# CLINICAL CASE

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# Cornelia de Lange Syndrome in a 3.5 Year Old Girl – Case Report

## Zespół Cornelii de Lange u 3,5-rocznej pacjentki – opis przypadku

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## Abstract

Cornelia de Lange syndrome (Brachmann syndrome) is a rare, multiple congenital anomaly defect. The etiology and pathogenesis are not clearly understood. About half of the cases are a mutation in the Nipped-B homolog (NIPBL), which is located on chromosome 5. Phenotypic features include: low birth body weight, short size (dwarfism) and facio-cranial dismorphia. Oral manifestations detected are micrognathia, macroglossia, microdontia and delayed tooth eruption. In addition to that, the syndrome includes defects of the heart, gastroesophageal reflux and mental retardation. Because of complicated pathogenesis of Cornelia de Lange syndrome, recognition is based on detailed medical history, physical examination and genotype analysis. The aim of this report is to present the phenotypic features of Cornelia de Lange syndrome in a 3.5 year old girl. A clinical examination of the oral cavity of a small girl was performed. Her parents came to the Children's Dental Clinic, worried about their daughter's delayed tooth eruption. In the patient's history, we found she was born in the 39$^{th}$ week of pregnancy after a caesarean section. Her weight as a newborn was 2640 g, the length of the body was 49 cm, the head circumference was 30 cm. The girl began teething in her 12$^{th}$ month. Contact with the child was limited (the girl did not talk).The dental examination revealed a small chin, thin lips, eyebrows grown together and long curly eyelashes. The intraoral examinations during the first and second visit (on Feb 8$^{th}$, 2010 and July 19$^{th}$, 2010) revealed a delayed tooth eruption in relation to her age group and widely spaced teeth. Children with congenital anomaly syndrome require multi-disciplinary medical care, because of the many different clinical symptoms (**Dent. Med. Probl. 2012, 49, 2, 305–308**).

**Key words:** Cornelia de Lange syndrome, Brachmann syndrome, symptoms.

## Streszczenie

Zespół Cornelii de Lange (*Brachmann syndrome*) jest rzadkim zespołem wad rozwojowych uwarunkowanych genetycznie. Przyczyna występowania tej choroby nie jest do końca wyjaśniona. Około połowa przypadków (CdLS1) powstaje w wyniku mutacji genu *NIBL* na chromosomie 5. Fenotypowo zespół Cornelii de Lange objawia się małą masą urodzeniową, niskim wzrostem i dysmorfią twarzoczaszki. W obrębie jamy ustnej może występować mikrognacja, makroglossia, gotyckie podniebienie, opóźnione ząbkowanie, oligodoncja, mikrodoncja. Objawom morfologicznym mogą też towarzyszyć: wada serca, refluks żołądkowo-przełykowy, a także różnego stopnia upośledzenie umysłowe. Ze względu na skomplikowaną patogenezę zespołu Cornelii de Lange rozpoznanie opiera się na dokładnym badaniu klinicznym podmiotowym i przedmiotowym oraz analizie genotypu. Celem pracy jest przedstawienie fenotypowych cech zespołu Corelii de Lange u 3,5-letniej dziewczynki. Wywiad lekarski oraz badanie kliniczne jamy ustnej przeprowadzono u dziewczynki, której rodzice zgłosili się do Kliniki Stomatologii Dziecięcej zaniepokojeni opóźnionym ząbkowaniem u córki. Z wywiadu ustalono, że dziecko pochodzi z ciąży rozwiązanej w 39. tygodniu cięciem cesarskim. Waga dziecka wynosiła 2640 g, długość ciała 49 cm, obwód główki 30 cm. Rozpoczęcie ząbkowania nastąpiło w 12. miesiącu życia. Kontakt z dzieckiem był utrudniony (dziewczynka nie mówi). W badaniu stomatologicznym zewnątrzustnym stwierdzono małą bródkę, drobne, cienkie wargi oraz zrośnięte brwi i długie rzęsy. Na podstawie wywiadu i badania wewnątrzustnego przeprowadzonego podczas 2 wizyt (8.02 i 19.07.2010 r.) stwierdzono opóźniony czas ząbkowania w stosunku do wieku metrykalnego dziecka oraz szerokie szpary międzyzębowe. Dzieci z rozpoznanymi zespołami genetycznymi z powodu mnogości i różnorodności objawów klinicznych wymagają wielospecjalistycznej opieki (**Dent. Med. Probl. 2012, 49, 2, 305–308**).

