the Russian literature [4, 5]. Furthermore, different authors mention different terms of first manifestations of the pathology: first 72 hours [6], 4–5 days [7], 6 days [9], or 6–7 days of life [2].

The disease developed in the period between 72 hours and 90 days after birth is currently classified as LONS. It can be caused by a wide spectrum of biopathogens. Most often, these are coagulase negative staphylococci, more rarely, gram-

negative bacilli and fungi [8, 11, 13, 17, 18, 20, 23, 28, 29, 32, 33]. Incidence of LONS is also inversely proportional to the weight of the newborn [12]. Risk factors also include prolonged invasive procedures (catheterization of blood vessels, artificial lung ventilation), late initiation of breastfeeding, prolonged parenteral nutrition, surgeries, concomitant cardiovascular and respiratory diseases [11, 18, 24, 28, 29].

Non-specific spondylodiscitis and tuberculous spondylitis are considered to be the most common spinal infections in children during the first years of life, which usually manifest as moderate pain or complications, such as paralysis or spine deformity [16, 19, 21, 31]. Neonatal sepsis extremely rarely involve vertebrae, and the reports of this disease usually regard degradation of one or two cervical vertebrae [14, 15, 16, 27, 30, 31].

The objective of this research was to analyze the characteristics of spinal lesions as a manifestation of late-onset neonatal sepsis.

Study design: retrospective clinical series. Evidence level – IV.

Material and Methods

We studied medical history and results of clinical and instrumental examinations of 9 children with destructive lesions of the spine, whose nature corresponded to previous late-onset neonatal sepsis. All the patients underwent basic (X-ray) and detailed (CT, MRI) preoperative examinations of the spine. X-ray spondylogram was the main method for postoperative monitoring.

Results

All patients were admitted to the Clinic of Pediatric Surgery and Orthopedics of the St. Petersburg Research Institute of Phthisiopulmonology with suspected tuberculous spondylitis. None of them had clinical and laboratory signs of active infection at the time of hospitalization. The average age of patients was 12.5 months (6 to 20 months) at admission. Medical history provided information about the disease onset time, which varied from 5 days to 2.5 months after birth. In all these children, the period of acute manifestations was characterized by febrile temperature and severe condition, and for this reason they were treated in the intensive care unit, having different detected infection foci: pneumonia (7 cases, including 3 cases of bilateral pneumonia), coxitis (2), rib osteomyelitis (1), soft tissue infection, including infection of skin and subcutaneous tissue (2), and intestinal infection (2). Importantly, in all these cases, neonatal sepsis has not been diagnosed during the period of acute manifestations of the disease and all patients received multiple courses of intravenous antibiotics. Only 2 of 9 case records included reports on detected microorganisms in diagnostic titers: *Staphylococcus sp.* (from feces) and *Klebsiella pneumonie* (from the tracheobronchial tree). One child with the most late (2.5 months) sepsis onset underwent surgery for congenital heart defect at the age of 1.5 months.

Vertebral syndrome was characterized by the following features:

– in all cases, detection of kyphotic deformity by child's parents during the period between 3 and 12 months after onset of the disease was the first manifestation of lesion;

– there were no neurological disorders;

– radiographic (X-ray, CT, MRI) examination at the time of detection of spinal pathology showed extensive paravertebral and epidural soft-tissue growths in all patients, which significantly decreased (6/9) or disappeared (3/9) during ongoing antimicrobial therapy;

– all patients had destruction of several (2 to 4) thoracic vertebrae at the level of kyphosis' apex between T4 and T11; 4 children had multilevel lesions in the form of deep erosion of ventral surfaces of the bodies of another three segments adjacent to the area of total destruction (1 case), or degradation of several vertebrae, which are not adjacent to the area of underlying pathology (3 cases): C5 and T2 in one case; C5–C7 and T12–L1 in other case, C5 in the third case, wherein these changes themselves had no clinical manifestations and were incidentally detected by radiography.

At the time of the operation, the average age of patients was 13.4 months (7 to 21 months.). Rigid angular kyphotic deformity of the spine with average Cobb angle of 55.4° (44 to 80°) without scoliotic component was an indication for surgical treatment. In all cases, there was deformation and compression of the dural sac by the remnants of the degraded vertebral bodies and epidural pathological component (abscess) at the apex of kyphosis. Characteristic radiographic changes suggested tuberculosis of the spine as the first diagnosis. As already noted, in none of the cases clinical manifestations of myelopathy were detected.

