I. Background: Pseudohypoparathyroidism (PHP) encompasses a group of rare disorders defined by target organ unresponsiveness to parathyroid hormone (PTH). Patients with PHP type 1A carry heterozygous mutations of the maternal GNAS gene that encodes the α-subunit of the G protein. This protein is coupled to the PTH receptor as well as to other heptahelical receptors: thyrotropin (TSH), growth hormone-releasing hormone (GHRH) and gonadotropins receptors.

II. Subject and methods:

- The patient was born at 36 weeks gestation weighing 3535 grams after an uncomplicated pregnancy. Physical examination at birth was unremarkable except for umbilical hernia.
- At the 5th day of life, he developed hypothermia. Blood tests revealed:
  - TSH - 76 mIU/l (normal range: 0.7 - 9.8)
  - FT4 - 9.9 pmol/l (7-16) and FT3 - 4 pmol/l (3.8-6).
- Thyroid scan showed a normally located thyroid gland.
- Levothyroxine treatment was initiated with normalization of TSH, FT4 and FT3 levels.
- Excessive weight gain ensued and at 6 months he weighed 11.3kg (+3.3 SDS for his age).

III. Results: Sequence analysis revealed a novel heterozygous frameshift mutation with a premature stop codon in exon 7 (c.518_521delACTG). This mutation has not been previously reported and is predicted to be deleterious. Neither parent carried the mutation.

IV. Conclusion: This case presents a novel de-novo GNAS mutation. Physicians should consider the rare diagnosis of PHP among neonates with congenital hypothyroidism with normally located gland and marked obesity in the newborn period.