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Research Article

Pontocerebellar Hypoplasia: Literature Review and Clinical Study

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1. Abstract

Pontocerebellar Hypoplasia (PCH) refers to a group of rare, progressive, and hereditary neurodegenerative disorders with prenatal onset. Different subtypes have been identified based on the mutations present, and all share common characteristics, such as severe cognitive, linguistic, and motor disabilities. The objective of this study was to conduct a literature review and describe the clinical case of a 79-month-old boy diagnosed with PCH in terms of cognitive, motor, communicative, and linguistic skills. We also report the implications of the results on the therapeutic process and family homeostasis, as well as our reflections on the matter. Four articles that met the inclusion criteria set by the study were added to the review. The results of the psychological and speech therapy assessment indicate intellectual disability, severe language disorder, and dysarthric speech. Knowledge regarding the severity of these cases and the implications for the family of afflicted individuals when the clinical prognosis is uncertain, can contribute to the therapeutic process.

2. Key words

Pontocerebellar hypoplasia; Language; Cerebellar abnormalities; Speech language disorders

3. Introduction

Pontocerebellar hypoplasia (PCH) refers to a group of progressive, severe, and rare neurodegenerative disorders with prenatal onset that affect the development and function of the brainstem and cerebellum, resulting in developmental disorders [1-3]. It is a genetically heterogeneous autosomal recessive condition [4-7]. PCH is a purely descriptive term that implies a reduced volume of the bridge and cerebellum [5].

As of January 2020, 13 PCH subtypes have been recorded in the OMIM Portal [5]. The incidence rate of each subtype is unknown [6, 7].

The disorder has only symptomatic treatment available and has a poor prognosis. Additionally, life expectancy is difficult to determine, since death can occur at any point of development. Typically, however, patients die in late childhood or adolescence, according to most of the cases mentioned, although there is a possibility of survival until adulthood [6].

Descrições neurorradiológicas e genéticas são encontradas na literatura [1-14], porém com poucas informações sobre a evolução desses casos em relação ao neurodesenvolvimento e aprendizado. Some studies report severe changes in motor development, microcephaly, motor and cognitive disorders [2, 5-9]. Despite the existence of descriptions of signs and symptoms in these areas, there are limited data available on the characterization of the development of the patient. Additionally, currently no studies present the phenotypic profiles of the disorder in terms of global development and communication. The families of patients with rare and severe disorders deal with the uncertainties of the future and the poor prognoses, which can cause additional suffering and difficulties in adhering to the therapeutic process [15].

In view of the above, the objective of this study was to conduct a literature review and describe the clinical case of a 79-month-old boy diagnosed with PCH, particularly in terms of cognitive, motor, communicative, and linguistic skills, as well as to report the implications of the results on the therapeutic process, as well as on family homeostasis.

4. Materials and Methods

Two bibliographic searches were carried out to find studies describing developmental skills and/or phenotypic profiles of cognitive, motor, communicative, and linguistic skills in individuals with PCH. The searches were performed in national and international databases: Lilacs, PubMed, Scopus, Scielo, Web of Science, and EMBASE. The descriptors were selected after consulting the Health Sciences Descriptors (DeCS-BVS). The survey period covers 2000-2020.

The descriptors were as follows: pontocerebellar hypoplasia OR cerebellar hypoplasia, AND (Language OR Cognition OR Cognition Disorders OR Speech OR Language Development Disorders

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OR Language Disorders OR Language Tests OR Language Therapy OR Rehabilitation of Speech and Language Disorders OR Speech-Language Pathology OR Speech Disorders OR Language Development) OR ("Language"[Mesh]) OR ("Cognition"[Mesh] OR "Cognition Disorders"[Mesh])) OR "Speech"[Mesh]) OR "Language Development Disorders"[Mesh]) OR "Language Disorders"[Mesh]) OR "Language Tests"[Mesh]) OR "Language Therapy"[Mesh]) OR "Rehabilitation of Speech and Language Disorders"[Mesh]) OR "Speech-Language Pathology"[Mesh]) OR "Speech Disorders"[Mesh]) OR "Language Development"[Mesh])) OR Communicative aspect) OR disorders communication) OR Development of communication).

The inclusion criteria were derived from articles describing neurodevelopmental skills and evolution in the areas of cognition, language, and communication. On the other hand, the exclusion criteria were taken from review articles describing genetic and/or medical aspects without pointing out the evolution in the areas of cognition, motor, language, and communication.

5. Description of the Clinical Case

Ethical procedures were followed (CAE: 42356815.1.0000.5417) and the legal guardian signed a Free and Informed Consent Form.