Given the pronounced angular spinal deformities, higher potential risk of complications and the need for substantial shortening of the spine in the vertebral column resection (VCR) operations, all patients underwent two-stage operation at the level of kyphotic deformity: reconstruction of the anterior column through the transthoracic approach and posterior instrumental fixation using low-profile multi-anchoring hook metal construct. When the initial deformity value exceeded 50°, posterior stage was accompanied by resection of the arch of the apical vertebra [1]. Both procedures were carried out simultaneously (one anesthesia) in 8 patients. In one patient, who had previous surgery for congenital heart disease, the stages were separated by 2-week pause. The average length of anterior column reconstruction was 4.2 vertebral segments (3 to 6), wherein autologous rib was used for the anterior fusion in five cases, titanium mesh with a diameter of 10–12 mm filled with autologous bone – in four cases. There were no postoperative neurological complications.

Morphology of surgical specimens from all patients showed signs of nonspecific inflammation. In none of the cases, microbiota was detected in the material by microscopy or inoculation, there was no mycobacterium tuberculosis DNA, which was confirmed by PCR in all 8 patients.

The average value of surgical deformity correction was 62.5 %, long-term out-

comes were followed during the period from 1 to 5 years. There were no relapses or late exacerbations of the disease. In 4 children, posterior metal constructs were removed 1.5–2 years after spinal reconstruction since the anterior block has formed. In one case, reoperation was carried out 1.5 years after the removal of the posterior constructs due to formation of proximal contact kyphosis with stable anterior and posterior bone blocks in the area of primary reconstruction.

Fig. shows clinical example of spinal lesion in LONS.

Discussion

According to the literature [16, 19, 31], spinal infections are extremely rare in infants and have no characteristic clinical presentation until the development of complications as confirmed in our clinical series, where spinal lesion was diagnosed in none of the cases until kyphotic deformation occurred.

Modern understanding of the neonatal sepsis diagnosis suggests that the patient has a number of characteristic symptoms, corresponding to the general concept of sepsis, including severe condition, evaluation of the signs of systemic inflammatory response syndrome, multiple organ failure, and certain diagnostic tests (procalcitonin test, characteristic changes in hemogram and ESR, platelet count, etc.). At the same time, isolation of microbiota is not critical for the diagnosis, which is, however, managed according to the principles of intensive syndromic therapy [22, 23].

Unfortunately, we did not evaluated these tests in patients in the acute phase of the disease. Despite long-standing consensus on sepsis in general and neonatal sepsis in particular [9, 10, 25], the international diagnostic criteria are not fully used in our country.

It is noteworthy that in none of our observations spinal lesion was the primary symptom in the clinical presentation of sepsis: severity of patient's condition was usually due to pneumonia, while spondylitis was detected only several months after its onset.

We present a small cohort of 9 patients, which is however the largest of those reported in the literature. Lesions of the cervical vertebrae are believed to be characteristic of LONS; however, in our group, they were found only in 3 cases and were not accompanied by complications. Lesions of middle and lower thoracic vertebrae prevail in terms of both incidence and clinical manifestations. Despite the angular kyphosis and epidural growths, determining the potential risks of neurological disorders, neurological status of patients was intact, which again confirms the high compensatory potential of infantile spinal cord with respect to compression, even in the particularly sensitive area of the thoracic terminal blood flow.

In all the cases, microbial agent (sepsis causative agent in pathological material from vertebral destruction area) could not be verified. On the one hand, this is indicative of the effective eradication of infection as a result of the preceding antibiotic therapy, which is however not able to stop the development of pathological vertebral syndrome in the form of progressive single-plain deformity. On the other hand, the absence of microbiota verification at the stage of acute manifestations of the disease in 7 of 9 cases diagnosed with neonatal sepsis reflects the initial underestimation of the pathology and limitations of the applied diagnostic tests.

The nature of vertebral lesions (multilevel destruction with significant paravertebral and epidural growth) requires, first of all, the differential diagnosis of spinal tuberculosis [1, 3], while previous pneumonia, which was detected in all patients, suggests generalized tuberculosis. Without going into the issue of the differential diagnosis of etiological variants of infectious spondylitis, we should point out that the tuberculin skin tests (TST), as well as modern IGRA-tests (including Russian Diaskintest) are not valid in the case of extrapulmonary tuberculosis: verification of the diagnosis should be based solely on the analysis of the material sampled directly from the pathologic area [3, 26].

Conclusion

Surgical treatment of orthopedic consequences of spondylitis arising from late neonatal sepsis is carried out, when the infection is under control. It is aimed at correcting kyphotic deformity, restoring the supporting ability of the anterior spinal column, and ensuring growth of the newly created spine as close as possible to the physiological growth. At the same time, isolated posterior fixation of the spine without reconstruction of the anterior column may be insufficient to prevent late progression of kyphosis [29].

