Uchida Y, J Altern Complement Integr Med 2023, 9: 351
DOI: 10.24966/ACIM-7562/100351

HSOA Journal of
Alternative, Complementary & Integrative Medicine

Review Article

Developmental Process and Interventions in Long-term Survivors of Campomelic Dysplasia: A Narrative Review

Yuka Uchida*

Abstract

Campomelic Dysplasia (CD) is a rare genetic disorder affecting skeletal, genital and facial development. It has been regarded as prognostically unnecessary, but in recent years the number of cases of long-term survival has increased. There is characteristic facial and bony dysplasia, often associated with respiratory failure. Delayed motor development and mental retardation are also often present. This review article reviews relevant research articles focusing on the developmental process of children with CD and discusses the need for developmental support. There are few studies on development in patients with CD, although there are studies on diagnosis and medical treatment. There are also no studies on the support needed by long-term survivors of CD in their daily and social lives, and further research is required.

Keywords: Campomelic dysplasia; Development; Genetic disorder; Physiotherapy; Skeletal dysplasia

Introduction

Campomelic dysplasia (CD) is a rare genetic disorder that affects the development of the skeleton, reproductive system, and face. It is characterised by symptoms such as cleft palate, flat front, curved and shortened long bones, hip dislocation, underdeveloped lungs and chest, laryngomalacia, and ambiguous genitalia. And it is also one of skeletal dysplasia. Many affected infants die in the neonatal period due to respiratory failure, and CD has been considered a poor prognosis. However, there have been reports of long-term survival cases in recent years. Long-term survival cases of patients with CD are known to be Ischiopubic-patella syndrome (IPP), with two possibilities concerning chromosomes: mosaicism of SOX9 mutations and chromosomal rearrangements involving chromosome 17q [1,2]. IPPs are characterised by dysplasia of their lower limbs.

We previously reported on developmentally supportive interventions for a child with CD undergoing long-term hospitalisation [3]. Despite the limited environment of the Growing Care Unit (GCU) and continuous use of respiratory support, we observed improvements in motor and cognitive development. However, there were no previous studies on physiotherapy interventions for children with CD at the time of our case report and present.

Developmentally supportive interventions are essential for children with CD as long-term survivors. This narrative review aims to (1) review the developmental process of children with CD, the risks associated with their growth and the treatment, and (2) discuss the necessity of physiotherapy interventions for children with CD.

Methods

The literature search was conducted between February and March 2023. The author carried out all searching, screening, and analysis. The following databases were used for the search: MEDLINE (Ovid), PubMed, Google Scholar®, and for Japanese searches Igaku Chuo Zasshi, CiNii.

Developmental process and treatment

The keywords 'campomelic dysplasia AND (treatment OR intervention)' were used in the literature search on the developmental process of children with CD, the risks associated with their growth and the treatment given. In addition, articles that did not clearly describe the development level, motor function and cognitive function of the cases during the review as their title, abstract and full-text content, and 18 were included in the analysis.

Physiotherapy interventions

The keywords 'campomelic dysplasia AND (child OR children OR infant) AND (physiotherapy OR therapy OR childcare)' were used in the literature search on developmentally supportive and physiotherapy interventions for children with CD. Articles were reviewed in their title, abstract and full-text content, and only one was included in the analysis.

Japanese articles

The keyword 'campomelic dysplasia' was used in the literature research on Japanese literature search, and 50 results were produced. These articles were also reviewed using the same procedure.

Results

Of the 22 studies reviewed, one was an intervention study [4], and 21 were case reports. Two studies related to developmentally supportive interventions through physiotherapy and childcare and 20 studies related to diagnosis and treatment by doctors, including intervention studies. One of these 20 studies specified physiotherapy interventions

***Corresponding author:** Yuka Uchida, Japan, E-mail: yukauchida1207@gmail.com

Citation: Uchida Y (2023) Developmental Process and Interventions in Long-term Survivors of Campomelic Dysplasia: A Narrative Review. J Altern Complement Integr Med 9: 351.

Received: April 26, 2023; **Accepted:** Mya 05, 2023; **Published:** May 12, 2023

for the case. Cases ranged in age from 18 months to 34 years and varied in severity. However, there were reports of relatively mild cases in which a mother was found to have CD herself after the birth of her child with CD [2], and most studies reviewed reported cases with multiple signs and clinical features specific to CD.

In the following sections, the analysis results are presented in terms of what developmental process they followed, what symptoms they experienced and what treatment they were given, categorised into developmental stages.

