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Comorbidity: alobar holoprosencephaly and pulmonary tuberculosis in a child (a case report)

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Aim: to demonstrate the features of detection and management of a child with simultaneous alobar holoprosencephaly and pulmonary tuberculosis (TB) by the example from our own clinical observation.

Materials and methods. A clinical case of our own observation of the simultaneous course of pulmonary TB and alobar holoprosencephaly in the child who was treated in the pediatric department of the clinical base of the Department of Phthysiatry and Pulmonology of Zaporizhzhia State Medical and Pharmaceutical University on Public Non-Profit Enterprise "Zaporizhzhia Regional Clinical and Diagnostic Center of Phthysiatry and Pulmonology" of Zaporizhzhia Regional Council.

Results. The 4-year-old child diagnosed with pulmonary TB was admitted to the Pediatric Department. Previously, the child was diagnosed with alobar holoprosencephaly in a children's hospital. His condition was severe due to the main disease. Family members, who had contact with the child, were examined to rule out TB. The index patient was a grandmother, who had recurrent drug-sensitive TB and was looking after the child living apart from the family. The treatment for TB was successful, but the child developed drug-induced hepatotoxicity. Also, the child had episodic convulsions when admitted to the department, which did not repeat after the prescribed treatment by a neurologist.

Conclusions. Alobar holoprosencephaly is a severe and rare structural brain abnormality with complex and multifactorial causes. This condition can be identified at the first screening examination of a pregnant woman, so prenatal diagnosis is quite important. The disease leads to severe disability and requires assistance of physicians in different specialties. Treatment for tuberculosis is successful but demands more monitoring of side effects during antimycobacterial therapy.

Key words: alobar holoprosencephaly, pulmonary tuberculosis, child, households, clinical case.

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Коморбідність: алобарна голопрозенцефалія та легеневий туберкульоз у дитини (клінічний випадок)

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Мета роботи – на прикладі власного клінічного спостереження описати особливості виявлення та ведення хворої дитини з одночасним перебігом алобарної голопрозенцефалії та легеневого туберкульозу.

Матеріали та методи. Наведено клінічний випадок одночасного перебігу легеневого туберкульозу (ТБ) на фоні алобарної голопрозенцефалії в дитини, яка перебувала на лікуванні в дитячому відділенні Комунального некомерційного підприємства «Запорізький регіональний фтизіопульмонологічний клінічний лікувально-діагностичний центр» Запорізької обласної ради, що є клінічною базою кафедри фтизіатрії і пульмонології Запорізького державного медико-фармацевтичного університету.

Результати. До дитячого відділення надійшла дитина віком 4 роки, якій встановлено діагноз легеневого туберкульозу. Раніше дитина перебувала в дитячій лікарні, де була діагнотована алобарна голопрозенцефалія. Дитина у тяжкому стані, що зумовлений основним захворюванням. Обстежили членів родини, які контактували з дитиною, для виключення у них ТБ. Індексним пацієнтом виявилася бабуся, в якої стався рецидив чутливого туберкульозу. Вона не проживала з родиною, але доглядала за дитиною. Лікування ТБ у дитини було успішним, але з'явилася побічна реакція – гепатотоксичний прояв. Крім того, на час надходження в відділення дитина мала епізодичні судоми, які не повторювалися після лікування, що призначив невропатолог.

Висновки. Алобарна голопрозенцефалія – тяжка й рідкісна структурна аномалія головного мозку, спричинена складними й різноманітними факторами. Цей стан можна виявити вже на першому скринінговому обстеженні вагітної, тому пренатальна діагностика є доволі важливою. Захворювання призводить до тяжкої інвалідизації, потребує допомоги лікарів різних спеціалізацій. Лікування туберкульозу в таких дітей є успішним, потребує більшого контролю за побічними явищами в процесі антимікобактеріальної терапії.

Ключові слова: алобарна голопрозенцефалія, легеневий туберкульоз, дитина, домогосподарства, клінічний випадок.

Запорізький медичний журнал. 2023. Т. 25, № 6(141). С. 563-570

Holoprosencephaly (HPE) is a brain malformation in which the prosencephalon or embryonic forebrain fails to divide into two separate lobes between the third and fourth weeks of gestation. This process results in varying degrees of the cerebral hemispheric separation failure. About 80 % of affected embryos or fetuses have craniofacial abnormalities. The most severe of the associated craniofacial abnormalities are cyclopia, synophthalmia and proboscis. Other less severe abnormalities include microcephaly, hypotelorism, depressed nasal bridge, single central incisor of the maxilla, and midline cleft lip and palate [1].

The classification of HPE is based on the complete absence of the interhemispheric fissure and the degree of the cerebral hemispheric separation. Usually, there are four degrees of HPE severity, according to descending severity: alobar, semilobar, lobar and middle interhemispheric variant.

Alobar HPE is the rarest and the most severe clinically. It is characterized by the absence of cerebral hemispheric separation and a single ventricle of the brain, the "monoventricle". The semilobar form is represented by the fusion of the left and right frontal and parietal lobes, while the posterior lobes remain intact, as the interhemispheric fissure exists posteriorly. In the lobar form, the frontal lobes are fused, especially ventrally, while most of the right and left cerebral hemispheres and lateral ventricles remain intact. In the middle interhemispheric type, the posterior frontal and parietal lobes are not separated, there is also a varying degree of insufficiency of the thalamic and basal ganglia splitting, and the corpus callosum is absent. The severity of craniofacial malformations and prognosis usually correlate with the degree of HPE: the alobar form is the most severe, both in terms of craniofacial malformations and neurological disorders [2].