The patient was male with a chronological age of 79 months, diagnosed with PCH, and born to non-consanguineous parents. The mother reported a planned pregnancy, with prenatal care and no complications. The patient underwent full-term birth, via cesarean delivery, at the 39th gestational week. He was born with a weight of 3,835 grams, a height of 51 cm, an Apgar score of 9/10 in the 1st and 5th minutes, and a head circumference of 33 cm. During early childhood, in addition to weak sucking, the baby had difficulty gaining weight and cried a lot. He was not breastfed, but instead fed from a bottle, from birth to three years of age. Considering neuropsychomotor development, he presented cervical balance at 8 months, sat with support at 12 months, sat without support at 18 months, and grabbed objects, stood up, and took his first steps with support at the age of 2 years. He started marching independently at the age of 3, with a history of constant falls and difficulties in balancing that persists until the present. In terms of communication skills, the patient did not produce sounds and did not smile. His first words occurred at around the age of 5, when he started gaining the ability to control sphincters. He underwent physiotherapy and speech therapy at 8 and 36 months, respectively. Additionally, up until the present, he needs help for all activities of daily living. To control attention and behavior, 1.5 ml of risperidone, divided in three doses, is being administered used daily since he was 63 months old.

At the age of 3, he also underwent imaging tests and the initial results were indicative of cerebellar dot hypoplasia. The neurologist's report pointed out "global developmental delay associated with gait instability (ataxic), with frequent episodes of imbalance" and microcephaly, which suggested the probability of PCH11. He was then referred for further investigation, which revealed hypoplasia of the cerebellum and, to a lesser extent, of the pons, thus confirming cerebellar hypoplasia (Figure 1).

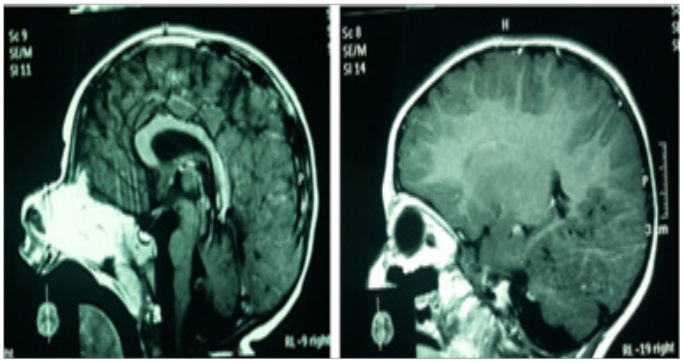

Figure 1: HD: Pontocerebellar hypoplasia

According to information provided by the family, as well as through clinical observations, he used gestures to be understood, pointed to the things he wanted, and produced simple words and phrases, mostly consisting merely of the subject and verb. He initiated communicative acts, and, to draw attention, touched people. The child attended a regular school at infant level IV. In terms of learning, he needed more explanations to understand things, and he acted more slowly than peers due to instability in his motor coordination, which is associated with learning difficulties (sic). He also underwent therapeutic accompaniment in the areas of psychology, occupational, and speech therapy. Professionals inferred that the difficulties observed in the fragile therapeutic evolution were due to failure in retention of stimulated and trained information, which interfered in the consolidation of learning. The family showed concern over the therapeutic processes since the therapeutic gains were considered insufficient.

6. Evaluation Process

The following development assessment procedures were carried out: Language Development Assessment – ADL [16], Development Screening Test DENVER II (Denver II) [17], MacArthur Communicative Development Inventory: First Words and Gestures [18], Nonverbal Intelligence Test (SON-R) [19], Columbia Mental Maturity Test [2], and Pré-WISC [21].

Complementary assessments were made to augment the subtypes in the PCH chart, whose manifestations include hearing loss, visual impairment, and vitamin A and hydroxyvitamin D deficiency. The patient underwent audiological, ophthalmological, and swallowing examinations, as well as complete blood count, all with indices within normative parameters.

7. Results

A total of 443 articles were found in the search involving the combined descriptors. The results of the analysis with the application of

the inclusion criteria are shown in (Figure 2).

