Coffin-Siris Syndrome In A Four-Year-Old Girl: A Case Presentation

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Citation

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Abstract

Coffin-Siris syndrome is a rare genetic abnormality with undetermined pattern of inheritance.
In this syndrome most frequent findings include: mental retardation associated with coarse features, hypoplasia or absence of the fifth fingernails and fifth distal phalanges, difficulties with feeding and muscular hypotonia in infancy.

We report a 4-year-old girl affected by this syndrome. All presented features apart from macrocephaly and rectal dislocation were typical of Coffin Siris syndrome. Therefore, this girl may represent a new variant of Coffin-Siris syndrome.

INTRODUCTION

Coffin-Siris syndrome (MIM 135900) is a rare genetic abnormality. The first description of the syndrome was published by Coffin and Siris in 1970; they described 3 girls with mental retardation, absent nails of the fifth fingers and hypoplastic distal phalanges [1]. Up to now the pattern of inheritance has not been ultimately determined. What is presumed is autosomal recessive inheritance, yet the disease occurs in girls much more frequently than in boys (4:1). One of the most typical features of the syndrome is absence or hypoplasia of the nails of the fifth fingers. Hence another name of the syndrome – “the fifth digit syndrome”.

So far, around 50 publications have come out, describing over 60 patients with Coffin-Siris syndrome [2]. In most cases, there occur different extents of intellectual handicap or the psychomotor development delay. Apart from changes in the area of fingers and toes, the most characteristic of the syndrome is the face phenotype, including coarse features, thick eyebrows, long eyelashes, flat nasal bridge, anteverted and wide nasal tip, and broad mouth with thick, prominent lips. The hair is usually thin; on the body, however, especially on the face, hypertrichosis may be observed. In single cases such characteristics may resemble MPS type I or syndrome Cornelia de Lange, as well as, in view of changes within the nails, fetal hydantoin syndrome [2, 3, 4].

A diagnosis of Coffin-Siris syndrome is based on a typical clinical picture. A radiological hand examination may be useful to detect hypoplasia or absence of distal phalanges, especially of the fifth finger. At present there are no biochemical or molecular tests capable of confirming the diagnosis [1].

CASE REPORT

A four-year-old girl born from the first, uneventful pregnancy in a spontaneous delivery after 37 week of gestation, with the birth weight of 2950 g, and the Apgar score 9 points. The family history was non-contributory. After birth an anatomic anomaly was recognized, the so-called narrow perineum. The psychomotor development was slightly delayed; she started sitting at the age of 10 months and walking – when she was 18 months old. In the first months of life muscular hypotonia and feeding difficulties were present.

Figure 1

Figure 1: Profile of the head: sparse hair, full cheeks, low set ear, up-turned nose.

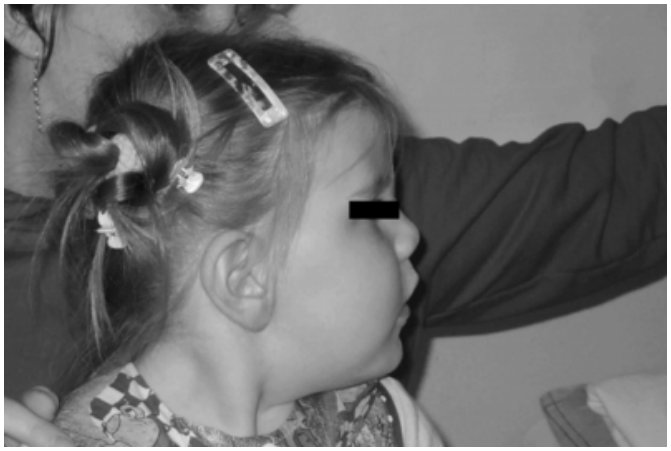


Figure 2

Figure 2: Face: flat nasal bridge with bulbous nasal tip.

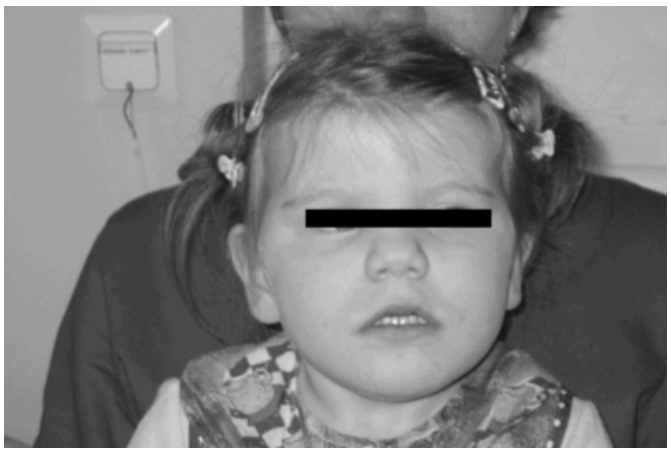


Figure 3

Figure 3: Right hand: hypoplastic nail in fifth digit.