HPE is a quite rare malformation, but at the same time, the most common malformation of the brain and face, with a frequency of 1.00–1.34 per 10,000 births. The prevalence is much higher among aborted embryos, with a prevalence of 1 in 200–250. Thus, the lower the gestational age, the higher the prevalence, and it can be explained by a high intrauterine mortality of fetuses with HPE, probably due to associated genetic and structural defects [3].

The etiology of this disease is multifactorial, including the influence of teratogenic factors, genetic abnormalities and syndromic association, so it is difficult to determine the exact cause of this pathology. Today, the majority of cases of this disease remain unknown, that leads to the "multiple lesion hypothesis", which considers both genetic and non-genetic causes. Among the non-genetic factors that can cause this disease are maternal diabetes, ethanol consumption, smoking, retinoic acid, drugs that affect cholesterol biosynthesis, and the use of salicylates. In addition, viral diseases, such as cytomegalovirus, toxoplasma and rubella, have also been identified recently [4]. There are also genotypic causes of development, which can be identified not in all cases. HPE is inherited by autosomal dominant manner. The most common cause of familial HPE is a mutation of the SHH gene. The majority of HPE cases are associated with multiple chromosomal abnormalities, such as trisomy 13 and 21, which account for 25 % to 50 %. The disease affects about 70 % of people with trisomy, which has a prevalence of 1/5000 at birth. Trisomy 13 can be suspected during pregnancy based on ultrasound findings and confirmed by fetal karyotype analysis [5,6].

Prenatal ultrasound diagnostics of the fetal brain is a necessary and reliable method of diagnosis. It is known that most brain abnormalities remain undiagnosed until the second trimester. However, a basic approach to scanning in the first trimester can be used to diagnose brain abnormalities according to the current recommendations of the International Society of Ultrasound in Obstetrics and Gynecology. Thus, the structure of the fetal head, which should be visualized, is limited to the skull bones, the midline of the parietal region and the ventricles filled with the neurovascular plexuses. Using this method, almost all cases of acrania, cephaloceles, and alobar holoprosencephaly can be detected [7].

The absence of a "butterfly" sign by brain ultrasound in the first trimester of gestation should cause a high level of suspicion and indicates the presence of brain malformations with an adverse outcome and is associated with a detection rate of 100 % [1,8]. In the alobar form, a significant distortion of the normal brain anatomy can be observed and a single ventricle and extracerebral, facial and karyotype abnormalities can be detected. These changes can be revealed as early as the first trimester of pregnancy [9]. This is reflected in one of the most recent studies, where a group of researchers, Yu Hu et al. suggested that all cases of alobar holoprosencephaly were diagnosed by ultrasound in the first trimester [10].

Postnatal mortality in all types of holoprosencephaly is very high but depends on the specific type. The reported survival rate after one year is 29 %. Children with alobar type of holoprosencephaly, who survive the newborn period, have profound developmental disorders. In particular, spasticity of the limbs and axial hypotonia are observed. In most cases, children are unable to sit independently, although in some cases they can only grab objects and knock on them, so they have elements of fine motor skills and minimal hand function. In addition, such patients are non-verbal, with profound cognitive impairment, which causes complete dependence on all daily activities [11]. Also, common conditions in surviving children may include epilepsy, electrolyte imbalance due to hypothalamic dysfunction, which leads to diabetes insipidus, neurocognitive deficits, and mental disorders such as anxiety and depression [4].

In summary, as we can see, this disease is quite severe and requires full information to be provided to parents at the prenatal screening stage, concerning prognosis, morbidity and mortality, and about the care of such children in the postnatal state. Healthcare professionals should take into account the values and beliefs of parents regarding further decision-making [12].

As for tuberculosis (TB) in children, this problem is currently relevant. Children who have contact with a TB patient are at the highest risk of contracting TB. Lack of vaccination is also a crucial factor in the development of TB and affects the course, prevalence, complications, and mortality.

After analyzing the available literature, we did not find any described clinical cases of simultaneous alobar holoprosencephaly and TB in children, which may be of interest to physicians of various specialties.

Aim

To demonstrate the features of detection and management of a child with simultaneous alobar holoprosencephaly and pulmonary tuberculosis by the example from our own clinical observation.

Materials and methods

A clinical case of our own observation of the simultaneous course of pulmonary TB and alobar holoprosencephaly in the child who was treated in the pediatric department of the clinical base of the Department of Phthysiatry and Pulmonology of Zaporizhzhia State Medical and Pharmaceutical University on Public Non-Profit Enterprise "Zaporizhzhia Regional Clinical and Diagnostic Center of Phthysiatry and Pulmonology" of Zaporizhzhia Regional Council (PNE "ZRCDCPP" ZRC).

Results

A 4-year-old boy G.

Medical history. The child was born to a mother with no previous pregnancies. She was not prenatally cared. Pregnancy was accompanied by chorioamnionitis, stage 2 anemia, colpitis (purulent discharge). The mother was not registered by a gynaecologist during pregnancy.

