

Presentation of an Infant with Nutritional Deficiency Dermatitis as the Initial Manifestation of Cystic Fibrosis

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SUMMARY

Introduction Cystic fibrosis (CF) is a multisystemic autosomal recessive disease most frequently recognized by characteristic respiratory and/or digestive manifestations. Exceptionally rare, as is the case with the infant we are presenting, the initial sign of the disease can be nutritional deficiency dermatitis (NDD).

Case Outline A three-month-old male infant of young and healthy non-consanguineous parents, born at term after the first uneventful pregnancy, was hospitalized due to atopic dermatitis (AD)-like skin changes, failure to thrive and normochromic anemia (Hb 60 g/L). As exclusively breast-fed, failure to thrive was attributed to hypogalactia and skin changes to nutritional allergy, so that, besides exclusion of cow's milk protein and other highly allergenic foods in mother's diet, hypoallergenic milk formula was added to the child's diet. However, dietetic measures were without effect, and the child was re-hospitalized at age 4.5 months, this time in the condition of severe malnutrition with hypoproteinemic edemas, extensive dermatitis, moderate hepatosplenomegaly and recurrent normochromic anemia (Hb 57 g/L). After plasma-free erythrocyte transfusion, correction of hypoalbuminemia and two-week parenteral and semi-elementary nutrition resulted in gradual recovery of the child, also including the resolution of skin changes. Having in mind the clinical course of the disease, as well as the response to applied therapeutic measures, CF was suspected as the cause of the child's problems, which was also confirmed by a high level of sweat chlorine (92 mmol/L) and DNA analysis ($\Delta F508/\Delta F508$).

Conclusion Our experience indicates that NDD, as the initial manifestation of CF, should be also kept in mind in differential diagnosis of the infant's AD-like changes.

Keywords: cystic fibrosis; infant; nutritional deficit dermatitis

INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disease of multisystemic and progressive character [1-3]. It is primarily seen in people of Caucasian origin (1:2000-3000), while in other population groups it is considerably or exceptionally rare [1-6]. The basic disease involves mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene located on the long arm of the chromosome 7 (7q31.2) [7, 8]. There are over 1500 discovered different mutations in this gene that encodes synthesis of the CFRT protein responsible for chloride ion transport at the luminal cell membrane of the respiratory, digestive, reproductive and cutaneous epithelium [2, 8, 9]. The absence, deficit or structural and functional abnormalities of the CFRT protein leads to mucus hyperviscosity of the respiratory, digestive and reproductive systems, and malabsorption of chlorine and sodium in sweat glands [2, 8-11]. Accordingly, clinical features of CF patients are predominantly characterized by respiratory, digestive and reproductive disorders, as well as tendency to dehydration under condition of the

increased sweating [1-6, 8, 9]. The classic form of the disease is manifested by characteristic digestive and/or respiratory disorders, so it is diagnosed before completed 18 years of age in 97%-98% of cases, out of which about 70% is diagnosed during the first two years of birth [6, 12]. In rarer cases, particularly those with milder mutations, the disease can have atypical onset or a milder course, so it remains unrecognized on time or is discovered under the features of some complications [6, 13]. Exceptionally rare, such as is the case of the infant we are presenting, the disease can be manifested by nutritional deficiency dermatitis (NDD) as its initial manifestation [13-17].

CASE REPORT

A 3-month male infant was hospitalized in October 2009 due to dermatitis manifested on the cheek area, perineum, extremities and trunk, with failure to thrive and normochromic (Hb 69 g/L) (Figure 1). He was born after the first uneventful term pregnancy to young and healthy non-consanguineous parents, with

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Figure 1. Our patient with NDD of CF, with erythematous, partially confluent and scaling papules in diaper distribution, face, extremities and trunk

body weight (BW) of 3080 g and body length (BL) of 49 cm. Since birth he has been exclusively breast-fed, with additional daily intake of 400 IU of vitamin D. Skin changes were observed at age of 2 months, first on the cheek, and 10 days before hospitalization in other areas as well. An average increase of BW was about 500 g per month. At that time, etiology of anemia was unknown, and it was corrected with erythrocyte-free transfusion. As exclusively breastfed, his failure to thrive was contributed to hypogalactia, and skin changes to atopic dermatitis (AD) so that, besides exclusion of cow's milk protein and other highly allergenic foods from mother's diet, hypoallergenic milk formula was added to the child's diet. However, these measures, with corresponding care and local application of corticosteroids, were without effect, so the child was re-hospitalized at age 4.5 months, this time in condition of severe malnutrition with generalized hypoproteinemic edemas (total proteins 34 g/L, albumins 16 g/L), extensive dermatitis and recurrent normochromic anemia (Hb 57 g/L). In addition, the child developed hepatosplenomegaly (liver 4 cm and spleen 1 cm below the costal margin), with an increased serum activity of gamma-GT (306 U/L, normal <200 U/L) and transaminases (AST 97 U/L, normal <55 U/L; ALT 79 U/L, normal <62 U/L). Neither alopecia nor nail and mucous membrane changes were present. Abdominal ultrasound detected, other than hepatosplenomegaly, a larger number of smaller cysts in the pancreatic body and tail. After plasma-free erythrocyte transfusion, correction of hypoalbuminemia and two-week parenteral

and semi-parenteral nutrition resulted in full recovery of the infant, also including the resolution of skin changes. Having in mind the clinical course of the diseases, as well as the response to the applied therapeutic measures, CF was suspected as the key cause of the child's problems, which was also confirmed by a high concentration level of sweat chlorine (89 and 92 mmol/L) and DNA analysis ($\Delta F508/\Delta F508$). Since, in the meantime, mother's breast milk dried up, the application of semi-elemental infant formula, additional pancreatic enzymes, essential fatty acids and liposoluble vitamins, as well as complementary feeding, resulted in that child's condition was fully normalized until completed 5.5 years. By 3 years 5 months of age, except for a mild obstructive respiratory syndrome, other CF manifestations were not recorded.

