

Incontinentia Pigmenti: A Description of a Clinical Case.

Andrei Adamchuk*

Pediatrician, Neonatologist, Healthcare Institution of the Republic of Belarus, Kletsk Central District Hospital, Republic of Belarus.

***Corresponding Author:** *Andrei Adamchuk, Pediatrician, Neonatologist, Healthcare Institution of the Republic of Belarus, Kletsk Central District Hospital, Republic of Belarus.*

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Abstract

Bloch-Sulzberger syndrome is a rare genetic disease that has both cutaneous and extra cutaneous manifestations, is more common in females and in most cases, intrauterine male fetuses are detected. There is a report of isolated cases of the presence of the syndrome in males. The pathology manifests itself as a result of the NEMO (nuclear factor- κ B essential modulator)/IKK- γ (inhibitor kappa kinase- γ) mutation of the gene located on the Xq28 chromosome. The skin is primarily affected by linearly arranged blisters. In this case, the inflammatory stage may be absent or manifest in utero. Skin manifestations are already present at birth and are difficult to differentiate between non-infectious and non-infectious manifestations. Treatment of skin symptoms of pigment incontinence is often not required as they may resolve spontaneously. However, it should be noted that the early diagnosis of skin manifestations, the significance of which, can be identified by identifying the affected target organs to identify and exclude the detection of fatal complications in the future. This disease is very important for the diagnosis of infectious and non-infectious skin diseases in young children and, in particular, neonatal periods. The presented case is a case from practice in the context of the work of a pediatrician, neonatologist with children with this pathology. In this clinical case, it is possible to trace the clinical picture of the disease in infancy with the further fate of the child for 7 years.

Keywords: *Bloch-Sulzberger syndrome; incontinentia pigmenti (IP); antibiotic resistance*

Introduction

Primarily with this pathology, pediatricians and neonatologists meet. The difficulty in accurate diagnosis lies in the need for rapid etiotropic therapy for a newborn with infectious purulent diseases in children with a high risk of intrauterine infection, which leads to frequent unreasonable therapy with antimicrobial drugs. Further spontaneous involution of these elements of the rash is regarded as a successful outcome of treatment. The newborn, together with his mother, is discharged home with a deliberately incorrect diagnosis, and the subsequent recurrence of the rash leads to stress for both the mother and the child.

Clinically, the pigment incontinence syndrome evolves (from vesicular elements to a linear or circular hypo pigmented stripe pattern with no hair or sweat glands) with frequent involvement of a number of tissues and organs, such as hair, teeth, nails, eyes, and the central nervous system. The prognosis for this disease is often favorable but depends on the degree of involvement of the above organs and systems. The diagnosis is made on the basis of signs of damage to the skin.

Using the example of this case, one can trace the complete clinical picture of the disease in infancy with the further fate of the child for 7 years. When working with such patients, we are guided by the principles of dynamic monitoring with parental consent and succession among specialists. Children with this pathology are observed by a dermatologist and pediatrician until they reach adulthood. After the age of majority, the patient is observed only by a dermatologist; patients with this pathology turn to therapists when there are already complications. A pediatrician and a dermatologist jointly examine children 2 times a year and have the opportunity to perform the necessary diagnosis and prescribe appropriate treatment at the early stages of the onset of symptoms of target organ involvement.

Case Presentation

The purpose of the work: to describe a clinical case of observation of a rare pathology "Bloch-Sulzberger"

Patient A. girl, 7 years old.