From the first day of birth, the child was treated at a clinical hospital in neonatal intensive care unit (NICU) from 03.07.2018 to 28.08.2018 and was transferred to a Neonatal Pathology Department for further treatment. The child's general condition was severe. The skin was pale. Soft tissue turgor was low. Breathing was spontaneous. Oxygenation was satisfactory. Auscultation: rough breath sounds, no wheezing; heart sounds were loud, rhythm was regular. Central hemodynamics was stable. The abdomen was soft, not swollen. Conscious, lethargic, motor activity was only in response to stimulus, convulsive equivalents. The large fontanelle was 4.0 × 4.0 cm, not tense, head circumference – 46 cm. Scoliotic deformity of the cranium. Severe hydrocephalic symptoms, oculomotor disorders (von Graefe's sign was noted). Rigidity involving all extremities. Tendon reflexes were increased, pathological reflexes were not provoked. Orientation sensitivity was preserved.

Brain spiral computed tomography (SCT) (18.12.2018): Hydrocephalus. Abscess.

Chest X-ray (17.12.2018): the lung fields were clear. The vascular pattern was unchanged. The shadows of the lung hilus were structural. A neonatal resuscitation procedure was performed in the emergency department (13.07.2018): placement of an external ventricular drainage. In the Neonatal Pathology Department (18.09.2018), a surgery was performed: ventriculopuncture, drainage of the anterior horn. Also, the brain abscess was drained through the large fontanelle.

On 02.02.2019, the child was discharged from the Department in a stable condition under the supervision of a neurologist at the place of residence. At discharge, the child was in moderately severe condition, stable. Diagnosis: Hydrocephalus. Postoperative condition (POC) (13.07.2018): external ventricular drainage placement. Postoperative status (POS) (18.09.2018): ventriculopuncture, drainage of the anterior horn of the right lateral ventricle of the brain. Severe delay in psychomotor development, spastic tetraparesis. Symptomatic epilepsy. Recurrent neonatal sepsis, necrotising enterocolitis of newborns, respiratory distress syndrome.

The child's mother visited the children's hospital to register the child's disability as planned on 01.01.2023. The child was examined using clinical, laboratory and instrumental methods and consulted by specialist physicians.

Magnetic resonance imaging (MRI) of the brain (02.02.2023): the basic structure of the cerebral hemispheres was lost and seen as multiple cavities with a substantial volume of fluid with varying amounts of residual cortex. The white matter of the cerebral hemispheres was absent. One median mono-ventricle (holo-ventricle) was detected, lateral and third ventricles were absent. Median structures and interhemispheric fissures were absent. Transparent membrane was absent. The corpus callosum was absent. The olfactory tract was absent. Normal optic nerves were detected. The brain stem and cerebellar hemispheres were preserved. The pons was moderately compressed. The fourth ventricle was formed, compressed. The pituitary gland was formed, measuring 4 × 3 × 3 mm. There was an upward displacement of the parietal bones due to a significant amount of fluid in the brain cavities. The cerebral skull was deformed. There was unilateral (left-sided) occipital craniostenosis. Conclusion: MRI signs of developmental anomaly – alobar holoprosencephaly. Loss of the main structure of the cerebral hemispheres seen as multiple cavities with a substantial volume of fluid and with different amounts of residual cortex. Preservation of the brain stem and cerebellar hemispheres. Anomaly of skull bone development – left-sided occipital plagiocephaly (*Fig. 1*).

During the examination, according to echocardiography (heart ultrasound), free fluid up to 5 mm at the apex was found in the pericardial cavity. At discharge, the diagnosis was made: Brain developmental anomaly: allobar holoprosencephaly. Spastic tetraparesis. Severe psycho-speech retardation. Alalia. Symptomatic epilepsy. Protein and energy deficiency of severe degree with hypostatura. Hearing loss. Moderate degree iron deficiency anemia. Flexion contractures of the limb joints. Flat – valgus feet. Effusive pericarditis with reduced left ventricular ejection fraction. Right-sided cryptorchidism, inguinal hernia. Physiological phimosis. Congenital partial atrophy of the optic nerve of both eyes. Purulent conjunctivitis.

The mother categorically refused hospitalization and further treatment in a ward. She was discharged under the supervision of her family doctor. Recommendations were given including repeated ultrasound examinations of the heart and the second cardiologist consultation after 10 days.

On 13.02.2023, echocardiography showed no free fluid in the pericardial cavity, but a cavity formation was incidentally found in the left half of the chest. A left lung abscess was suspected. On 15.02.2023, the child was admitted to the surgical department of the Children's Hospital. Clinical, laboratory and instrumental examinations of the child were again performed using X-ray TCO and computed tomography (chest CT scan).

X-ray TCO dated 17.03.2023: the projection of the left lingual segments of the left lung demonstrated moderate reduction of pneumatisation due to infiltration of a homogeneous structure with indistinct irregular contours. Conclusion: Signs of infiltrative changes in the left lung lobes (differentiate between pneumonia and a specific process) (*Fig. 2*).

The child also underwent chest CT (16.02.2023): In the lingual segments of the left lung, a 5 mm subpleural calcified focus, above the diaphragm, an area of consolidation (infiltration) measuring 5 × 18 mm with small dense inclusions. In the basal regions from the paravertebral to the scapular line, thickening of the visceral pleural up to 4.5 mm. The right side was normal. The chest was deformed due to severe right-sided scoliosis. Conclusion: probable specific changes in the left lung (*Fig. 3*).