Neonatal Period and Fformer Infancy (during admission)

Some neonates with very mild cases of CD may have no respiratory compromise in the neonatal period [4-6]. Still, even in long-term survivors, many have respiratory failure and are often intubated and managed [2,3,7-14]. Patients are admitted to the hospital until their respiratory status is stabilised. The length of hospitalisation varies but can last up to a year or more [3,12,13]. The problem with long-term hospitalisation is that development can be delayed. After extubation, the patient remains connected to a ventilator, nasogastric tube and other lines during admission. In addition, there are reports of hypotonia [2,3,14,15], and it is expected that spontaneous movement in the neonatal period is expected to be overwhelmingly low due to environmental restrictions and impairment of motor functions.

However, only two studies reported developmentally supportive intervention. In the Growth Care Unit (GCU), the physiotherapist encouraged turning and helped a child with CD undergoing long-term hospitalisation to assume supine and sitting positions that they could not take on her own, which showed not only motor but also cognitive development [3]. In the other study, a childcare worker's intervention with a child with CD during a long-term stay in the NICU helped increase responses to stimulation and spontaneous movement [13].

Infancy (after leaving the hospital)

After a prolonged treatment period, infants are discharged from the hospital when their respiratory status has stabilised [3,12]. This is also the time when cleft palate repair surgery begins to be undertaken. A cleft palate is known to be a major complication of CD. Among the analysed studies, 13 out of 22 cases reported having a cleft palate [2,3,4-6,10,11,14,16-20]. In addition, three studies noted surgery for cleft palate by infancy [17,18,20]. Narimatsu et al., [20] also reported that the appropriate time for cleft palate repair is 18 months and 15 years. Regarding speech development, three cases reported dysarthria [15-17].

Children with CD have gross motor developmental delay and tend to be able to sit up from the age of 1 year onwards; Giordano et al. reported a case of sitting with support at the age of 1 year, Corbreported a case of sitting up at 13 months of age [9], and Fonseca et al., reported a case in which the child achieved a supported sitting position at the age of 1 year and six months [11]. Ray and Bowen also reported a case in which the patient first sat up at 22 months of age, followed by rapid progression of scoliosis [7].

Regarding spinal deformity, some studies have reported progressive spinal deformity from earlier than 22 months of age. For example, Mansour et al. reported cases of progressive spinal kyphosis from 3 months of age and progressive scoliosis from 9 months of age [2]. Neither they indicated when the child was sitting. In the interventional study in which spinal fusion was performed on six children with CD who had spinal deformities, the age of the cases ranged from 2 to 8 years [21]. A case of posterior spinal fusion from the cervical spine to the thoracic spine at 30 months of age and another case of posterior spinal fusion in another area of the cervical spine at the age of 4 years has also been reported [7].

Children with CD begin to stand at around 1.5 years of age and tend to be able to walk at 2 to 3 years of age [2,7,11,15-17]. There are reports of plastic braces and Achilles tendon lengthening and dissection in cases of severe clubfoot; Ray and Bowen showed a case which started walking with plastic lower limb braces at 2 to 3 years of age, but after surgical treatment such as lengthening Achilles tendon at five years and seven months, and spinal fusion A case is reported in which the patient was able to walk again with a brace and plastic lower limb orthosis [7]. Maffulli et al. reported a case where the patient was able to walk at the age of 17 years and was treated conservatively with massage, physiotherapy intervention and strapping. However, one lower limb was treated with Achilles tendon lengthening and posterior dissection at the age of 5 years and was able to walk again [16]. Still, the child had restricted range of motion of the hip and flexion contracture of the knee [16].

School age and adolescence

In this stage of development, school begins. No reports focused on school life, but there were studies of cases with special support needs; Mansour et al. reported a case of a child with moderate learning difficulties who attended a special needs school [2]; Corbani et al., reported a case of a child with mild mental retardation who entered a special needs school [15]; Okamoto et al., reported a case of a child with motor skills difficulties with sitting and standing and mental retardation who entered a special needs school [12]; Castori et al., reported a case of a child who received a programme of special support in school [7].

Some articles reported that intelligence was normal [1,2,11,16,17], but many studies reported that the children with CD had mental retardation as well as gross motor developmental delay [2,3,4,6,12,14,15,19,22].

