Morphologie (2014) xxx, xxx—xxx

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

CASE REPORT

Clinical features in adult patient with Wolf-Hirschhorn syndrome

Caractéristiques cliniques chez des patients adultes atteints du syndrome de Wolf-Hirschhorn

E. Martínez-Quintana[a,*], **F. Rodríguez-González**[b]

[a] *Cardiology Service, Insular-Materno Infantil University Hospital, Complejo Hospitalario Universitario Insular-Materno Infantil, Avd. Marítima del Sur s/n, 35016 Las Palmas de Gran Canaria, Spain*
[b] *Ophtalmology Service, Dr. Negrín University Hospital of Gran Canaria, Las Palmas de Gran Canaria, Spain*

KEYWORDS
Wolf-Hirschhorn syndrome;
Pitt-Rogers-Danks syndrome;
Cardiac;
Genetic;
Rehabilitation

Summary The Wolf-Hirschhorn syndrome (WHS) encompasses deletions at the distal part of the short arm of one chromosome 4 (4p16 region). Clinical signs frequently include a typical facial appearance, mental retardation, intrauterine and postnatal growth retardation, hypotonia with decreased muscle bulk and seizures besides congenital heart malformations, midline defects, urinary tract malformations and brain, hearing and ophthalmologic malformations. Pathogenesis of WHS is multigenic and many factors are involved in prediction of prognosis such as extent of deletion, the occurrence of severe chromosome anomalies, the severe of seizures, the existence of serious internal, mainly cardiac, abnormalities and the degree of mental retardation. The phenotype of adult with WHS is in general similar to that of childhood being facial dysmorphism, growth retardation and mental retardation the rule in both adults and children. Avoid long-term complications and provide rehabilitation programs and genetic counseling may be essential in these patients.

MOTS CLÉS
Syndrome de Wolf-Hirschhorn ;
Syndrome de Pitt-Rogers-Danks ;
Cardiaque ;
Génétique ;
Rééducation

Résumé Le syndrome de Wolf-Hirschhorn englobe différentes délétions de la partie distale du bras court d'un des chromosomes 4 (région 4q16). Les signes cliniques habituels sont un faciès typique, un retard mental, un retard de croissance intra-utérine et post-natale, des anomalies musculaires (hypotonie, diminution de masse, crises convulsives, malformations cardiaques), des anomalies de la ligne médiane, des malformations des voies urinaires et des malformations cérébrales, auriculaires et ophtalmiques. Le syndrome de Wolf-Hirschhorn est une pathologie multigénique. Le pronostic est multifactoriel selon l'étendue de la délétion, la présence d'anomalies chromosomiques importantes, l'intensité des crises convulsives, la présence d'anomalies internes (surtout cardiaques) et l'importance du retard mental. En

* Corresponding author.
E-mail address: efrencardio@gmail.com (E. Martínez-Quintana).

1286-0115/$ – see front matter © 2014 Published by Elsevier Masson SAS.
http://dx.doi.org/10.1016/j.morpho.2014.02.002

général, le phénotype est similaire chez l'adulte et chez l'enfant : dysmorphose faciale, retard de croissance, retard mental. Il est essentiel d'éviter des complications chroniques, de prévoir des programmes de rééducation et de proposer des conseils génétiques pour ces patients.

Introduction

In the mid 1960's, Wolf et al. [1] and Hirschhorn et al. [2] described a clinically recognizable syndrome caused by partial deletion of the short arm (p) of chromosome 4 [3]. Actually, the Wolf-Hirschhorn syndrome (WHS) (phenotype MIM number 194190) has a reported frequency of 1 in 50,000 births, occurring more frequently in females with a male to female ratio of 1:2 [4].