Undoubtedly, spinal reconstruction at such an early age (less than 2 years) is a least-evil solution and it is determined by both early-onset severe angular kyphosis and the potential risk of neurological complications associated with its natural course. Favorable outcomes obtained in our series are limited to a relatively short follow-up period (up to 5 years), while the first growth spurt is not complete in most of the children and they did not reach school age. Therefore, we cannot assess to what extent further formation of the spine will be different from physiological one. These questions are of great interest, however, they are outside the scope of this publication and the answers are likely to be obtained, when continuing the study.

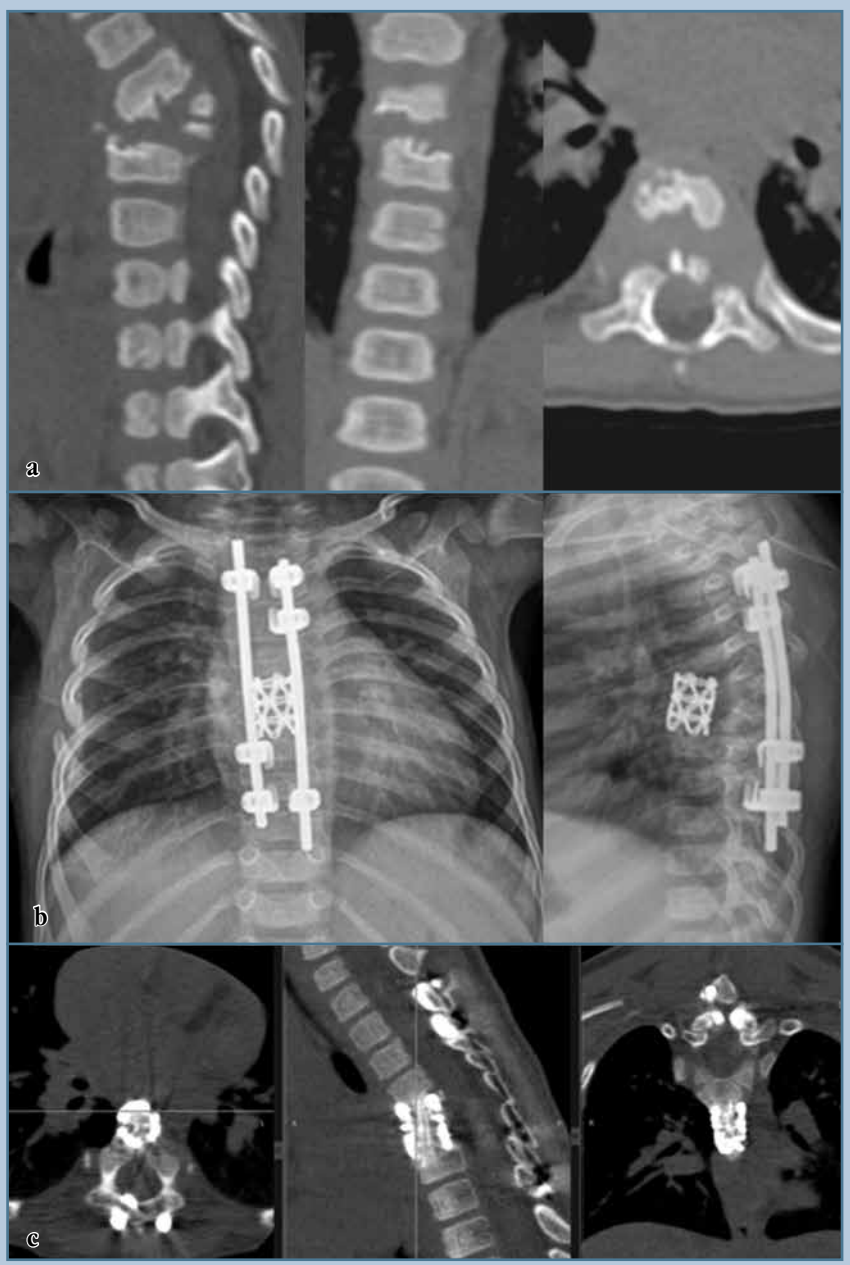

Fig.
Patient A. with late-onset neonatal sepsis has a history of bilateral pneumonia and left-sided coxitis; spondylitis was detected at the age of 5 months: **a** – sagittal, coronary, and axial CT slices at admission (age 1 year): subtotal destruction of T6, T7, contact destruction of T5, T8; kyphotic deformity of 44°; **b** – anteroposterior and lateral x-ray spondylograms immediately after reconstruction of the anterior column, anterior fusion with a titanium mesh with autologous bone, posterior instrumental fixation of the spine (age 1 year and 1 month); residual kyphosis of 8°; **c** – sagittal, coronary, and axial CT slices (age 2 years and 2 months) 1 year and 1 month after the operation; bone block of the vertebral bodies was formed without kyphosis, removal of posterior metal construct was planned

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