Pregnancy reduces severity and frequency of attacks in hyperkalemic periodic paralysis due to the mutation c.2111C>T in the *SCN4A* gene

Sir,

Hyperkalemic periodic paralysis (hyperPP) is due to mutations in the muscular sodium-channel gene *SCN4A*, clinically characterized by episodes of sudden-onset, mild to severe weakness lasting between seconds and hours.[1] Episodes usually go along with hyperkalemia.[2] Improvement of hyperPP during pregnancy has been reported only once.[3]

A 30-year-old Caucasian female experienced recurrent episodes of muscle weakness since age 1 year. The attacks lasted 15 min to

3 h. During severe attacks, she could not walk or turn her body and developed dysarthria. During mild attacks, weakness of the lower limbs allowed her to walk unaided and weakness of the upper limbs prevented her from lifting heavy weights. Attacks could be triggered by alcohol 1–2 h after consumption. Mild attacks could be relieved by walking or urination. HyperPP was diagnosed and calcium and acetazolamide prescribed, which she took until age 26 year, without effect. Attacks could be prevented by eating every 4 h and restriction of fruits and vegetables. Since age 29 year, she recognized that carbohydrates shortly after onset of an attack prevented further deterioration or even stopped an ongoing attack. At age 29 year, detection of the *SCN4A* mutation c.2111C>T confirmed hyperPP.

At age 28 year, she became pregnant for the first time. Shortly after recognizing her pregnancy, frequency and intensity of hyperPP attacks became markedly less. During the entire pregnancy, only a few mild attacks and four severe attacks occurred. During the same period without pregnancy, she had approximately one severe attack/week. After delivery of a healthy child at term, frequency and intensity of attacks increased to the pregestational level.

The family history was positive for hyperPP in her 57-year-old mother. Against the advice of her treating physicians, who feared deterioration of hyperPP during pregnancy, the mother became pregnant without deterioration of hyperPP during pregnancy. Severity and duration of the attacks became less with increasing age. The mother was on a low-potassium diet, avoided heavy work, and cold, and took Na-polystyrene sulfonate (15 g) three times/week, acetazolamide, and salbutamol on demand.

The presented case shows that contrary to previous experience, pregnancy can reduce severity and frequency of hyperPP attacks. Relief from hyperPP attacks during pregnancy has been previously reported in a single patient carrying the *SCN4A* mutation p.T407M.[3] In this patient, attacks completely resolved during the second and third trimester to recur after delivery.[3] The present and previously reported beneficial effect of pregnancy on hyperPP is unique since it is generally believed that pregnancy deteriorates hyperPP.[1,4] Improvement of hyperPP during pregnancy could be explained by the potassium-lowering effect of a pregnancy or by hyperglycemia due to hormonal changes. A further explanation could be a direct effect of gestagens on sodium channels since the treatment of *Xenopus laevis* oocytes with progesterone resulted in complete abolishment of transmembrane sodium currents. It was also speculated that hormonal changes may induce hypokalemia.[3] There are also indications that gestagens reduce contractility of smooth muscle cells[5] by reducing transmembrane calcium currents.[6] Whether the beneficial effect of pregnancy on hyperPP is restricted to the mutations c.2111C>T and p.T407M remains speculative. The beneficial effect of walking and urination could be explained by lowering potassium through these activities. Most likely, multiple factors such as fluid retention, progesterone, and diet may have contributed to the beneficial effect of the pregnancy on the attacks of weakness.

This case shows that duration and intensity of attacks in hyperPP may decline during pregnancy. Contrary to previous reports, pregnancy may have a beneficial effect on disease severity in certain hyperPP patients.

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Conflicts of interest
There are no conflicts of interest.

Josef Finsterer, Salma Majid Wakil[1], Franco Laccone[2]

Department of Neurology, Krankenanstalt Rudolfstiftung, [2]Institute of Medical Genetics, Medical University of Vienna, Währinger Strasse 10, 1090, Vienna, Austria, [1]Department of Genetics, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

For correspondence:
Dr. Josef Finsterer, Postfach 20, 1180, Vienna, Austria.
E-mail: fifigs1@yahoo.de

References

1. Weber F, Jurkat-Rott K, Lehmann-Horn F. Hyperkalemic Periodic Paralysis; 18 Jul, 2003. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJ, editors. GeneReviews®. Seattle, WA: University of Washington; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1496/. [Last updated on 2016 Jan 28].
2. Jurkat-Rott K, Lehmann-Horn F. Genotype-phenotype correlation and therapeutic rationale in hyperkalemic periodic paralysis. Neurotherapeutics 2007;4:216-24.
3. Finsterer J. Disappearance of episodic weakness during pregnancy in hyperkalemic periodic paralysis from the SCNA4 mutation T704M. Neurologist 2009;15:289-90.
4. Therby D, Guionnet B, Vaast P, Rajabally R, Krivosic-Horber R, Puech F. Gamstorp's disease and pregnancy. A case report. J Gynecol Obstet Biol Reprod (Paris) 1996;25:832-5.
5. Perusquía M, Hernández R, Montaño LM, Villalón CM, Campos MG. Inhibitory effect of sex steroids on guinea-pig airway smooth muscle contractions. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol 1997;118:5-10.
6. Bielefeldt K, Waite L, Abboud FM, Conklin JL. Nongenomic effects of progesterone on human intestinal smooth muscle cells. Am J Physiol 1996;271(2 Pt 1):G370-6.

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