Case report

We report the case of an 18-year-old male patient referred to our congenital heart disease unit for evaluation. The patient presents a typical facial appearance (Fig. 1) and has a profound intellectual disability, with speech limited to guttural sounds and minimal communication skills. The patient also has a ponderoestatural delay with a weight of 27 kg and a height of 130 cm, dorsal kyphosis (Fig. 2A), generalized hypotonia, reduced reflexes, equinus foot, hallux valgus (Fig. 2B) and walks one or two steps without support but has needed corrective orthotics and surgical interventions of both feet due to progressive deformity. The patient has no sphincter control, has no autonomy with eating, dressing or undressing and no improvement has been observed over time in his adaptive behaviour assessments. Generalized seizures and absences disappeared at the age of 12 years while the patient continues treatment with valproic acid. Although the patient, in childhood, showed electroencephalographic (EEG) abnormalities, the EEG is now within normality. The patient dose not has hearing loss and has not had recurrent respiratory tract infections, otitis media or psychotic behaviour. Cardiologically the patient is asymptomatic and the echocardiogram shows a corrected double outlet right ventricle (Fig. 2C and D). No antibody deficiencies or hematopoietic dysfunction were found.

The genetic study showed a microdeletion in the short arm of one of the pairs of the chromosome 4 (46,XY, del 4p16.3) using fluorescence in situ hybridization (FISH) technique. Meanwhile, his mother and his maternal aunt had the same but balanced translocation (46,XX, t(4,8)) (p16.3, q35.1) [5]. Similarly, his sister, who genetic study was performed by examination of the amniotic fluid, showed the

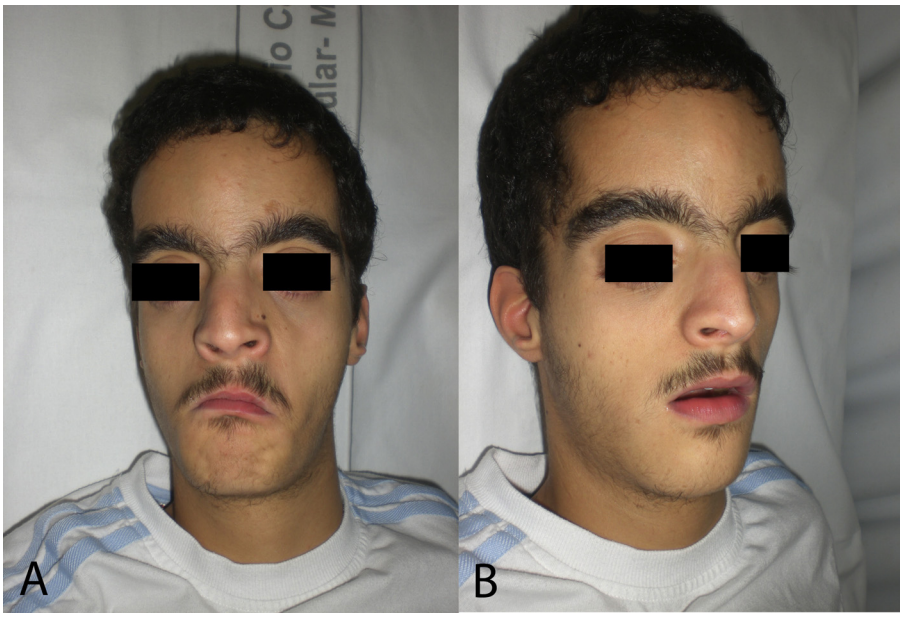

Figure 1 Anterior (A) and lateral (B) views of the patient's face showing a craniofacial disproportion with cranial predominance, normal hair, a high forehead with a prominent glabella, a large nasal bridge with a beaked nose, hypertelorism, high arched eyebrows, protruding eyes, a poorly defined upper lip, bilateral microtia with low-set ears, hypoplastic lobule, narrow helix, prominent antihelix and a triangular concha.
Dysharmonie cranio-faciale vue de face (A) et de profil (B) : crâne proéminent, cheveux normaux, grand front, nez large et crochu, hypertélorisme, sourcils hauts et arqués, exophtalmie, lèvre supérieure mal délimitée, microtie bilatérale avec implantation basse du pavillon, hypoplasie lobulaire, hélix étroit, proéminence de l'anthélix et conque triangulaire.

Please cite this article in press as: Martínez-Quintana E, Rodríguez-González F. Clinical features in adult patient with Wolf-Hirschhorn syndrome. Morphologie (2014), http://dx.doi.org/10.1016/j.morpho.2014.02.002