A diagnosis of left-sided pneumonia was made, but the mother categorically refused further examination and treatment in the pediatric department. The child was recommended to be monitored and treated by a family doctor at the place of residence and consulted with a pediatric phthisiologist.

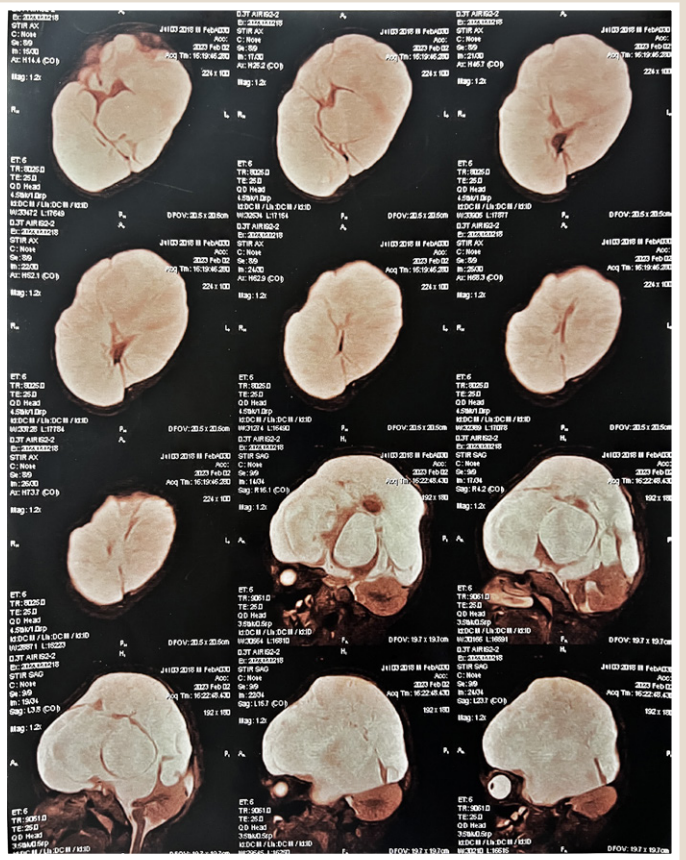

Fig. 1. MRI of the child's brain at the children's hospital.

On 01.03.2023, the child was hospitalized for further examination and treatment to the pediatric department of PNE "ZRCDCPP" ZRC (*Fig. 1*). Upon admission, no respiratory complaints were detected. The child was not vaccinated with BCG (for medical reasons). Family members were examined to detect TB. It was found that the parents had no changes in the lungs according to X-ray TCO results, but changes were found in a grandmother. Further inspection revealed that she had previously TB, and this case was considered as recurrent sensitive TB, MDR+. The child had no previous history of TB and was not registered with the dispensary.

On examination: the child's general condition was severe due to the main disease. He did not stand, sit, walk, and has no productive contact. His mother said that he sometimes shuddered and stretched his limbs. The skull and chest were deformed. The skin was pale and dry. Visible mucous membranes were clean. Tissue turgor was decreased. The peripheral lymph nodes of the neck and axilla were enlarged by the micropolyadenopathy type. Over the lungs, breathing sounds were rough, no wheezing. The heart was rhythmic, heart sounds were muffled. The abdomen was soft, painless to palpation. The lower edge of the liver was near the costal arch. Costovertebral tenderness on percussion was negative on both sides. Urination and bowel movements were not disturbed.

Data from clinical, laboratory and instrumental methods of examination:

Blood tests for HIV (02.03.2023) – negative.

The results of general blood analysis (GBA) (02.03.2023): hemoglobin (Hb) – 99 g/l, erythrocytes (RBC) – 3.26 × 10^{12}/l, platelets (PLT) – 185 × 10^{9}/l, leukocytes (WBC) – 9.9 × 10^{9}/l, eosinophils (EOS) – 4 %, banded neutrophils (b/n) – 3 %, segmented neutrophils (s/n) – 62 %, lymphocytes (LYM) – 21 %, monocytes (MONO) – 10 %, erythrocyte sedimentation rate (ESR) – 6 mm/h.

Biochemical blood analysis (10.03.2023): total bilirubin – hemol, thymol test – 1.33 U, alanine aminotransferase (ALT) – 1.0, aspartate aminotransferase (AST) – 1.8, total protein (TP) – 72.8 g/l, glucose – 5.22 mmol/l, albumin – 42.8 g/l, creatinine – 71.4 μmol/l, urea – 2.48 μmol/l.

General urine analysis (GUA) (02.03.2023): color – yellow, transparency – clear, specific gravity – not enough urine, reaction – alkaline, protein, glucose, ketone bodies – absent, leukocytes – 2–4, erythrocytes – 0–1, phosphates – many.

The results of bacteriological and molecular genetic (MG) analyses of gastric lavage (GL) were negative.

Abdominal ultrasound (02.03.2023): ultrasound signs of significant hepatomegaly, right-sided nephroptosis.

Electrocardiographic (ECG) data (02.03.2023): sufficient voltage. Sinus tachycardia – 125 bpm. The electrical axis of the heart was not deviated. Diffuse changes in the ventricular myocardium. QTcF – 382 msec.

