


10. Per M. Humpert1* Marco J. Battista1 Alexander Lammert2 Peter Reismann2 Zdenka Djuric1 Gottfried Rudofsky, Jr.1 Markus Zorn3 Michael Morcos4 Hans-Peter Hammes5 Peter P. Nawroth1,5 Angelika Bierhaus1

1 Medizinische Klinik I
University of Heidelberg
Heidelberg, Germany

2 V. Medizinische Klinik
University Clinics Mannheim
Mannheim, Germany

3 Sektion Laboratoriumsmedizin der Inneren Medizin I
Heidelberg, Germany

* Address correspondence to this author at: Medizinische Klinik I, University of Heidelberg, Im Neuenheimer Feld 410, 69120 Heidelberg, Germany. Fax 49-6221-100300; e-mail per.humpert@med.uni-heidelberg.de.

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**Association of Polycystic Ovary Syndrome and Fibromyalgia in a Patient with Primary Hyperparathyroidism: A Novel Triad?**

To the Editor:
The recent report by Panidis et al. (1), defining a novel mechanism for increased serum parathyroid hormone (PTH) driven by hyperandrogenism in polycystic ovary syndrome (PCOS), challenges the better established theory that secondary hyperparathyroidism observed in PCOS is related to hypovitaminosis D associated with obesity. Since its characterization by Stein and Leventhal (2), decades before its recognition as part of the metabolic syndrome, PCOS has been associated with the triad of obesity, oligoamenorrhea, and hirsutism. The molecular connection between insulin resistance and hyperandrogenism remained enigmatic until these 2 cardinal features of PCOS were elegantly unified by the discovery of a mutant serine kinase that hyperphosphorylates P450c17 and the insulin receptor β-chain (3). The linkage, in PCOS, of increased PTH to primary hyperparathyroidism constitutes a revolutionary theory for the cause of this disorder. To provide further insight, we describe a patient with PCOS with increased serum PTH and hypercalcemia associated with fibromyalgia. This case may represent a new triad, and it indicates that primary hyperparathyroidism itself may lead to a predisposition to PCOS and subsequently may be accentuated through positive feedback by PCOS-linked hyperandrogenism.

The case patient, a 40-year-old woman, presented on June 9, 2005, with generalized worsening body aches over 9 months that incapacitated her independent baseline functional status. PCOS had been diagnosed several years earlier at a women's infirmary when the patient presented with oligomenorrhea, hirsutism, obesity, and polycystic ovaries. Her medical history was remarkable for 2 hospitalizations for hypercalcemia that resolved with rehydration. During her most recent previous admission, the patient had had hypercalcemia of 2.71 mmol/L [reference interval (RI), 2.15–2.55 mmol/L] with an inappropriately high serum PTH of 8.6 pmol/L (RI, 1.3–7.6 pmol/L). Tumor markers for ovarian neoplasms such as serum human chorionic gonadotropin-β and CA-125 were negative. The patient was hirsute, obese, normotensive, and had 18/18 fibromyalgic spots, per the 1990 American College of Rheumatology multicenter criteria for fibromyalgia. Relevant serum chemistries included calcium, 2.74 mmol/L; phosphatase, 0.87 mmol/L (RI, 0.77–1.38 mmol/L); magnesium, 0.84 mmol/L (RI, 0.7–1.05 mmol/L); PTH, 9.7 pmol/L; and 25-hydroxyvitamin D3, 7.7 μg/L (RI, 10.1–40.3 μg/L). Her renal and thyroid functions were biochemically normal, her 24-h urinary calcium was 6.9 mmol/day (RI, <6.25 mmol/day), her serum C-reactive protein was <0.7...
mg/L, and her leukocyte count was 5500 cells/μL. Treatment with 20 mg of amitriptyline nightly dramatically ameliorated the patient’s pain, as indicated by a reduction in disability scores from 10 to 1 on a visual analog scale. Results of a double-phase septal scan were negative. After rehydration, her serum calcium was 2.67 mmol/L at discharge on June 23, 2005.

Panidis et al. (1) surmised that increased serum PTH is related to PCOS, a theory that was applicable in our case. However, the converse is equally compelling, given that dysregulated balance of calcium and vitamin D can perturb oocyte maturation, leading to meiotic arrest. In a series of women with PCOS and hypovitaminosis D–related secondary hyperparathyroidism, repletion of vitamin D with calcium normalized the menstrual cycles within 2 months in 7 of 13 women (4). Our patient’s profile differed because her low vitamin D stores, increased PTH, and hypercalcemia were synchronous, suggesting that her hypercalcemia was fueled by hyperparathyroidism, as supported by the hypercalciuria in her urine. After rehydration, our patient’s calcium was 2.67 mmol/L at discharge on June 23, 2005.

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