Grebe syndrome
Case report

Jessica A. Suárez Zarrate,[*] Ricardo Arias Arguello,[**] Sebastián Rodríguez Serna[**]

[*]*Fundación Universitaria Sanitas, Bogotá, Colombia*
[**]*Clínica Universitaria Colombia, Bogotá, Colombia*

Received on December 8th, 2016; accepted after evaluation on August 1sth, 2017 • JESSICA A. SUÁREZ ZARRATE, MD • jessi_k10@hotmail.com

Abstract

Grebe chondrodysplasia is a rare autosomal recessive disorder included in the group of osteochondrodysplasias. From the medical point of view it is characterized by severe dysmorphism and remarkable micromelia, and deformities in upper and lower limbs. Recognizing this type of syndrome leads doctors to make better diagnoses and make differential diagnosis with commoner conditions such as achondroplasia.

We present a 35-year-old patient diagnosed with Geber syndrome at 10 years of age.

The Grebe syndrome is associated with very low incidence rates; therefore, it is hardly acknowledged by medical doctors in general and even less by orthopaedists, who will be in charge of these patients' management.

Key words: Grebe syndrome; osteochondrodysplasia; dysplasia, acromesomelic dysplasia.
Level of evidence: IV

Síndrome de Grebe. Reporte de un caso

Resumen

La condrodisplasia de Grebe es un trastorno raro autosómico recesivo que pertenece al grupo de las osteocondrodisplasias. Clínicamente se caracteriza por un severo dismorfismo con una marcada micromelia y deformidad de las extremidades inferiores y superiores. Conocer este tipo de síndrome orienta a dar mejores diagnósticos y permite el diagnóstico diferencial con patologías más comunes, como la acondroplasia.

Se presenta una paciente de 35 años con diagnóstico de síndrome de Grebe desde los 10 años.

El síndrome de Grebe tiene una muy baja incidencia; por este motivo, es poco conocido por el cuerpo médico en general y aun menos para los ortopedistas, quienes serán los encargados de tratar a estos pacientes.

Palabras clave: Síndrome de Grebe; osteocondrodisplasia; displasia, acromesomélico.
Nivel de Evidencia: IV

Introduction

Grebe chondrodysplasia is a rare autosomal recessive disorder included in the group of osteochondrodysplasias; there are reports on 25 cases. The gene that accounts for this condition has already been identified—it codes for the cartilage-derived morphogenetic protein-1 (CDMP-1) and it is located in the chromosome 20q11.2.1

From the medical point of view, it is characterized by severe dysmorphism with remarkable micromelia and deformity in lower and upper limbs, with a typical pattern of increasing severity from the proximal end to the distal one. Fingers become just globe-like appendixes (soft tissue-bridges), thumb apparently does not develop, neither apparently do it toe-joints (no motion), and there is limitation on elbows, wrists, knees, ankles and fingers

Conflict of interests: The authors have reported none.

movement. Dislocation in proximal limb-joints is common. The axial skeleton, head and face aspect is normal. Patients are short—they are approximately 100 cm-tall.[1]

From the radiological point of view, it is characterized by deformity and shortening in long bones, fusion in carpal and tarsal bones, severe metatarsal and metacarpal dysplasia and, sometimes, lack of middle and proximal phallanxes.[2] By recognizing this type of syndrome it is possible to make better diagnoses, rule out similar conditions such as achondroplasia, and clarify what type of medical and radiologic findings these patients show.

Case

She is a 35-year-old female who weighs 40 kg and is 100 cm-tall, and who has been diagnosed with Grebe syndrome when she was 10 years of age. One sister and two second-grade maternal aunts of hers suffer the same syndrome (Figure 1).

In 2009 she consults for right elbow pain caused by mouse manipulation at work, and with images she is diagnosed as having right radial head dislocation. She is decided to undergo right radial head-resection arthroplasty. Five months after the procedure, she consults for elbow pain (dysesthesia), functional limitation and subjective sensation of paresia in her right upper limb. She is suspected to have neurapraxia at the level of her posterior interosseous nerve. At physical examination she shows preserved range of motion and strength, with allodyina in right elbow and forearm; therefore, she is referred to the pain management unit and prescribed physiotherapy and lidocaine patches. She undergoes electomyography, with normal results.

Some medical findings in the Grebe syndrome are severe dwarfism (100 cm), micromelia and deformity in upper and lower limbs, with different degrees of severity. The patients' face appearance, intelligence and axial skeleton are normal, while upper and lower limbs have short proximal segments and mid-segments even shorter. Ranges of motion are limited in elbows, wrists, elbows, ankles and fingers. There are severe deformities in hands and feet, with toes which are just globe-like appendixes (soft tissue-bridges); there is no apparent thumb development, neither is there apparent joints in toes (no motion) (Figure 2).