**Słowa kluczowe:** zespół Cornelii de Lange, zespół Brachmanna, objawy kliniczne.

Multisystem developmental disorder is a set of several congenital conditions which create a particular clinical picture. The kind of conditions depends on the type of tissue, the disorder of the development mechanism and the time the condition occurred. Multisystem developmental disorders, which most often result from gene mutations [1], became a separate condition after several similar cases were reported.

Cornelia de Lange syndrome (CdLs), otherwise known as Brachmann syndrome, is a rare multisystem developmental disorder with a genetic background. It is more likely to occur in females than males (F : M ratio 1.3 : 1) with the incidence estimated at 1 in 30,000 to 1 in 50,000 births [2]. 105 cases of CdLs have been diagnosed since 2001 [3]. The name comes from Cornelia de Lange (1933) and Brachmann (1916) who first described the syndrome [4]. The cause of the condition is not very clear. Around half of the cases (LdCs1) have been found to result from NIPBL gene mutation which is located on chromosome 5. The mutation of the SMC1L1 gene, which is located on the X chromosome, as well as of the SMC3 gene from chromosome 10, are responsible for less than 5% of cases and are connected to CdLs type II [5–8].

The physical phenotype of Cornelia de Lange syndrome includes low birth body weight, short size (dwarfism) and facio-cranial dismorphia. The latter includes low-set auricles, hirsutism, synophrys, hypertelorism, long eyelashes and anteverted nostrils, while the oral cavity may manifest micrognathia, macroglossia, high arched palate, delayed tooth eruption, oligodontia, and microdontia. Other common conditions include polidactyly (extra fingers), syndactyly (fingers grown together), oligodactyly (lack of fingers), and an extra rib. Beside morphological characteristics, other conditions may occur, for example gastroesophageal reflux disorder, cardiac disorder, mental retardation of varying degrees, hyperactive behavior and autism [4, 9].

Due to the complex pathogenesis of the syndrome, its diagnosis relies on a detailed medical history, physical examination and genotype analysis.

The aim of the present work is to show the phenotypic features of Cornelia de Lange syndrome in a 3.5 year old girl.

Medical history taking and a dental clinical trial were conducted at the request of the parents, who reported to Pediatric Dentistry at Poznań Medical University concerned about the delay in their daughter's teething. General health history data was gathered from medical records.

The history showed that the patient was born to a first-time mother by means of Caesarean section in her 39$^{th}$ week of pregnancy. The child weighed 2640 g, measured 49 cm and had a head circumference of 30 cm. She was fed artificially. She started teething at 12 months, sitting at 9 months and walking at 14 months.

Currently the patient is under the constant supervision of a neurologist, cardiologist (due to cardiac disorder), and nephrologist (due to vesicoureteral reflux).

Clinical examination showed short fingers. Communication is hindered – the girl does not talk.

Extraoral examination demonstrated a small chin, thin lips, eyebrows that meet at the midline, long eyelashes and low-set and protruding auricles (Fig. 1). The first intraoral examination indicated the existence of eight teeth (51, 52, 54, 61, 62, 64, 71, and 81), many of them widely spaced, mainly in the mandible (Fig. 2). The follow up examination 5 months later showed three more teeth which had erupted (72, 82, and 74). No dental caries or other dental abnormalities were found. Nevertheless, teething could be described as late in relation to her age group.

During both visits, to prevent dental caries, the fluoride varnish Duraphat® by Colgate® was applied.