A consultation with a neurologist (06.03.2023). Conclusion: Anomaly of brain development – holoprosencephaly. Spastic tetraplegia. Symptomatic therapy. It was recommended to prescribe levetiracetam 10 mg/kg twice daily (1.1 ml – twice daily) with an increase in dosage to 15 mg/kg in 3–7 days for anticonvulsant therapy.

According to the obtained data, the diagnosis was made: Newly diagnosed TB (NDTB) of the left lung (infiltrative) Destr–, MBT–, M–, MG–, K–, Resist 0, Hist 0, Cog 1 (2023). Brain developmental anomaly: alobar holoprosencephalopathy. Spastic tetraparesis. Severe retardation of psycho-speech development. Alalia. Symptomatic epilepsy. Protein and energy deficiency of severe degree with hypostatura. Hearing loss. Flexion contractures of the appendicular joints. Flat – valgus feet. Right-sided cryptorchidism, inguinal hernia. Physiological phimosis. Congenital partial atrophy of the optic nerve of both eyes.

Treatment according to the scheme for susceptible TB was prescribed: 2 months with isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E), 2 months with HR. The child first tolerated the treatment relatively satisfactorily. 05.24.2023, a case of hepatotoxic reaction was registered due to an increase in transaminases: bilirubin – 11.3 μmol/l, thymol test – 1.14 U, ALT – 3.48. AST – 1.42, total protein – 67.7 g/l, albumin – 41.4 g/l. Antituberculosis drugs withdrawal from the child was done for 2 weeks. It was also recommended to examine the child for the presence of cytomegalovirus and Epstein–Barr virus.

Anti – CMV Ig G – negative, Anti – CMV Ig M – negative. Anti-Epstein–Barr viral capsid antigens IgG – positive, Epstein–Barr virus, IgG antibodies to nuclear antigen (anti-EBNA IgG) – positive.

Consultation with the neurologist (12.05.2023): The child's condition was severe. Seizures were periodic 1–2 times a day. Inability to move the eyes to look at items. Productive contact was not available. Roving eye movements, sunset sign. Spastic tetraplegia. Positive tension

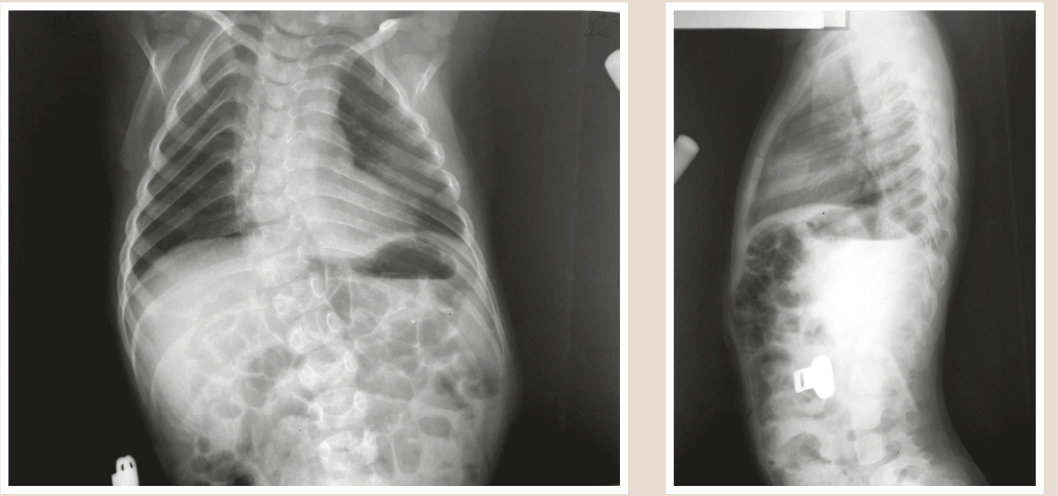

Fig. 2. X-ray TCO in direct and lateral position of the child in the surgical department of the children's hospital.

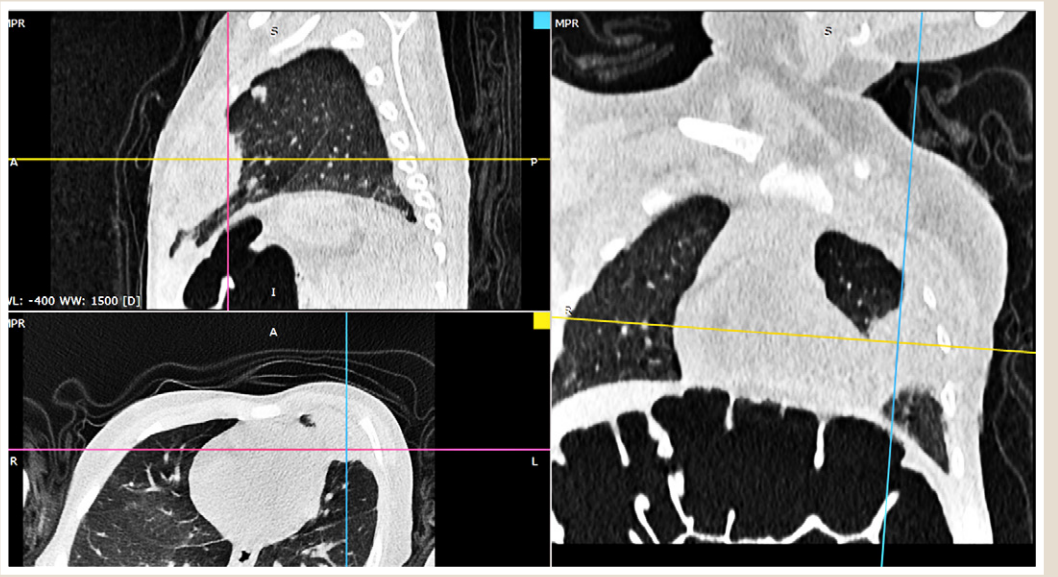

Fig. 3. CT scan in the surgical department of the children's hospital.

symptoms. Torpid tendon reflexes of the lower extremities with clonuses. It was recommended to continue therapy and dynamic follow-up.