Adulthood

Only one study described the motor function and intellectual level in adulthood: Takano et al. reported a 34-year-old woman with CD who had short stature, cervicothoracic deformity, cleft palate (with previous post-repair surgery), severe intellectual disability and leg length difference [22]. She was able to stand and walk but easily tripped and fell on her longer lower limbs and had a history of five fractures between the ages of 28 and 31 years. She also had hypertension, tachycardia and mild aortic regurgitation, for which she had been on medication since she was 33.

Discussion

For low birth weight infants with low tone and significant motor developmental immaturity, combined tactile stimulation and joint exercises [23] have been reported to improve motor development at four months and psychomotor development at two years of age [24,25]. Many reports of birth weight greater than 2500 g for children with CD and low birth weight infants, but it has been reported that they do not develop as per normal milestones after discharge from the hospital. This has been reported even in mild cases without symptoms of respiratory distress in the neonatal period, with delayed acquisition of sitting and walking, learning disabilities and delayed mental

development [5,15]. Therefore, developmental support from the neonatal period could encourage the development of children with CD. However, as this review revealed, there are very few studies on developmentally supportive interventions, and further research is needed.

A case of a child with CD who has a respiratory failure in the neonatal period, but was able to take oral intake after her respiratory status had stabilised, has been reported [12]. The problem here is oral sensitivity. It has been suggested that there is an appropriate period for the start of suckling, including taste and touch and pressure stimulation of the pharynx [26,27]. Not experiencing oral intake at the most appropriate period can lead to hypersensitivity, leading to feeding refusal. Interventions are needed from the neonatal period to prevent feeding refusal later in development. It is important for the development of children with CD that physiotherapists, as well as speech-language pathologists, gently touch the oral cavity to assess sensations and help make the experience stimulating.

Regarding spinal fusion for spinal deformity in CD, Thomas et al. stated that although there is a risk of paraplegia, it affects cardiopulmonary function and early, aggressive treatment is important [21]. They also concluded that bracing is an option but does not stop progression, suggesting that surgical treatment is more effective [21]. However, research is needed on the long-term changes in quality of life after surgery for spinal deformity. This is because even if the spinal deformity improves, the quality of life (QOL) could still be reduced. A study on changes in QOL after surgery for scoliosis in patients with neuromuscular diseases reported improved QOL in cerebral palsy and muscular dystrophy but not in spina bifida, concluding that the quality of evidence is low [28]. It has also been reported that a 16-year-old child with athetotic cerebral palsy who underwent spinal fusion surgery had difficulty turning over after surgery, which he was able to do before surgery [29]. Therefore, it can be said that careful consideration should be given to the children's QOL regarding surgery for spinal deformity.

No studies have investigated the difficulties in daily life, and it is not clear what support is needed by long-term survivors with CD. As is the case for skeletal dysplasia, most studies have focused on medical models such as medical treatment and diagnosis. In contrast, very few studies have focused on social models. For non-CD skeletal diseases, very few studies related to social models, e.g. in congenital spondyloepiphyseal dysplasia aged 2 to 69 years [30]. Takigawa et al. reported a study in which patients aged 2-69 were surveyed about their social life [31]. Furthermore, for chondrodysplasia, the most frequent skeletal dysplasia, Penny et al. reviewed the literature on lifelong musculoskeletal, neurological, cardiopulmonary, ear, nose and throat disorders and complications, using an extended model of ICF, and discussed the support needed [32]. For patients with osteoporosis, the Screening Tool for Everyday Mobility and Symptoms (STEMS) has been developed to assess mobility and symptoms such as pain patients with osteoporosis. If more cases are collected, changes over time can be monitored to determine the need for intervention and treatment. With the recent increase in the number of long-term survivors among patients with CD, research related to social models is needed. The knowledge of the reality of social life and the prediction of functional prognosis would be beneficial not only for supporters but also for the patients themselves and their families.

Conclusion

In recent years, with an increasing number of long-term survivors with CD, it is expected that they will have to live with and treat a variety of complications. Interprofessional interventions tailored to developmental and life stages will become increasingly important. Developmentally supportive interventions will be necessary as this disease, such as CD, is slow but developing. As the patient grows, spinal deformities and joint pain problems will emerge. Physiotherapy interventions, as well as orthotics and surgery, will need to be provided accordingly. Further research on the long-term course of children with CD is required to know when and what interventions are necessary.