DISCUSSION

Cystic fibrosis presents a multisystemic disease with variable initial presentation [1, 2, 3]. In the neonatal and early infantile period, the classic form of disease is most frequently manifested by meconium ileus, cholestasis syndrome and failure to thrive, and by respiratory and other disorders at the end of the infantile period and later. In a lower number of patients, mainly those with milder mutations, the disease can have a milder and atypical course, so that it is disclosed later, sometimes even in the adult age [12, 18, 19]. An additional problem of timely diagnostics of CF is its concomitant development with diseases featuring similar clinical expression, such as food protein allergy, bronchial asthma, celiac disease and other [20, 21].

Nutritional deficiency dermatitis represents a rare finding in CF [13, 22, 23]. It occurs due to multi-nutritional deficit, above all of essential fatty acids (EFA), of vitamin E, zinc and possibly taurine and copper [13-17, 22-26]. Therefore, it primarily appears in severe and timely unrecognized or neglected forms of disease, and exceptionally rare as its basic initial manifestation, which was the case in our patient [13-17, 24]. NDD in CF presents at 2 weeks to 6 months of age, develops considerably earlier in non-breast than breastfed infants, as erythematous and scaling papules that may be annular in configuration [13, 22]. They develop first in the diaper distribution, periorbital and perioral regions, and then spread to the extremities and progress into extensive desquamating plaques [13, 23, 24]. Alopecia is possible, while mucous membrane or nail involvement is not observed [22]. Besides, more frequent and large stools, failure to thrive, anemia, hypoalbuminemia with periorbital and extremity edema and reduced blood level of zinc, essential fatty acids and vitamin E are recorded in a patient [13]. After confirmed diagnosis and introduction of therapy that implies adequate diet regime (human milk and/or semi elemental formula), pancreatic enzymes, as well as nutritional supplementation with EFA, multivitamins and trace metals, NDD often leads to resolution within 2 weeks [13, 22, 23].

The presented infant is an example of CF with NDD as the first and predominant sign. Although the diagnosis was made at age 4.5 months, a retrograde clear conclu-

sion can be reached that the first signs of NDD of CF occurred already at age 2 months. The diagnosis was made with a delay, because the infant at age 3 months, when first observed, except for dermatitis, severe normochromic anemia (Hb 69 g/L) and a milder form of failure to thrive (500 g per month), had no other signs of CF. Thus, as the child was exclusively breast-fed, the skin changes were diagnosed as sensibilization to nutritional allergens through the mother's milk, which is not so rare at this age, and failure to thrive disorder due to hypogalactia, and accordingly, adequate dietetic measures were undertaken. Explanation for anemia, which was corrected by plasma-free erythrocyte transfusion, was based on possible bleeding or

inadequate tying off the umbilical cord at birth. However, one and a half month later the clinical features of CF and consequently the nature of dermatitis became clear. The diagnosis of CF was confirmed by a high concentration of sweat chlorine (89 and 92 mmol/L) and DNA analysis ($\Delta F508/\Delta F508$). The corresponding treatment resulted in the complete recovery of the infant, also including the disappearance of cutaneous lesions.

In conclusion, CF should be included in differential diagnosis in any infant with AD-like skin changes and failure to thrive. The recognition of NDD as a sign of CF will allow earlier diagnosis and treatment of these patients and may improve their outcome.

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Приказ одојчета с нутритивним дефицитним дерматитисом као почетном манифестацијом цистичне фиброзе

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КРАТАК САДРЖАЈ

Увод Цистична фиброза је мултисистемско аутозомно рецесивно обољење које се најчешће препознаје по типичним респираторним и/или дигестивним манифестацијама. Изузетно ретко, као што је то случај с одојчетом кога приказујемо, почетни знак болести може бити нутритивни дефицитни дерматитис (НДД).

Приказ болесника Тромесечни дечак, дете младих и здравих родитеља рођено из прве нормалне терминске трудноће, примљен је у болницу због промена на кожи налик атопијском дерматитису, заостајања у расту и нормохромне анемије (ниво хемоглобина био је 69 g/l). Пошто је само дојено, лошије напредовање је приписано хипогалактији, док су промене на кожи приписане нутритивној алергији, те је, уз искључење протеина крављег млека и других високоалергогених намирница мајци, исхрани детета додата хипоалергогена млечна формула. Како дијететске мере нису дале жељене резултате, дете је у узрасту од четири

и по месеца поново хоспитализовано, и то у стању тешке малнутриције с хипопротеинемичким едемима, проширеним дерматитисом, умереном хепатоспленомегалијом и рецидивом нормохромне анемије (ниво хемоглобина био је 57 g/l). Након трансфузије деплазматисаних еритроцита, корекције хипоалбуминемije и двонедељне парентералне и семиелементарне исхране, дете се постепено опоравило, а промене на кожи су нестале. Имајући у виду клинички ток болести, као и одговор на примењене терапијске мере, посумњало се на цистичну фиброзу као узрок тегоба детета, што је и доказано високим нивоом хлора у зноју (92 mmol/l) и ДНК анализом ($\Delta F508/\Delta F508$).

Закључак Наше искуство показује да у диференцијалној дијагнози кожних промена налик на атопијски дерматитис код одојчади треба имати у виду и нутритивни дефицитни дерматитис као почетну манифестацију цистичне фиброзе.

Кључне речи: цистична фиброза; одојче; нутритивни дефицитни дерматитис