A full-term girl from the first pregnancy, which occurred against the background of periodic exacerbations of chronic pyelonephritis, the first birth at 39-40 weeks (274 days). Birth weight 3520g, height 51cm, chest circumference 34cm, head circumference 35cm, Apgar score 9/9. At birth, it was visualized on the inner surface of the thighs and lower legs as vesicular rashes in the form of multiple flaccid vesicles up to 2 mm in diameter with transparent serous contents. The results of enzyme immunoassay for toxoplasmosis, cytomegalovirus infection, ureaplasmosis, herpes simplex virus 1, chlamydia are negative. Wasserman's reaction is negative. Blood parameters were within the age norm (RBC- $5.6 \cdot 10^{12}$, HB-156g/l, PLT- $256 \cdot 10^9$, WBC- $18.6 \cdot 10^9$), with the exception of a single manifestation of eosinophilia (18%), which, upon further blood tests, did not repeat. A diagnosis of intrauterine infection, vesiculopustulosis was made, empirical therapy with cefotaxime 50 mg/kg was prescribed, and the rash was treated with potassium permanganate solution. The general somatic condition of the child is not disturbed, the appetite is good, breastfeeding. Within 7 days, the elements dried up, antibiotic therapy was completed, the child was discharged home with further recommendations for observation. Within a month, my mother noted frequent intestinal colic. Mom continued breastfeeding. In the study of the stool, inflammatory changes were detected (color - yellow-green, mushy consistency, squamous epithelium 0-1, WBC 8-10, RBC 4-6, pH 5.9, bacterial flora +++) *St. Aureus* resistant to amoxicillin. Treatment with a 10 day course of probiotics and bacteriophage was positive.

By the end of the first month, the rash returned in the same volume and at the same location. The child was sent to the regional children's hospital.

The infectious nature of the disease was not confirmed. Consultations were held with a dermatologist, neurologist, ophthalmologist, and cardiologist. Associated pathology was not revealed, only the abnormally located chord of the left ventricle without changes on the ECG. The final diagnosis was made: pigment incontinence syndrome, additional chord of the left ventricle. The child received antibiotic therapy to prevent bacterial infection, glucocorticoids, antiseptic solutions and aniline dyes. The dynamics of the condition is positive: the elements of the rash have dried up, the crusts have been torn off, and the erythema has subsided. The child was discharged home in a satisfactory condition.

During the first year of life, the child had colds without complications. Up to 3 months, the child once again underwent a course of treatment with a probiotic and a bacteriophage due to the increase in the mother's complaints about mucus in the stool and restless sleep.

Relatively late teething (the upper incisors erupted only by the end of the 8th month of life). Subsequent teeth erupted gradually with a difference of 3-5 weeks. No tooth deformities were found.

In the second year of life, the mother began to notice the appearance of warts on the former sites of the rash. When examined by a dermatologist and a pediatrician, it was found that these are hypertrophic papules. A decision was made, taking into account the possible cause of their appearance as a phase of pigment incontinence syndrome development, on dynamic observation for 3 months. The papules began to self-reduce after 2.5 months. The child received no treatment.

Further observation of the child was carried out 1 time in half a year. Neurological examination once a year does not reveal developmental disorders of the nervous system. At the moment, the girl is growing and developing according to the norms. Rash recurrence or progression to other phases has not been established. Further contact with the child and parents continues. During this time, 2 more girls were born in the family, according to the mother, there was one spontaneous miscarriage at 8 weeks.

Discussion

Incontinentia pigmenti (IP) or Bloch-Sulzberger syndrome is a rare (frequency of occurrence 1: 90,000 newborns) genetic anomaly in the development of the ectoderm with a predominant lesion of the skin, hair, nails, teeth and eyes. It is characterized by dysplasia of the outer and middle germ layers and the inability of the basal cells of the epidermis to retain melanin. The pigment begins to accumulate in the intercellular space and melanophores of the dermis.

This disease is mosaic, since genetically distinct tissues from one zygote are present in the body. Caused by IKBKG at the Xq28 locus in approximately 80% of probands, or by X-linked dominant mutations in the NEMO gene. Affected females have a 50% risk of passing the mutant IKBKG allele to offspring. The estimated percentage of live births is 33% unaffected girls, 33% affected girls, 33% healthy boys. Male fetuses are not viable due to inheritance. There are also frequent spontaneous miscarriages in women carriers of the mutant gene.