References

1. Unger S, Scherer G, Furga A (2021) Campomelic dysplasia. University of Tsukuba, Japan.
2. Mansour S, Offiah AC, McDowall S, Sim P, Tolmie J, et al. (2002) The phenotype of survivors of campomelic dysplasia. Journal of medical genetics 39: 597-602.
3. Uchida Y, Mikiko H, Yuu U, Naoko S, Ono H, et al. (2021) A Case of Developmentally Supportive Interventions for a Child with Campomelic Dysplasia. Physical Therapy Japan 48: 420-426.
4. Normann EK, Pedersen JC, Stiris G, Hagen CB (1993) Campomelic dysplasia--an underdiagnosed condition? European journal of paediatrics 152: 331-333.
5. Matsushita M, Kitoh H, Kaneko H, Mishima K, Kadono I, et al. (2013) 'A novel SOX9 H169Q mutation in a family with overlapping phenotype of mild campomelic dysplasia and small patella syndrome. American journal of medical genetics. 161: 2528-2534.
6. Castori M, Bottillo I, Morlino S, Barone C, Cascone P, et al. (2016) Variability in a three-generation family with Pierre Robin sequence, acampomelic campomelic dysplasia, and intellectual disability due to a novel ~1 Mb deletion upstream of SOX9, and including KCNJ2 and KCNJ16. Birth defects research Part A Clinical and molecular teratology 106: 61-68.
7. Ray S, Bowen JR (1984) Orthopaedic problems associated with survival in campomelic dysplasia. Clinical orthopaedics and related research 185: 77-82.
8. Thong MK, Scherer G, Kozlowski K, Haan E, Morris L (2000) Acampomelic campomelic dysplasia with SOX9 mutation. American journal of medical genetics 93: 421-425.
9. Giordano J, Prior HM, Bamforth JS, Walter MA (2001) Genetic study of SOX9 in a case of campomelic dysplasia. American journal of medical genetics 98: 176-181.
10. Khoshhal K, Letts RM (2002) Orthopaedic manifestations of campomelic dysplasia. Clinical orthopaedics and related research 401: 65-74.
11. Fonseca AC, Bonaldi A, Bertola DR, Kim CA, Otto PA, et al. (2013) The clinical impact of chromosomal rearrangements with breakpoints upstream of the SOX9gene: two novel de novo balanced translocations associated with acampomelic campomelic dysplasia. BMC medical genetics 14: 50.
12. Okamoto T (2014) Climocal Courses of Five Patients with Various "Lethal" Skeletal Dysplasia. J Jpn Pediatr Soc 118: 1229-1236.
13. Oka M, Tsuchiya Y (2015) Initial Movements and Interactions of a Child With Profound and Multiple Disabilities and Severe Medical Complications: A Case Study. Jpn J Spec Educ 53: 275-284.
14. Matsumoto A, Imagawa E, Miyake N, Ikeda T, Kobayashi M, et al. (2018) The presence of diminished white matter and corpus callosal thinning in a case with a SOX9 mutation. Brain & development 40: 325-329.

15. Corbani S, Chouery E, Eid B, Jalkh N, Ghoch JA. et al. (2011) Mild Campomelic Dysplasia: Report on a Case and Review. Molecular syndromology 1: 163-168.

16. Maffulli N, Blakeway C, Fixsen JA (1993) Long-term follow up of a case of kyphomelic dysplasia. Orthopedics 16: 86-89.

17. Lecointre C, Pichon O, Hamel A, Heloury Y, Calemard LM, et al. (2009) Familial acampomelic form of campomelic dysplasia caused by a 960 kb deletion upstream of SOX9. American journal of medical genetics 149: 1183-1189.

18. Kaissi AA, Fröhlich AE, Ryabykh S, Ochirov P, Kenis V, et al. (2016) Spine malformation complex in 3 diverse syndromic entities: Case reports. Medicine 95: 5505.

19. Pasupathy M, Radhakrishnan V, Adenwalla H, Narayanan P (2016) A case report of acampomelic campomelic dysplasia and operative difficulties in cleft palate reconstruction. Indian journal of plastic surgery: official publication of the Association of Plastic Surgeons of India 49: 253-257.

20. Narimatsu K, Iida A, Kobayashi T (2022) Palatoplasty for the patient with campomelic dysplasia-report of a case and review of the literature. Cleft Palate Craniofac J 59: 132-136.

21. Thomas S, Winter RB, Lonstein JE (1997) The treatment of progressive kyphoscoliosis in camptomelic dysplasia. Spine 22: 1330-1337.

