Rare Presentations of Congenital Hypothyroidism
Tatiana Smolkin MD, Irena Ulanovsky MD, Shraga Blazer MD and Imad R. Makhoul MD PhD

Department of Neonatology, Meyer Children’s Hospital and Rambam Health Care Campus, affiliated with Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

**KEY WORDS:** congenital hypothyroidism, neonatal screening, abdominal distension, weak pulse, newborn infant

**COMMENT**
In this report we wish to raise the awareness of neonatologists regarding uncommon clinical presentations of CH, where the clinical signs disappeared following thyroid hormone supplementation. In the first patient, abdominal distension was likely the sole sign of CH and was apparently caused by decreased intestinal motility often observed with CH [2]. In the second patient, weak pulses could have been due to CH which has been associated with decreased beat-to-beat variability of fetal heart rate [4] and with decreased left ventricular function [5].

**PATIENT DESCRIPTIONS**

**PATIENT 1**
A 2550 g term female infant, born to a group B Streptococcus-carrier mother, had abdominal distension at discharge examination [Figure A]. The infant nursed well without vomiting and passed meconium. There was no organomegaly or palpable abdominal masses. Sepsis workup was performed and empiric ampicillin and cefotaxime were started.

A decompressive nasogastric tube was inserted and intravenous fluids were initiated. Abdominal radiograph was normal except for mild bowel distension [Figure B]. Sepsis workup was negative. Abdominal ultrasonography was normal. On day 4 of life, the Israeli National Neonatal Screening Program reported a high thyroid-stimulating hormone level (> 400 mU/L). Venous sample of free thyroxine 2.4 pmol/L (normal 12–22) and TSH > 100 mU/L (normal < 10 mU/L) were compatible with CH. Thyroid hormone supplementation was started and 10 days later the pulses became normal and were easily palpable.

**PATIENT 2**
A term female infant weighing 4110 g presented with a systolic murmur and barely palpable pulses. Blood pressure (four limbs) was normal. Echocardiography was normal except for patent foramen ovale. The infant was asymptomatic but pulses remained weak. At day 4, the Israeli National Neonatal Screening Program reported a high TSH level (> 400 mU/L). The venous sample of FT4 = 2 pmol/L and TSH > 100 mU/L was compatible with CH. Thyroid hormone supplementation was started and 4 days later abdominal distension subsided; the infant nursed well and was discharged home. Follow-up 2 weeks later revealed a healthy infant with normal FT4 and TSH.

**Abdominal radiographs:** [A] Significant bowel distension at discharge examination (day 2), [B] Mild bowel distension (day 4).
These cases also demonstrate the crucial role of neonatal screening, which allowed early and timely treatment of CH.

**References**


---

**Capsule**

**Tissue factor-protease-activated receptor 2 signaling promotes diet-induced obesity and adipose inflammation**

Tissue factor, the initiator of the coagulation cascade, mediates coagulation factor VIIa-dependent activation of protease-activated receptor 2 (PAR2). Badeanlou et al. delineate a role for this signaling pathway in obesity and its complications. Mice lacking PAR2 (F2H1) or the cytoplasmic domain of tissue factor were protected from weight gain and insulin resistance induced by a high-fat diet. In hematopoietic cells, genetic ablation of tissue factor-PAR2 signaling reduced adipose tissue macrophage inflammation, and specific pharmacological inhibition of macrophage tissue factor signaling rapidly ameliorated insulin resistance. In contrast, non-hematopoietic cell tissue factor-VIIa-PAR2 signaling specifically promoted obesity. Mechanistically, adipocyte tissue factor cytoplasmic domain-dependent VIIa signaling suppressed Akt phosphorylation with concordant adverse transcriptional changes of key regulators of obesity and metabolism. Pharmacological blockade of adipocyte tissue factor in vivo reversed these effects of tissue factor-VIIa signaling and rapidly increased energy expenditure. Thus, inhibition of tissue factor signaling is a potential therapeutic avenue for improving impaired metabolism and insulin resistance in obesity.

*Nature Med* 2011; 17: 1490

Eitan Israeli

---

**Capsule**

**Melanopsin signaling in mammalian iris and retina**

Non-mammalian vertebrates have an intrinsically photosensitive iris and thus a local pupillary light reflex (PLR). In contrast, it is thought that the PLR in mammals generally requires neuronal circuitry connecting the eye and the brain. Xue et al. report that an intrinsic component of the PLR is in fact widespread in nocturnal and crepuscular mammals. In mouse, this intrinsic PLR requires the visual pigment melanopsin; it also requires PLCβ4, a vertebrate homologue of the Drosophila NorpA phospholipase C which mediates rhabdomeric phototransduction. The Plcb4−/− genotype, in addition to removing the intrinsic PLR, also essentially eliminates the intrinsic light response of the M1 subtype of melanopsin-expressing, intrinsically photosensitive retinal ganglion cells (M1-ipRGCs), which are by far the most photosensitive ipRGC subtype and also have the largest response to light. Ablating in mouse the expression of both TRPC6 and TRPC7, members of the TRP channel superfamily, also essentially eliminated the M1-ipRGC light response but the intrinsic PLR was not affected. Thus, melanopsin signaling exists in both iris and retina, involving a PLCβ4-mediated pathway that nonetheless diverges in the two locations.

*Nature* 2011; 479: 67

Eitan Israeli

---

“Every man is a damned fool for at least five minutes every day. Wisdom consists in not exceeding the limit”

Elbert Hubbard (1856-1915), American writer, publisher, artist and philosopher

“Lots of people want to ride with you in the limo, but what you want is someone who will take the bus with you when the limo breaks down”

Oprah Winfrey (born 1954), American talk show host and philanthropist