There are 2 forms:

The first form is staged, which has 4 stages or phases: inflammatory, hypertrophic, pigmentary, atrophic.

The second form - there is no inflammatory phase, manifested by warty growths that can be confused with nevi. These growths can begin to wither as early as 2 years of age and persist until puberty or beyond.

The staged form, as mentioned above, has 4 phases:

1. **Inflammatory:** manifested at birth or in the first days after birth as linear stripes or plaques consisting of vesicles with transparent contents, more often located on the limbs or along the circumference of the body. The number of rashes may increase as repeated outbreaks appear, which can last from several days to 1.5 months. For a neonatologist, it is necessary to conduct a differential diagnosis with mastocytosis, bullous impetigo, herpes. When opening the vesicles, erosions with serous crusts are formed. The mucous membranes are not affected, the general condition of the child does not suffer. In the study of peripheral blood, pronounced eosinophilia (30-65%) can be detected. By the end of the 4th month, the stage is resolved, but in acute febrile diseases, relapses may occur throughout the entire childhood period.
2. **Hypertrophic:** after the resolution of the first phase, hypertrophic growths (papules) can form at the site of the rash, similar to warts, which tend to be reduced after 6 months. Most often located on the limbs. Diffuse hyperkeratosis can be found on the soles and palms.
3. **Pigmentary:** the most characteristic phase. It can appear simultaneously with the previous phases and gradually gaining a peak after a few weeks or months. It is characterized by the appearance of areas of hyperpigmentation, always in the axillary and inguinal areas, not always at the site of former rashes, in the form of curls, mesh spots, linear stripes along Blaschko's lines. Having arisen once, it persists throughout the entire period of childhood. During adolescence begins to fade and sometimes disappears, but may persist for life.
4. **Atrophic:** characterized by the presence of patches of depigmentation, which lack hair and sweat glands. These areas are areas of skin atrophy and focal sclerosis, located on the flexor surface of the legs, arms and torso. The phase appears on average after 20-30 years.

About 80% of cases, other defects are observed: alopecia in the parietal region (40%), anomalies of the teeth (80%) and their late eruption, in a third of cases CNS damage and delayed psychomotor development, paralysis, microcephaly. Eye damage occurs in approximately 30% of cases: strabismus, microphthalmos, cataracts. Very rare lesions of the nails and skeleton.

The diagnosis is made on the basis of clinical data, a general physical examination and laboratory tests, with the participation of consulting doctors, in particular, geneticists and dermatologists.

Differential diagnosis is carried out depending on the stage: in the first phase - with bullous dermatosis, the second and third phase - with nevi, warts, keratosis.

The prognosis in most cases is favorable and depends on the degree of involvement of systems and organs.

Treatment also depends on the degree of extracutaneous manifestations and is more often symptomatic, aimed at preventing inflammatory changes and infection. With secondary infection, external therapy with antiseptic solutions and powders is used, with generalization - antibiotics, glucocorticoids.

Conclusion

Newborns and infants with vesiculobullous rashes require careful observation and examination. The main problem is a clear early diagnosis of this pathology, due to the similarity with other epidermal bullous diseases. Since the disease is multisystemic in nature and the staging of manifestations, long-term monitoring of patients with an established diagnosis of Bloch-Sulzberger Syndrome is necessary. Constant dynamic monitoring and timely assistance in detecting target organ damage can improve the quality of life of children and reduce the cost of treatment and rehabilitation. Drawing up a genetic map is also important for the diagnosis of this pathology. Due to the development of high antibiotic resistance of most microorganisms, unreasonable prescription of antibiotic therapy at an early age can lead to serious adaptation disorders (in particular, changes in the intestinal microbiota with subsequent digestive disorders, both transient and chronic) and the formation of a resistant pathological microflora to the most common antimicrobial drugs, which is a clear example of this case.

Conflict of Interest

The authors declare no conflict of interest.

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