Is Gorlin-Chaudhry-Moss syndrome associated with aortopathy?
Legue, J.; Francois, J.H.M.; Rijswijk, C.S.P. van; Brakel, T.J. van

Citation
Legue, J., Francois, J. H. M., Rijswijk, C. S. P. van, & Brakel, T. J. van. (2020). Is Gorlin-Chaudhry-Moss syndrome associated with aortopathy? European Journal Of Cardio-Thoracic Surgery, 58(3), 654-655. doi:10.1093/ejcts/ezaa108

Version: Publisher's Version
License: Creative Commons CC BY-NC 4.0 license
Downloaded from: https://hdl.handle.net/1887/3184005

Note: To cite this publication please use the final published version (if applicable).
Is Gorlin–Chaudhry–Moss syndrome associated with aortopathy?

Juno Legueá*, Jules H.M. Françoisb, Carla S.P. van Rijswijkb and Thomas J. van Brakel c, a

a Department of Cardiothoracic Surgery, Leiden University Medical Center, Leiden, Netherlands
b Department of Radiology, Leiden University Medical Center, Leiden, Netherlands

* Corresponding author. Department of Cardiothoracic Surgery, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, Netherlands. Tel: +31-(0)71–5264022; e-mail: j.legue@lumc.nl (J. Legueá).

Received 21 November 2019; received in revised form 3 March 2020; accepted 9 March 2020

Abstract

Gorlin–Chaudhry–Moss syndrome (GCMS) is a rare disorder consisting of craniofacial dysostosis, hypertrichosis, underdeveloped genitalia, and ocular and dental anomalies. Recently, GCMS has been reclassified together with Fontaine syndrome as Fontaine progeroid syndrome (FPS), after a common genetic basis was found. It was previously thought that GCMS/FPS was not associated with aortopathy, but in recent years 3 patients with aortic disease have been described. We describe the fourth case, who is the oldest patient with GCMS/FPS reported in the medical literature: a 45-year-old patient who presented with acute aortic dissection. We therefore recommend screening patients previously diagnosed with GCMS/FPS for aortic pathology to aid early detection and avoid patient presentation in an acute setting.

Keywords: Gorlin–Chaudhry–Moss syndrome • Fontaine progeroid syndrome • Aortopathy dissection

INTRODUCTION

Gorlin–Chaudhry–Moss syndrome (GCMS) is a rare disorder consisting of craniofacial dysostosis, hypertrichosis, underdeveloped genitalia, and ocular and dental anomalies [1]. It has thus far not been associated with aortopathy. Ehmke et al. [2], who demonstrated that the syndrome is caused by recurrent mutations affecting the 217th amino acid in SLC25A24, did describe 2 GCMS patients with aortic ectasia. The same mutation is associated with Fontaine syndrome [3]. These syndromes show overlapping clinical features but have different life expectancies: patients with Fontaine syndrome do not survive beyond a year, whereas patients with GCMS are assumed to have a normal life expectancy. The cause of the different life expectancies is still unclear. Fontaine syndrome and GCMS, due to their common genetic basis, have been reclassified as Fontaine progeroid syndrome (FPS, OMIM: Fontaine progeroid syndrome; https://www.omim.org/entry/612289). A 15-year-old male with FPS has since been described with aortic dilatation. We present the case of a 45-year-old woman, with GCMS, who presented with an acute type A aortic dissection. Written consent was obtained from the patient.

CASE

A 45-year-old female, diagnosed with GCMS in childhood, displays typical features of the syndrome (Table 1). The patient had an otherwise unremarkable medical history. She was admitted to the hospital with sharp pains behind the sternum, that had been present for 10 days. The patient was in stable haemodynamic and respiratory conditions. Thoracic computed tomography (CT) showed an aneurysm of the ascending aorta and the proximal part of the aortic arch, with a maximal diameter of 51 mm (patient length 142 cm, weight 31 kg). Proximally, the aneurysm had a saccular aspect and a mural thrombus (Fig. 1). The patient was...
transferred to a tertiary medical centre where she underwent urgent surgery.

Inspection revealed an aneurysmatic dilatation with a local partially chronic and partially acute dissection with fresh thrombus. A supracoronary ascending aorta and a zone 2 partial arch replacement (with reimplantation of brachiocephalic and left common carotid artery as an island) was performed using 18-mm Hemashield protheses. Surgery was performed under deep hypothermia, circulatory arrest, and bilateral antegrade cerebral perfusion.

