[1]Patient Area Endocrinology and Nephrology, Karolinska University Hospital, Stockholm, Sweden
[2]Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden
[3]Hôpital des enfants, Centre de référence du Syndrome de Prader-Willi, Centre Hospitalier Universitaire de Toulouse, Toulouse, France
[4]Pediatric Endocrinology, NYU Winthrop Hospital, Mineola, New York
[5]Centre for Pediatric Endocrinology, University of Zürich, Zürich, Switzerland
[6]Chair, IPWSO Clinical & Scientific Advisory Board, University of Florida College of Medicine, Gainesville, Florida
[7]Past President IPWSO, Division of Medical Genetics, University of California, San Francisco, California
[8]President IPWSO, Department of Psychiatry, University of Cambridge, Cambridge, UK

Correspondence
Charlotte Höybye, Patient Area Endocrinology and Nephrology, Karolinska University Hospital and Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden.
Email: charlotte.hoybye@sll.se

ORCID

Charlotte Höybye https://orcid.org/0000-0001-6412-166X

REFERENCES

1. Donze SH, Damen L, Alfen-van der Velden J, et al. Prevalence of growth hormone (GH) deficiency in previously GH-treated young adults with Prader-Willi syndrome. *Clinl Endocrinol (Oxf)*. 2019;1-6.
2. Schilbach K, Olsson DS, Boguszewski M, Bidlingmaier M, Johannsson G, Jørgensen J-O. Biomarkers of GH action in children and adults. *Growth Hormon IGF Res*. 2018;40:1-8.
3. Deal CL, Tony M, Höybye C, Allen DB, Tauber M, Christiansen JS. Growth hormone research society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi Syndrome. *J Clin Endocrinol Metab*. 2013;98(6):E1072-1087.
4. Angulo M, Castro-Magana M, Mazur B, Atilio Canas J, Vitollo PM, Sarrantonio M. Growth Hormone secretion and effects of growth hormone therapy on growth velocity and weight gain in children with Prader-Willi Syndrome. *J Ped Endocrinol Metab*. 1996;9:393-400.
5. Kuppens RJ, Bakker NE, Siemensma E, et al. Beneficial effects of GH in young adults with Prader-Willi Syndrome: a 2-Year crossover trial. *J Clin Endocrinol Metab*. 2016;101(11):4110-4116.

Received: 17 July 2019 | Accepted: 21 July 2019

DOI: 10.1111/cen.14066

Reply to Commentary on 'Prevalence of growth hormone (GH) deficiency in previously GH treated young adults with Prader-Willi syndrome'

Dear Editor,

We would like to thank the authors for their commentary as it gives us the opportunity to repeat our conclusion that adults with Prader-Willi syndrome (PWS) should be treated with growth hormone (GH), regardless of GH stimulation test results. Our findings show that conventional testing for adult growth hormone deficiency (GHD) is not reliable in adults with PWS. Children and adults with PWS have a hypothalamic dysfunction and several features that resemble those seen in GHD. The fact that they respond very well to GH treatment, with a significant improvement in body composition, health profile, normalization of stature in children, and a significant increase in serum IGF-I and IGFBP-3 levels strongly supports the likelihood of GHD in these patients.

However, GH treatment for adults with PWS is currently not reimbursed if they do not fulfil the consensus criteria of adult GHD. We, therefore, performed GHRH-Arginine tests in 60 young adults with PWS who had attained adult height after long-term GH treatment during childhood, to have an opportunity to treat them. In contrast to our expectations, none of them fulfiled the adult GHD consensus criteria. The insulin tolerance test was not feasible because of its side effects in subjects with PWS. We agree with the authors of the commentary that even though adult GHD could not be demonstrated by the GHRH-Arginine test, it does not mean that it does not exist, as we know that subjects with PWS have a hypothalamic dysfunction. Also, 27 of the 60 patients participated in our randomized double-blind placebo-controlled cross-over GH trial and had positive effects on body composition during 1 year of GH treatment compared with a deterioration during 1 year of placebo. In our opinion, our publication provides essential information for all (paediatric) endocrinologists involved in the care for subjects with PWS, as it shows that testing for adult GHD by GHRH-Arginine is not useful in (young) adults with PWS.