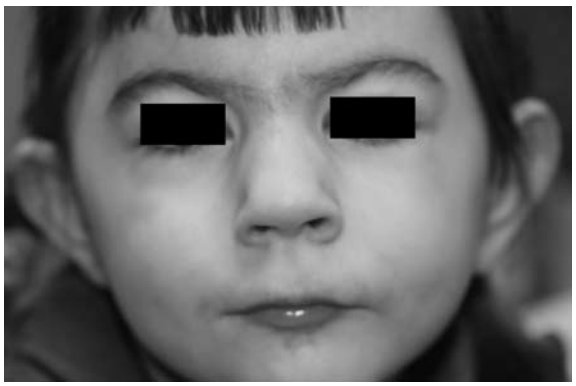

**Fig. 1.** Facial appearance of patient with Cornelia de Lange syndrome

**Ryc. 1.** Twarz pacjentki z zespołem Cornelii de Lange

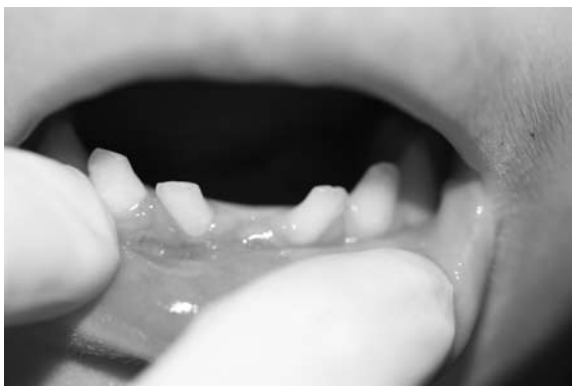

**Fig. 2.** Intraoral appearance of the patient

**Ryc. 2.** Obraz jamy ustnej u pacjentki

The parents were also instructed about the importance of brushing the girl's teeth with a toothpaste containing fluoride, about the correct diet and advised against giving the girl sweet drinks at night, a mistake they had often made.

Six months later the child was admitted with dental caries symptoms. The examination showed the presence of all the deciduous teeth in the maxilla, lack of the second mandibular molars and symptoms of acute dental caries which was visible on the labial surfaces of teeth no. 52, 51, 61, and 62 and on the occlusal surfaces of teeth no. 64 and 54. As a consequence of the child being uncooperative and the type of defects (large and even areas), which make retention difficult, the ACT (Arresting Caries Treatment) method was applied. This non-invasive preventive and healing method includes manual treatment of cavities, application of silver compounds and brushing teeth with toothpaste containing fluoride.

During the visit, silver nitrate ($AgNO_3$) was applied, then Lugol iodine for precipitation. Four follow-up visits, once a week for four weeks, in her place of living, were recommended. Ozone therapy was considered as an alternative, but eventually, it was discarded due to the parents' inability to travel with their child to the nearest health center equipped with the required apparatus.

Due to the variety and the composition of disorders, as well as the different functional states of patients with Cornelia de Lange syndrome, an individual prevention and treatment plan is required for each of them with continuous control from a number of specialist physicians. Because of the common occurrence of hypertonia and epilepsy, neurological care is indispensable. Virtually all cases include gastroesophageal reflux disease. However, if the condition is diagnosed at a young age, the symptoms disappear thanks to preventive measures. Ophthalmological care may prevent conjunctival and corneal ulcer (caused by thick eyelashes growing into the meibomian glands area) and blepharoptosis [10]. Patients with the Brachmann's syndrome often have a congenital cardiac disorder.

Among the specialist physicians, dentists should also definitely be a part of the team monitoring the health of pediatric patients with Cornelia de Lange syndrome. Various methods of dental caries prophylaxis need to be seriously considered. Moreover, mental retardation, autism and increasing self-injurious behavior may result in specific oral cavity conditions such as dental trauma and soft tissue trauma [4]. Another serious issue is gastroesophageal reflux disease, because its prolonged conditions result in tooth erosion. Intensive prevention and parents' health education covering hygiene and eating habits is of utmost importance, as through such measures, the formation of carious cavities, whose treatment frequently require general anesthesia, may be averted. Eventually, proper dental care may bring about positive results not only for the patient's oral cavity, but for the whole well-being of the children affected by Cornelia de Lange syndrome.

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