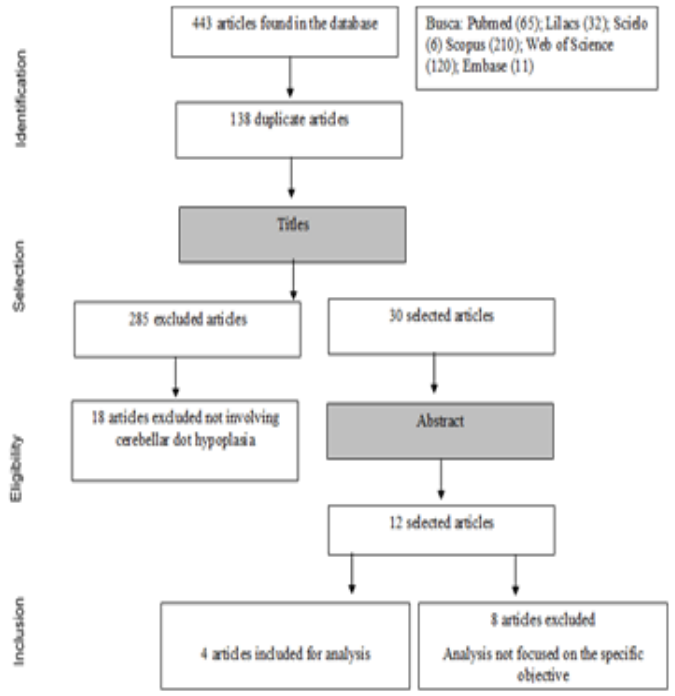

Figure 2: Results of the analysis using the inclusion criteria

Note: Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyzes: the PRISMA Statement. PLoS Med. 2015; 6 (7): e1000097. doi: 0.5123 / S1679-49742015000200017

Chart 1 presents the results of the literature review, with the studies that reported information on clinical characteristics and communication skills of individuals with PCH (Chart 1).

Chart 1: Articles included in the study that report information on cognition, motor, language and communication

Included Articles	Development data
Qian et. al (2014) [11]	- Cerebellar ataxia - Unsteady gait and a tendency to fall, accompanied by signs of dysphagia with liquids (coughing while drinking) speech problems (slurred speech)).
Sonmez et. al (2013) [12]	- Intellectual disability; - Monotonous voice and unintelligible vocalizations; - Speak with isolated words - Short and unsteady gait
Steinlin et. al. (2007) [13]	- Movement disorder and developmental delay - Breathing and / or suction problems during the neonatal period - The children analyzed showed inability to sit, walk or talk (there was no speech development - vocalization of sounds only in one child). - Non-verbal social communication - Hearing deficiency
Laugwitz et al. (2020) [14]	Global psychomotor deficits, involving gross and fine motor skills, as well as language development. Ataxic march. Vocalization of isolated words. Dysphagia. ADHD. The signs of regression and stagnation were noticed until the age of 12.

8. Language and Communication

Table 1 presents the results obtained in the speech and language assessment using the following instruments: ADL: Language Acquisition and Development [16], Denver-II Development Screening Test [17], MacArthur Inventory [18]; Nonverbal Intelligence Test (SON-R)[19]; Columbia Mental Maturity Test [20]; and Pré-WISC [21] (Table 1).

Table 1 - Results of tests applied to speech and psychological assessment

Speech Therapy Evaluation	
Assessment tools	**Results**
ADL	Scores below EP 69: Severe language disorder
DENVER – II	
Language	30 months
Coarse motor	36 months
Fine-adaptive motor	30 months
Personal-social	36 months
MacArthur Inventory	Can name objects, people's names and simple action verbs
Behavior observation	Speaks words alone - uses nouns and verbs. Tell facts from concrete contexts with simple sentences, without using low semantic words. There is distortion in speech, characterized as a dysarthric condition.
	Psychological Assessment
Nonverbal Intelligence Test (SON-R)	It presents diffuse involvement of the various functions, causing fundamental difficulty in learning and developing, mainly, conceptual abilities. Picture suggestive of intellectual disability, of non-specific severity, for associating cognitive deficits and adaptive behavior, that is, distortion in the chronology, in the rhythm and in the sequence of the basic functions for its development, impairing the efficiency in reaching the expected standards for its age and cultural group, in areas such as: social skills, communication / language, personal independence, responsibilities and self-sufficiency.
Columbia Mental Maturity Test	
Pré-WISC	

9. Discussion

The literature review on the subject of Pontocerebellar Hypoplasia (PCH) presents studies mostly related to the neurological, radiological, and genetic evaluation of the condition, generally describing anatomical measurements, mutations [1-10], and general characteristics of the different PCH subtypes [1-13]. Many of these refer to clinical case studies [1, 8-11].

In the present case, the clinical picture and the progression of the symptoms indicate the possibility of PCH11. This suggests the need for a genetic examination; however, the family is yet to accomplish this. Rudnik-Schonebom et al. [2] stated that the differential diagnosis of PCH is a challenge, considering its early onset and unspecific clinical presentations. Rüsch et al. [5] showed that a systematic analysis of images and clinical characteristics could aid in the differential diagnosis.

Van Dijk et al. [6] revealed that new genes and phenotypes related to PCH have been described through the use of state-of-the-art sequencing techniques, and that the classification of the types presented in literature is still confusing, given the heterogeneity of the disorder. They reported that there exist several patients with PCH, who do not possess mutations in any of the genes related to PCH.

There are clear descriptions regarding the disease progression of the different PCH types in literature [1-12], except for PCH8 and PCH11. According to the articles compiled [1-9], the manifestations in the linguistic and communicative cognitive areas that are commonly reported involve phenotypes associated with cognitive and behavioral changes, in addition to delays in and/or loss of motor skills, as well as difficulties in maintaining therapeutic gains, given the progressive nature of the disorder.

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