As several studies have documented the beneficial effects of GH treatment on body composition and health profile in adults with PWS, we agree with the authors of the commentary that treating adults with PWS with GH is highly recommended. For that reason,

Data sharing is not applicable to this article as no new data were created or analysed in this study.

we aim to attain a registration of GH treatment for adults with PWS, regardless of whether they fulfil the consensus criteria of GHD—just like in children with PWS. This will be based on the data of our randomized controlled trial, supported by the positive findings of previous GH studies in adults with PWS.

In conclusion, the take-away message of our publication was not that adults with PWS should not be treated with GH, but rather that conventional testing for GHD is not reliable in adults with PWS. We strongly agree with the authors of the commentary that, although adult GHD could not be confirmed by conventional testing, leaving adults with PWS without GH treatment is detrimental as GH treatment has well documented beneficial effects in both children and adults with PWS.

Keywords

growth hormone, growth hormone deficiency, Prader-Willi syndrome

Stephany H. Donze[1,2]

Anita C. S. Hokken-Koelega[1,2]

[1]*Dutch Growth Research Foundation, Rotterdam, The Netherlands*
[2]*Erasmus University Medical Center / Sophia Children's Hospital, Department of Pediatrics, Subdivision of Endocrinology, Rotterdam, The Netherlands*

Correspondence

Stephany H. Donze, Dutch Growth Research Foundation, Rotterdam, The Netherlands.
Email: S.Donze@kindengroei.nl

ORCID

Stephany H. Donze https://orcid.org/0000-0002-9249-4284

Received: 25 June 2019 | Revised: 23 July 2019 | Accepted: 29 July 2019

DOI: 10.1111/cen.14070

Spontaneous simultaneous bilateral quadriceps tendon rupture associated with severe vitamin D deficiency

Dear Editor,

Herein we report a young woman presenting with bilateral spontaneous quadriceps tendon rupture resulting from secondary hyperparathyroidism consequent to vitamin D deficiency. Simultaneous rupture of bilateral quadriceps tendon is extremely rare and has usually been reported in association with chronic kidney disease (CKD), diabetes mellitus, systemic lupus erythematosus, rheumatoid arthritis, gout and steroid use. Secondary hyperparathyroidism has been implicated as the underlying mechanism in CKD.[1] In addition, primary and tertiary hyperparathyroidism has also been incriminated in anecdotal case reports as a cause of spontaneous tendon rupture.[2,3] Our case stands unique in that the cause of bilateral quadriceps tendon rupture was vitamin D deficiency and resulting secondary hyperparathyroidism.

A 24-year-old lady presented with acute onset pain and swelling in both knees compounded with an inability to extend her legs after a trivial fall following a minor slip. On enquiry, she gave a history of diffuse bony pains for the past 3 months. Her past medical history was otherwise insignificant. There was no history of any over-the-counter or chronic medication intake. Physical examination revealed bilateral knee swellings. Bilateral suprapatellar gaps were palpable. She could not actively extend her knees, and quadriceps contraction did not result in movement of the patellae. She was lean with a body mass index of 20.3 kg/m^2.

Lateral radiographs of the knees showed bilateral inferior displacement of the patellae along with diffuse cortical thinning of the lower end of femur and upper end of tibia (Figure 1A). Fractures or calcification of the quadriceps tendon was not seen. Magnetic resonance imaging showed complete thickness tear in suprapatellar quadriceps tendon with inferior displacement of the patella and buckling of infrapatellar segment of the tendon (Figure 1B). Investigations revealed normal complete blood count and normal renal function. She had hypocalcemia (corrected serum calcium 8.4 mg/dL [range: 8.8-10.2]), hypophosphatemia (serum phosphate 2.4 mg/dL [range: 2.7-4.5]) and elevated total alkaline phosphatase (serum ALP 574 IU/L [range: 24-78]). Her serum 25-hydroxyvitamin D level was very low (3.1 ng/mL), and reciprocally her serum intact PTH was elevated (iPTH 1166 pg/mL [range: 15-65]). Rest of the investigations including serum albumin, magnesium, uric acid, fasting blood glucose, glycated haemoglobin and thyroid function tests were normal. Antinuclear and antidouble stranded DNA antibodies were not detectable in serum.

Ultrasonography of the neck did not reveal any parathyroid enlargement, and ^{99m}Tc-SESTAMIBI scan did not show any evidence of tracer-avid lesions. Hence, she was diagnosed as having simultaneous

Sailesh Lodha and Rimesh Pal are joint first authors.