Results of the child's examination at discharge: GBA (19.06.2023): Hb – 121 g/l, RBC – 3.94 × 10^{12}/l, WBC – 8.8 × 10^{9}/l, PLT – 185 × 10^{9}/l, EOS – 15 %, b/n – 3 %, s/n – 69 %, LYM – 11 %, MONO – 2 %, ESR – 2 mm/h.

Biochemical blood analysis (19.06.2023): total bilirubin– 8.1 μmol/l, thymol test – 0.73 U, ALT – 0.49, AST – 0.28, TP – 73.0 g/l, albumin – 50.5 g/l, glucose – 5.13 mmol/l.

GUA (14.06.2023): color – light-yellow, transparency – moderate, specific gravity – 1024, reaction – alkaline, protein, glucose, ketone bodies – absent, leukocytes – 0–1, erythrocytes – 2–4, phosphate salt amounts – high.

Abdominal ultrasound (15.06.2023): ultrasound signs of significant hepatomegaly, right-sided nephroptosis.

ECG data (14.06.2023): sufficient voltage. Sinus tachycardia – 136 bpm. The electrical axis of the heart was not deviated. Compared to the ECG dated 02.03.2023, there were more pronounced changes in the myocardium in the chest leads. QTcF – 386 msec.

Chest CT (28.06.2023): normal state of lung parenchyma inflation, equal pneumatization. A 5.5 mm subpleural calcified focus below the diaphragm and a 22.0 × 8.5 mm subpleural consolidation area with single calcifications were seen in S5 on the left. Thickening of the pleural layers up to 5.6 mm with single calcifications in the structure of 2 mm in size was determined in the left paravertebral region at the lower lobe level. There were no focal or infiltrative changes in all other lung fields on both sides. The hilum and mediastinum lymph nodes were not enlarged. Conclusion: CT scan showed signs of metatuberculous changes in the left lung in the form of the calcified focus and the subpleural area of consolidation with calcification and local pleural thickening at the lower lobe paravertebral level. Newly focal and infiltrative changes, volumetric pathology of the lungs and mediastinum were not detected. Compared to the chest CT scan dated 17.02.2023, a decrease in the size of the

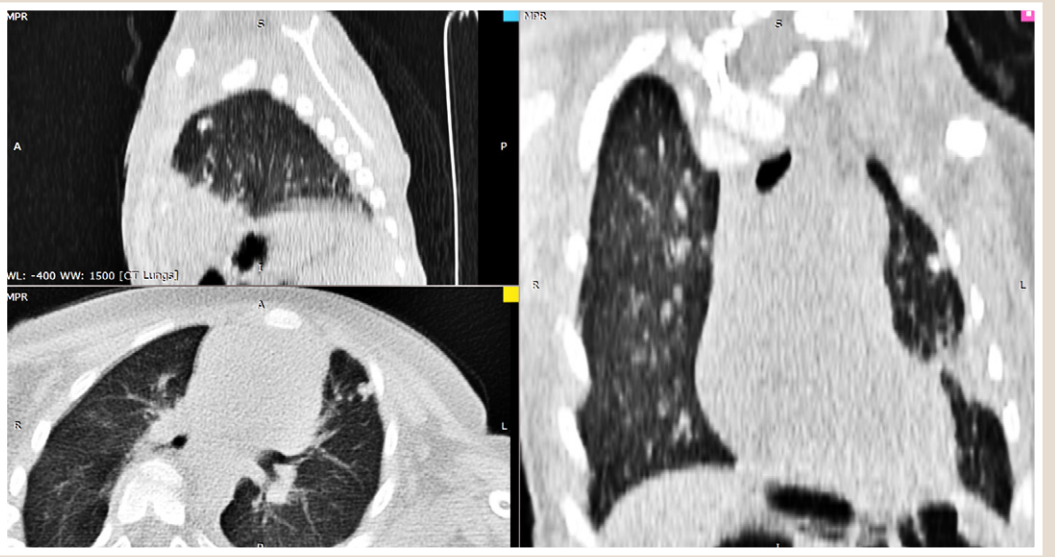

Fig. 4. Chest CT scan of the child in the pediatric department of PNE "ZRCDCPP" ZRC.