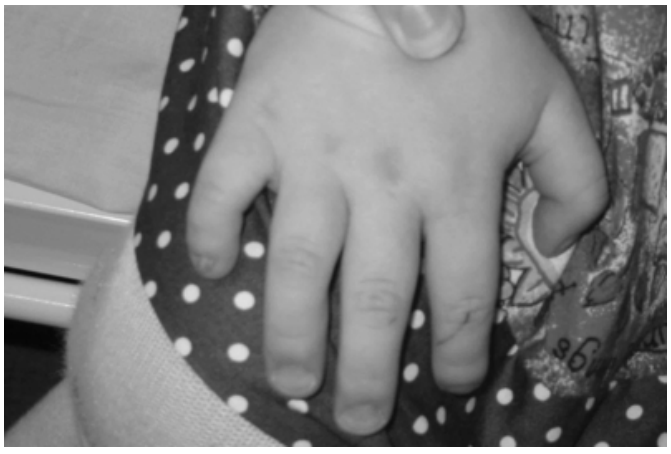
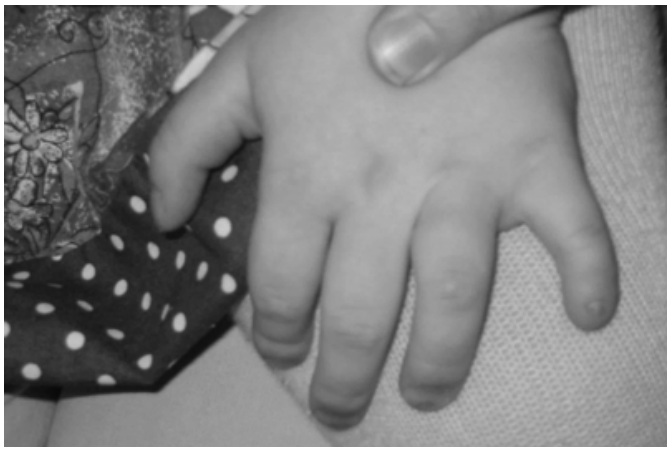


Figure 4

Figure 4: Left hand: hypoplastic nail in fifth digit.

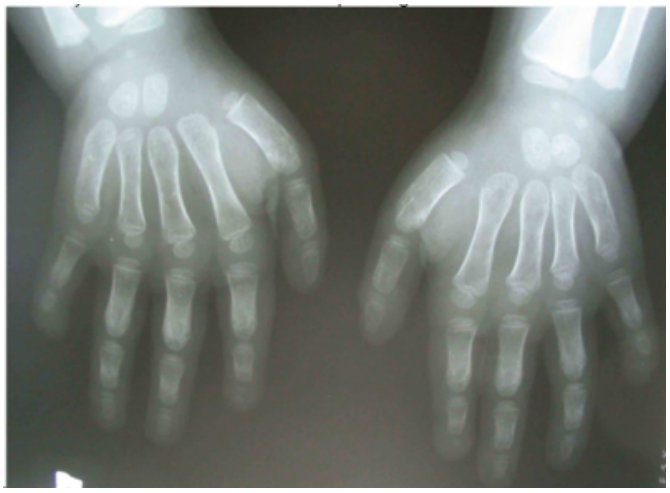


Frequent infections of the upper respiratory tract and urinary system, and febrile seizures twice, at the age of 13 and 17 months were observed. MRI of the head, performed at the age of 3 years, did not present any abnormalities within the brain structures.

A physical examination revealed macrocephaly (head circumference of 59 cm > 97th pc), dismorphic, thickened facial features (flat bridge and anteverted nasal tip, broad mouth and bilateral epicanthal folds), hypoplasia of the fifth finger nails and toenails, brachydactyly, umbilical hernia, slight rectal dislocation and lichenoid changes all over the skin (photos 1, 2, 3 – face; 4, 5 – hands). A neurological examination was normal. The intelligence quotient according to the Leiter scale equaled 75, which is below the average. The passive language was well developed, parallel to the underdeveloped active speech. An X-ray picture of the hand revealed absent distal phalanx of the right fifth finger and the hypoplastic distal phalanx of the left one (fig. 5). In a cytogenetic examination we found the normal female karyotype 46, XX. Metabolic diseases co-occurring with macrocephaly, such as lysosomal storage disorders, peroxisomal disorders, biotinidase deficiency and hypothyroidism were excluded.