The postoperative course was complicated by temporary respiratory distress caused by pulmonary oedema and pneumonia, which was treated with antibiotics. The patient was discharged from the hospital 2 weeks after surgery in a good clinical condition. Regular follow-up, including thorax CT, will occur in an outpatient setting.

Histopathological analysis on the resected aortic tissue showed an aortic dissection with fibrosis but no signs of connective tissue disorders (no cystic media necrosis) or vasculitis.

Genetic analysis revealed the recurrent mutation c.650G>A (p.Arg217His) in the SLC25A24-gene, confirming the diagnosis of FPS.

**COMMENTS**

This case report describes the oldest patient with GCMS in the medical literature. The 2 patients first described with GCMS were again described several years later, at 36 and 34 years of age, along with 2 new patients, including a 33-year-old [1, 5]. No information was provided on whether these patients had aortic abnormalities. Other patients described were either children or adolescents. Ehmke et al. [2, 4] were the first to report 2 patients with aortic ectasia and a later case described a 15-year-old male with FPS and aortic dilatation. We now describe a 45-year-old patient with an ascending aorta aneurysm and a local dissection who underwent urgent surgery. Due to the small patient population, the association between the syndrome and aortopathy is difficult to prove but 4 patients, including our patient, have recently been described with aortic disease [2, 4]. We would therefore recommend screening patients previously diagnosed with GCMSFPS for aortic disease.

**ACKNOWLEDGEMENTS**

We thank Hilhorst-Hofstee for her critical remarks and contribution to this case report.

**Conflict of interest:** none declared.

**REFERENCES**

[1] Gorlin RJ, Chaudhry AP, Moss ML. Craniofacial dysostosis, patent ductus arteriosus, hypertrichosis, hypoplasia of labia majora, dental and eye anomalies-a new syndrome? J. Pediatr 1960;56:778–85.

[2] Ehmke N, Graul-Neumann L, Smorag L, Koenig R, Segebrecht L, Magoulas P et al. De novo mutations in SLC25A24 cause a craniosynostosis syndrome with hypertrichosis, progeroid appearance, and mitochondrial dysfunction. Am J Hum Genet 2017;101:833–43.

[3] Writzl K, Maver A, Kovacic L, Martinez-Valero P, Contreras L, Satrustegui J et al. De novo mutations in SLC25A24 cause a disorder characterized by early ageing, bone dysplasia, characteristic face, and early demise. Am J Hum Genet 2017;101:844–55.

[4] Rodriguez-Garcia ME, Cotrina-Vinagre FJ, Cruz-Rojo J, Garzón-Lorenzo L, Carnicero-Rodríguez P, Sánchez-Del Pozo J et al. A rare male patient with Fontaine progeroid syndrome caused by p. R217H de novo mutation in SLC25A24. Am J Med Genet 2018:176:2479-86.

[5] Ippel PF, Gorlin RJ, Lenz W, van Doorne JM, Bijlsma JB. Craniofacial dysostosis, hypertrichosis, genital hypoplasia, ocular, dental, and digital defects: confirmation of the Gorlin-Chaudhry-Moss syndrome. Am J Med Genet 1994;44:518-22.

**Table 1:** Patient features of GCMS

| Short stature | Orofacial findings  |
|---------------|---------------------|
|              | • Brachycephaly     |
|              | • Midface hypoplasia |
|              | • Craniosynostosis   |
|              | • Microphthalmia with impaired vision |
|              | • DOWNSLANTING palpebral fissures |
|              | • Narrow palpebral fissures |
|              | • Parietal alopecia   |
|              | • Low frontal hairline |
|              | • Coarse hair and hypertrichosis |
|              | • High arched narrow palate |
|              | • Small prominent ears |

| Extremities | Bilateral distal phalangeal hypoplasia of the 4th–5th finger |
|------------|--------------------------------------------------------------|
|            | Cutaneous syndactyly of 4th–5th toes of the left foot       |

| Hyperopia | Hypo- and microdontia                                      |
|-----------|------------------------------------------------------------|
|           | Conductive hearing loss.                                   |

| Labia majora hypoplasia | Umbilical hernia |

GCMS: Gorlin–Chaudhry–Moss syndrome.