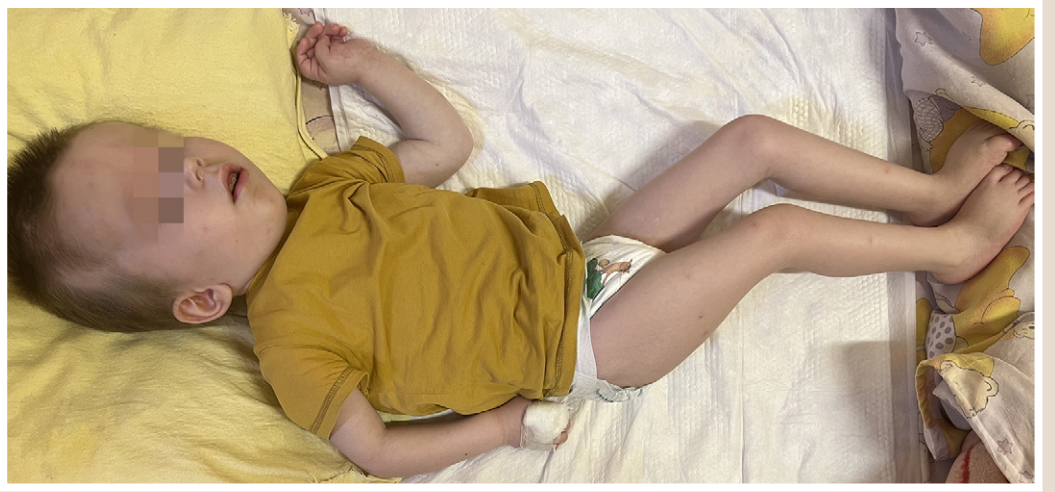

Fig. 5. The child 1 month before discharge from the department.

consolidation area in left S5 was determined, also without dynamics (*Fig. 4*).

A month before discharge, the child had no seizures (*Fig. 5*). In the future, he was recommended to be followed up by a family doctor and a pediatric neurologist at the place of residence.

Discussion

In this clinical case, we can see a comorbidity in the context of a combination of severe brain malformation and pulmonary TB. After birth, the child spent almost six months in the neonatal intensive care unit. After that, the child was not examined by a pediatrician, as the family was in difficult life circumstances. When the child was almost 4 years old, the family decided to register a disability for the main disease. It was during this period that changes were accidentally detected, which were initially regarded as pneumonia. On discharge, appropriate treatment was prescribed, but the mother refused further treatment and examination.

After a short period of time, the child was admitted to the pediatric department of PNE "ZRCDCPP" ZRC for further examination for TB, where he was later diagnosed with pulmonary TB. First of all, all family members were examined. The enquiry reviled that the child was taken care of not only by parents, but also by the grandmother living apart from the family. On X-ray TCO examination, the parents were not detected with changes in the lungs found in the grandmother. When gathering information about her health status, it was learnt that she had previously suffered from TB and received treatment in another region. During further examination, sensitive *Mycobacterium tuberculosis* (MBT) strains were found in her sputum. This condition was considered as recurrent TB with subsequent hospitalization and treatment.

Thus, in that situation, the grandmother was the index patient (IP). In that case, the child was a household contact defined by the WHO as a person, who used the same living space for at least 7 consecutive days during the 3 months prior to the diagnosis of TB in the index case [13].

When the child was hospitalized, his neurological condition was severe, with a serious motor deficit and profound cognitive impairment. The boy was completely dependent on all types of daily activities, but at least he was able to swallow liquid food. The child also had mild facial dysmorphism without any classic manifestations of HPE. This confirms the study data that a lower degree of craniofacial defects correlates with a higher life expectancy [14].

In summary, the treatment of pulmonary TB affected by holoprosencephaly is difficult and requires the involvement of medical specialists. The physicians of the department had two main problems. Firstly, on admission to the department, the child had episodic seizures, so before prescribing antituberculosis treatment, the child was examined by the pediatric neurologist and then prescribed anticonvulsant therapy which was quite effective since no repeated episodes were observed. According to a recent review, seizures are common in HPE and can occur in almost 50 % of patients. The specific type of seizure is not considered to be characteristic of the disease, and its frequency may vary during evolution. Also, seizures usually respond well to anticonvulsant therapy, as in our case [15].

Secondly, during the treatment, the child had the single hepatotoxic reaction. This required the drug withdrawal for two weeks and prompted physicians to perform the additional examination of the child. The presence of chronic Epstein–Barr infection was detected, which, in this case, could have been the cause of hepatobiliary adverse effects.

Prenatal screening of pregnant women is important because it allows the detection of alobar holoprosencephaly in the first trimester of pregnancy. Early fetal screening gives parents more time for medical counselling and further decision-making. In this case, the mother was not monitored during pregnancy and did not have any screening and karyotyping.

As we can see, this clinical case confirms that household contacts remain the most important factor in the development of TB in children. An additional important risk factor is the absence of vaccination against TB.

Conclusions

1. Alobar holoprosencephaly is a rare but quite severe brain malformation that leads to severe disability and requires a multimodal approach to the management of children in the postnatal period.

2. Prenatal diagnosis is an important and effective tool for detecting this defect in the first trimester of pregnancy, determining its severity and prognosis, which may also require fetal karyotyping.

3. Household contacts remain one of the most important risk factors for the development of tuberculosis in children due to their close proximity.

4. The work on identifying the index patient should be performed not only among parents, but also with other family members related to this household, that is, it should be more extensive.

5. Treatment of tuberculosis in children generally has positive results but requires the involvement of physicians in different specialties due to main diseases and possible side effects.

Prospects for further research in this area are to continue the study on features of TB management in children with comorbidity.