Figure 5

Figure 5: X-ray of hands: absence of distal phalanges in both hands.



On the basis of the specific phenotype and the result of the radiological examination of the hand, Coffin-Siris syndrome has been recognized.

DISCUSSION

Coffin-Siris syndrome occurs very rarely. Its genetic background has not been determined so far. In most patients presented in the literature, there were no chromosomal abnormalities. Until now only 2 cases have been diagnosed with balanced translocations within chromosome 7: 46, XY, t(1;7) (q21.3;q34) and 46, XY, t(7;22) (q32;q11.2) [5, 6]. Therefore, the gene responsible for the syndrome occurrence is likely to be located in the q32-q34 region of chromosome 7. In most cases the disease is a result of a de novo mutation, but familial occurrences have also been reported [3, 7, 8].

The cytogenetic examination performed by the method of GTG revealed no abnormalities. The diagnosis was based on both typical dismorphic features of the face: coarse facial features, broad mouth, chubby cheeks, flat and broad nasal bridge, and absent/hypoplastic distal phalanges and the nails of the fifth fingers at both hands, which are pathognomonic of Coffin-Siris syndrome. Apart from that, the psychomotor development delay was noted, especially in the area of active language; in infancy, moreover, muscular hypotonia was present, another typical component of Coffin-Siris syndrome.

In accordance with the literature on the subject, the developmental retardation observed is global; it concerns motor activity, the development of language, especially active speech, and social contacts [9]. Besides, in infancy we may observe feeding difficulties, muscular hypotonia, and excessive flabbiness of joints. While structural defects within CNS such as Dandy-Walker syndrome appear relatively rarely, there frequently occurs microcephaly [10]. The eye's disorders such as myopia, astigmatism, nystagmus or strabismus are characteristic and so are delayed teething and defects of dentition. Cleft palate has been described in this context as well; typically, however, the palate of an individual with Coffin-Siris syndrome is excessively arched. Quite frequently, auricles are also abnormal.

In many cases spinal abnormalities have been recognized: spina bifida, scoliosis, kyphosis and delayed bone age. Less frequently, there occur blepharoptosis or macroglossia. In extreme cases we may come across cardiological disorders (Fallot's tetralogy, ventricular and atrial septal defect), genitourinary abnormalities (cryptorchism, hypospadiasis, absence of the uterus, horseshoe kidney) and hernias (umbilical and inguinal) [9].

Children with the syndrome often have the respiratory system infections. Also typical, mostly in infancy and childhood, are feeding difficulties. In the presented case both of these symptoms, infections and feeding problems were present. We did not detect any developmental abnormalities of the internal organs; however, it is worth to emphasize, that after delivery umbilical hernia and an anatomic anomaly that has not been described in the syndrome before, rectal dislocation were recognized.

Moreover, there is another symptom which makes our case remarkable. This is macrocephaly, with negative family history. In all the individuals with Coffin-Siris syndrome so far described in the literature, the head circumference was normal or there occurred slight microcephaly. The macrocephaly present in the girl was an indication to perform diagnostic tests for some inborn errors of metabolism. The MRI of the head performed at the age of 3 years excluded structural disorders of the brain. Since the mentioned above examinations did not reveal abnormalities, while other clinical characteristics are consistent with descriptions of the disease, it may be presumed that macrocephaly and other developmental anomalies, such as rectal dislocation, are newly-discovered symptoms of the fifth digit syndrome, symptoms that have not been described yet. In our opinion, the presented case broadens the description of this rare syndrome. We also like to note, that among other genetic disorders characterized by increased head circumference, we considered Simpson-Golabi-Behmel syndrome as a possible diagnosis. This condition, besides

macrocephaly, may present: coarse facial features with wide mouth, developmental delay with seizures, umbilical hernia and nail hypoplasia as features. Although because of the mode of inheritance (X-linked recessive), no other symptoms of overgrowth and characteristic fifth fingers in presented case we decided for Coffin-Siris syndrome diagnosis and conclude that co-occurrence of macrocephaly and typical changes within distal phalanges of the fifth fingers should become an additional diagnostic hint.

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