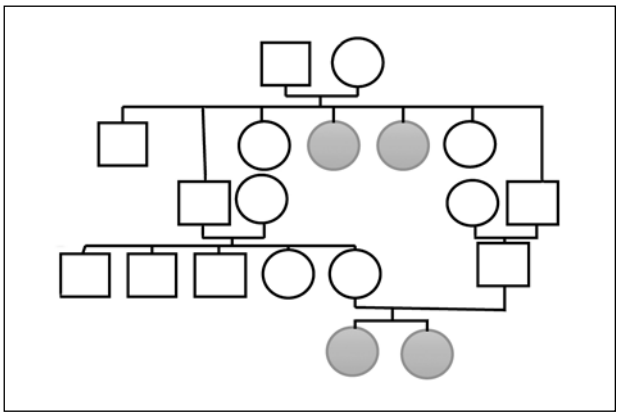

Figure 1. Patient's family genogram showing two generations—two people affected by the Grebe syndrome.

Ours is a completely functional patient; she has got a university degree and works with no difficulties whatsoever. She is completely independent for activities of daily living, including self-cleaning. She only reports difficulties in public transport access (buses) and acquisition of comfortable shoes.

In X-rays, we detect a normal axial skeleton (Figure 3), shortening of long bones with no changes in morphology, fusion in carpal and tarsal bones, severe metatarsal and metacarpal dysplasia (Figure 4), and bilateral radial head dislocation (Figure 5).

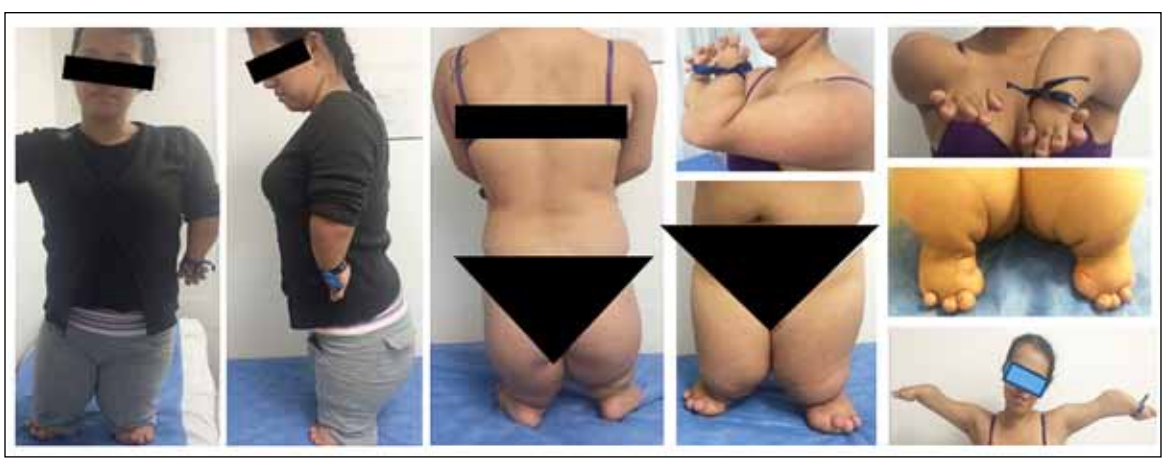

Figure 2. 35-year-old patient with Grebe syndrome.

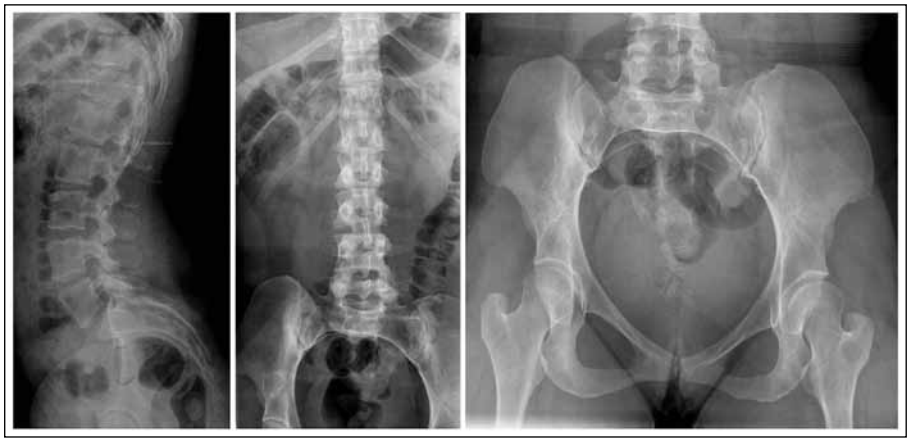

Figure 3. X-rays of lumbosacral spine and hips with left acetabular dysplasia.