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References

1. Society for Maternal-Fetal Medicine (SMFM), & Monteagudo, A. (2020). Holoprosencephaly. *American journal of obstetrics and gynecology, 223*(6), B13-B16. https://doi.org/10.1016/j.ajog.2020.08.178
2. Nakawa, W., Alkhalil, S., Martini, N., & Alawad, I. (2023). Rare manifestations of alobar holoprosencephaly and the potential causes: a report of two cases. *Annals of medicine and surgery (2012), 85*(2), 252-256. https://doi.org/10.1097/MS9.0000000000000176
3. Ionescu, C. A., Vladareanu, S., Tudorache, S., Ples, L., Herghelegiu, C., Neacsu, A., Navolan, D., Dragan, I., & Oprescu, D. N. (2019). The wide spectrum of ultrasound diagnosis of holoprosencephaly. *Medical ultrasonography*, *21*(2), 163-169. https://doi.org/10.11152/mu-1614
4. Honey, E. M., Bütow, K. W., & Zwahlen, R. A. (2019). Holoprosencephaly with Clefts: Data of 85 Patients, Treatment and Outcome: Part 1: History, Subdivisions, and Data on 85 Holoprosencephalic Cleft Patients. *Annals of maxillofacial surgery*, 9(1), 140-145. https://doi.org/10.4103/ams.ams_50_19
5. Meryem, B., Amine, N., Houssein, O., Siham, E. H., Nazik, A., & Latifa, C. (2023). Antenatal and Postnatal Diagnosis of Semilobar Holoprosencephaly: Two Case Reports. *Global pediatric health*, *10*, 2333794X231156037. https://doi.org/10.1177/2333794X231156037
6. El-Dessouky, S. H., Aboulghar, M. M., Gaafar, H. M., Abdella, R. M., Sharaf, M. F., Ateya, M. I., Elarab, A. E., Zidan, W. H., Helal, R. M., Aboelsaud, S. M., Eid, M. M., & Abdel-Salam, G. M. H. (2020). Prenatal ultrasound findings of holoprosencephaly spectrum: *Unusual associations. Prenatal diagnosis, 40*(5), 565-576. https://doi.org/10.1002/pd.5649
7. Volpe, N., Dall'Asta, A., Di Pasquo, E., Frusca, T., & Ghi, T. (2021). First-trimester fetal neurosonography: technique and diagnostic po-

tential. *Ultrasound in obstetrics & gynecology, 57*(2), 204-214. https://doi.org/10.1002/uog.23149
8. Ariyo, I. J., Mchaile, D. N., Magwizi, M., Kayuza, M., Mrindoko, P., & Chussi, D. C. (2022). Alobar holoprosencephaly with cebocephaly in a neonate: A rare case report from Northern Tanzania. *International journal of surgery case reports, 93*, 106960. https://doi.org/10.1016/j.ijscr.2022.106960
9. Montaguti, E., Cariello, L., Brunelli, E., Youssef, A., Livi, A., Salsi, G., & Pilu, G. (2022). Sonography of fetal holopr osencephaly: a guide to recognize the lesser varieties. *The journal of maternal-fetal & neonatal medicine*, *35*(25), 9717-9723. https://doi.org/10.1080/14767058.2022.2050900
10. Hu, Y., Sun, L., Feng, L., Wang, J., Zhu, Y., & Wu, Q. (2023). The role of routine first-trimester ultrasound screening for central nervous system abnormalities: a longitudinal single-center study using an unselected cohort with 3-year experience. *BMC pregnancy and childbirth, 23*(1), 312. https://doi.org/10.1186/s12884-023-05644-z
11. Malta, M., AlMutiri, R., Martin, C. S., & Srour, M. (2023). Holoprosencephaly: Review of Embryology, Clinical Phenotypes, Etiology and Management. *Children, 10*(4), 647. https://doi.org/10.3390/children10040647
12. Elfarawi, H., Tolusso, L., McGowan, M. L., Cortezzo, D., & Vawter-Lee, M. (2022). Alobar holoprosencephaly: Exploring mothers' perspectives on prenatal decision-making and prognostication. *Prenatal diagnosis*, 42(5), 617-627. https://doi.org/10.1002/pd.6130
13. World Health Organization. (2018). *Latent tuberculosis infection: updated and consolidated guidelines for programmatic management*. Retrieved from https://apps.who.int/iris/handle/10665/260233
14. Weiss, K., Kruszka, P., Guillen Sacoto, M. J., Addissie, Y. A., Hadley, D. W., Hadsall, C. K., Stokes, B., Hu, P., Roessler, E., Solomon, B., Wiggs, E., Thurm, A., Hufnagel, R. B., Zein, W. M., Hahn, J. S., Stashinko, E., Levey, E., Baldwin, D., Clegg, N. J., Delgado, M. R., … Muenke, M. (2018). In-depth investigations of adolescents and adults with holoprosencephaly identify unique characteristics. *Genetics in medicine, 20*(1), 14-23. https://doi.org/10.1038/gim.2017.68
15. Weiss, K., Kruszka, P. S., Levey, E., & Muenke, M. (2018). Holoprosencephaly from conception to adulthood. *American journal of medical genetics. Part C, Seminars in medical genetics, 178*(2), 122-127. https://doi.org/10.1002/ajmg.c.31624