22. Takano T, Ota H, Ohishi H, Hata K, Furukawa R, et al. (2021) Adult acampomelic campomelic dysplasia and disorders of sex development due to a reciprocal translocation involving chromosome 17q24.3 upstream of the SOX9 gene. Eur J Med Genet 64: 104332.

23. Field TM, Schanberg SM, Scafidi F, Bauer CR, Vega-Lahr N, et al. (1986) Tactile/kinesthetic stimulation effects on preterm neonates. Pediatrics 77: 654-658.

24. Procianoy RS, Mendes EW, Silveira RC (2010) Massage therapy improves neurodevelopment outcome at two years corrected age for very low birth weight infants. Early Hum Dev 86: 7-11.

25. Ho YB, Lee RS, Chow CB, Pang MY (2010) Impact of massage therapy on motor outcomes in very low-birthweight infants: randomized controlled pilot study. Pediatr Int 52: 378-385.

26. Illingworth RS, Lister J (1964) The critical or sensitive period, with special reference to certain feeding problems in infants and children. J Pediatr 65: 839-848.

27. Shinozaki M, Kawasaki Y, Uchida T (2004) Difficult cases of training for ingestion in a rehabilitation clinic for disabed children. The Japanese Journal of Dysphagia Rehabilitation 8: 55-63.

28. Mercado E, Alman B, Wright JG (2007) Does spinal fusion influence quality of life in neuromuscular scoliosis? Spine 32: 120-125.

29. Oohira, D, Ichiki K, Ishizaka I (2010) The influence of instrumentation for scoliosis on posture and movement in a child with athetospastic cerebral palsy. Research bulletin of Special Education Center 2: 95-102.

30. Takigawa K, Haga N (2002) Social life of patients with congenital spinal epiphyseal dysplasia. The Japanese Journal of Rehabilitation Medicine 39: 719-726.

31. Ireland PJ, Pacey V, Zankl A, Edwards P, Johnston LM, et al. (2014) Optimal management of complications associated with achondroplasia. Appl Clin Genet 7: 117-125.

32. Ireland PJ, Savarirayan R, Pocovi T, Tate T, Coussens M, et al. (2021) Development of the Screening Tool for Everyday Mobility and Symptoms (STEMS) for skeletal dysplasia. Orphanet J Rare Dis 16: 40.

HERALD

Advances In Industrial Biotechnology | ISSN: 2639-5665

Advances In Microbiology Research | ISSN: 2689-694X

Archives Of Surgery And Surgical Education | ISSN: 2689-3126

Archives Of Urology

Archives Of Zoological Studies | ISSN: 2640-7779

Current Trends Medical And Biological Engineering

International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X

Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276

Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292

Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370

Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594

Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X

Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562

Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608

Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879

Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397

Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751

Journal Of Aquaculture & Fisheries | ISSN: 2576-5523

Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780

Journal Of Biotech Research & Biochemistry

Journal Of Brain & Neuroscience Research

Journal Of Cancer Biology & Treatment | ISSN: 2470-7546

Journal Of Cardiology Study & Research | ISSN: 2640-768X

Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943

Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771

Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844

Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801

Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978

Journal Of Cytology & Tissue Biology | ISSN: 2378-9107

Journal Of Dairy Research & Technology | ISSN: 2688-9315

Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783

Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X

Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798

Journal Of Environmental Science Current Research | ISSN: 2643-5020

Journal Of Food Science & Nutrition | ISSN: 2470-1076

Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X

Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566

Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485

Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662

Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999

Journal Of Hospice & Palliative Medical Care

Journal Of Human Endocrinology | ISSN: 2572-9640

Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654

Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493

Journal Of Light & Laser Current Trends

Journal Of Medicine Study & Research | ISSN: 2639-5657

Journal Of Modern Chemical Sciences

Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044

Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X

Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313

Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400

Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419

Journal Of Obesity & Weight Loss | ISSN: 2473-7372

Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887

Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052

Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X

Journal Of Pathology Clinical & Medical Research

Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649

Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670

Journal Of Plant Science Current Research | ISSN: 2639-3743

Journal Of Practical & Professional Nursing | ISSN: 2639-5681

Journal Of Protein Research & Bioinformatics

Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150

Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177

Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574

Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060

Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284

Journal Of Toxicology Current Research | ISSN: 2639-3735

Journal Of Translational Science And Research

Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193

Journal Of Virology & Antivirals

Sports Medicine And Injury Care Journal | ISSN: 2689-8829

Trends In Anatomy & Physiology | ISSN: 2640-7752