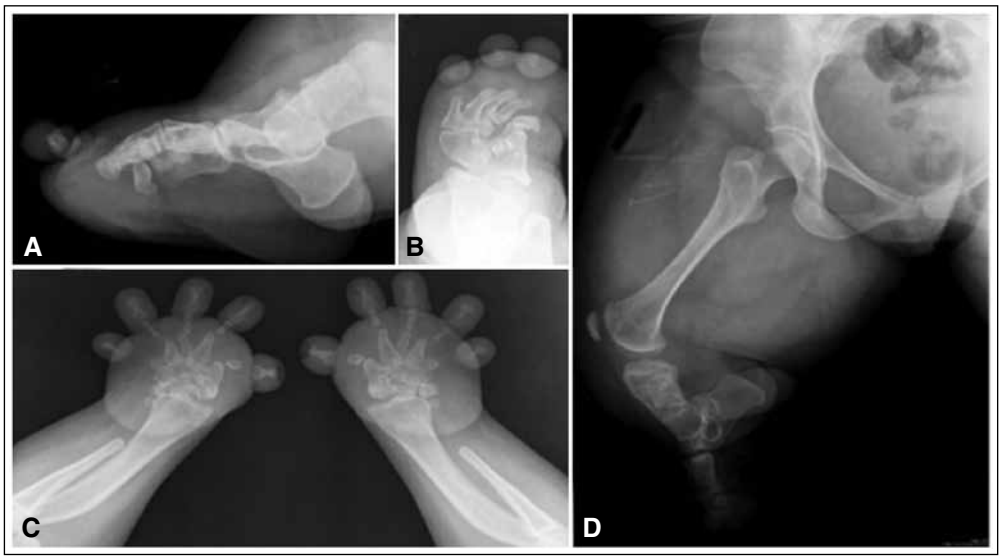

Figure 4. X-ray of femur and humerus showing bone shortening without morphologic changes. **B**. Bone shortening with changes in radial and ulnar morphology, and tibia and fibula. **C.** X-ray of bilateral forearm and hand. Partial absence of 1st and 5th metacarpal bones, absence of middle phalanxes and fusion of trapezium and trapezoid bones, and that of capitate and hamate bones in left hand. **D.** Lateral X-ray of right foot. Partial absence of 1st metatarsal bone, absence of middle phalanxes and fusion of scaphoid with 1st cuneiform bone, and that of cuboid with 2nd and 3rd cuneiform bones.

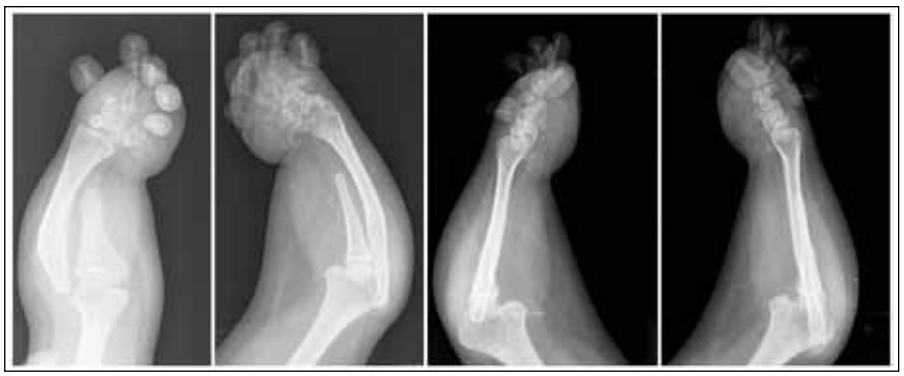

Figure 5. Lateral X-ray of right forearm and elbow. Forearm bones shortening with bilateral dislocation of radial head.

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Discussion

The patient's phenotype coincides with the diagnosis of Grebe-type chondrodysplasia. There are reports on newborn deaths, but this patient has got adult age with no complication anybody has known about. Severe micromelia is a frequent disorder in patients with atelosteogenesis type 2 (lethal chondrodysplasia); other characteristics are skeletal disorders such as vertebral bodies' crown cleft, epiphyseal and metaphyseal anomalies, clubfeet, and trigger fingers.[3] In general, these patients' skeletal anomalies are totally different from the ones in ours.

Other types of mesomelic shortening, such as the Grebe syndrome, are characterized by acromesomelic dysplasia, and very short phalanxes with button-like fingers very similar to one another. Radiologic findings include lack of fibular bone, forearm hypoplasia or dysplasia, dysplasia or absence of middle and proximal phalanxes and, in some patients, carpal fusion.[4]

In 1981, Langer et al. describe the Grebe syndrome as a clinical entity similar to Du Pan and Hunter-Thompson syndromes. Phenotypes in these syndromes are different, however; therefore, the Grebe syndrome is considered to be a totally different entity. Patients with Grebe-type chondrodysplasia have complex disorders in the peripheral skeleton, what shows in long bones shortening with greater involvement at distal level, especially at that of feet and hands.[5]

Conclusions

The Grebe syndrome is associated with very low incidence rates; therefore, it is hardly acknowledged by medical doctors in general and even less by orthopaedists, who due to their contact with muscle-skeletal conditions will be the ones in charge of these patients' management.

Recognizing this syndrome allows doctors to make differential diagnosis with commoner conditions, such as achondroplasia, and get acquainted with the medical and radiological findings these patients show, such as, in this case, bilateral radial head dislocation. Thus, these patients can be focused on more objectively and doctors achieve integral management of their patients' disorders.

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