

Contents

Preface.....	IX
Chapter 1 Acute Renal Failure Secondary to Inadvertent Propylene Glycol Overdose with Single-Day High-Dose Vitamin D (Stosstherapy).....	1
David H. Jelley, Deborah Zayneb Mohamad Ali and Michelle Condren	
Chapter 2 Vitamin D-Resistant Rickets Diagnostics and Treatment Challenges at Muhimbili National Hospital, Tanzania	4
Evanke K. Godfrey, Fatima Mussa, Parvina Kazahura, Aika Shoo, Helga Naburi and Karim P. Manji	
Chapter 3 Myxedema Coma Associated with Macroprolactinoma: Case Report and Review of the Literature.....	10
Elizabeth Jasola Omoniyi and Richard J. Robbins	
Chapter 4 Hypertension Accompanied by Hyperaldosteronism, Hyperkalemia and Hyperchloremic Acidosis: A Case Report and Literature Review	14
Yunyun Yang, Yang Ou, Yan Ren, Haoming Tian and Tao Chen	
Chapter 5 Association of Central Precocious Puberty with a Rare Presentation of Schimmelpenning-Feuerstein-Mims Syndrome in a Peruvian Girl	20
Miguel Angel De los Santos-La Torre, Carlos Manuel Del Águila-Villa, Luis Rômulo Lu-de Lama, Oswaldo Nuñez-Almache, Eliana Manuela Chávez-Tejada, Oscar Antonio Espinoza-Robles, Paola Marianella Pinto-Ibárcena and Martha Rosario Calagua-Quispe	
Chapter 6 Two Cases of Pituitary Stalk Interruption Syndrome in Syrian Children.....	25
Ibrahim Alali, Reem Saad and Younes Kabalan	
Chapter 7 A Case Report of Graves' Disease Induced by the Anti-Human Programmed Cell Death-1 Monoclonal Antibody Pembrolizumab in a Bladder Cancer Patient.....	30
Ken Yajima and Yushi Akise	
Chapter 8 Acute Heart Failure as a First Presentation of Pheochromocytoma Complicated with "Inverted" Takotsubo Syndrome.....	34
Jerrold Spapen, Jeroen de Filette, Stijn Lochy and Herbert Spapen	
Chapter 9 Adrenal Mass in a 70-Year-Old Woman.....	38
Kiana Karimi, Mohsen Nikzad, Sohrab Kulivand and Shiva Borzouei	
Chapter 10 Primary Aldosteronism Associated with Multiple Adrenocortical Micronodules in a Patient with Renal Cell Carcinoma.....	43
Kazuhito Oba, Yuko Chiba, Yoko Matsuda, Takeshi Kumakawa, Rie Aoyama, Miho Akahoshi, Seiji Hashimoto, Aya Tachibana, Koichi Toyoshima, Remi Kodera, Kenji Toyoshima, Yoshiaki Tamura, Takashi Nagata, Yuto Yamazaki, Hironobu Sasano and Atsushi Araki	

Chapter 11	Clinical Characteristics and Treatment Outcomes in Endogenous Cushing's Syndrome: A 15-Year Experience from Thailand.....	49
	Wasita Warachit Parksook, Nitchakarn Laichuthai and Sarat Sunthornyothin	
Chapter 12	Co-Occurrence of Exogenous and Endogenous Cushing's Syndromes – Dilemma in Diagnosis.....	56
	Chin Voon Tong and Subashini Rajoo	
Chapter 13	Addison's Disease Presenting as Acute Renal Failure and Hyperkalemic Paralysis: A Rare Presentation	59
	Kundan Jana, Kalyana Janga, Sheldon Greenberg and Amit Gulati	
Chapter 14	Vitamin D Intoxication and Nephrocalcinosis in a Young Breastfed Infant.....	63
	Abdullah Al-Kandari, Hussain Sadeq, Rita Alfattal, Maryam AlRashid and Mayra Alsaaid	
Chapter 15	Primary Hypothyroidism with Pituitary Hyperplasia in an Omani Girl.....	67
	Wafa Abdallah Fadle, Ali Al Reesi, Saud Al-Shabibi and Maryam Khamis Al-Badi	
Chapter 16	A New MEN2 Syndrome with Clinical Features of Both MEN2A and MEN2B Associated with a New RET Germline Deletion.....	73
	Carlotta Giani, Teresa Ramone, Cristina Romei, Raffaele Ciampi, Alessia Tacito, Laura Valerio, Laura Agate, Clara Ugolini, Michele Marino, Fulvio Basolo, Alessandro Franchi, Simona Borsari, Angela Michelucci, Cesare Selli, Gabriele Materazzi, Filomena Cetani and Rossella Elisei	
Chapter 17	Malignant Insulinoma with Multiple Liver Metastases and Hypercalcitoninemia in a Patient with Type 2 Diabetes Mellitus Presenting as Recurrent Episodes of Diaphoresis due to Severe Hypoglycemia.....	80
	Marco Ciacciarelli, Gianluca Caruso, Marco Rengo, Piero Maceroni, Carmen Misurale, Eleonora D'Armiento, Alessandro Polidoro, Cristina Napoli, Alberto Lombardini, Umberto Ceratti, Ruben Manuel Luciano Colunga Biancatelli, Leonardo Calvosa, Romina Milanese, Sonia Ferri, Teresa Massaro, Andrea Lorusso, Veronica Sorrentino, Vincenzo Petrozza and Luigi Iuliano	
Chapter 18	Multifocal Multisystem Langerhans Cell Histiocytosis Involving Pituitary Masquerading as Crohn's Disease: A Case Report and Review of the Literature.....	88
	Mohd. Ashraf Ganie, Bhanu Malhotra, Manpreet Saini, Arshiya Dutta, Atul Sharma, Kim Vaiphie and Pinaki Dutta	
Chapter 19	Heparin-Induced Pituitary Apoplexy Presenting as Isolated Unilateral Oculomotor Nerve Palsy: A Case Report and Literature Review	93
	Bakr Swaid, Frank Kalaba, Ghassan Bachuwa and Stephen E. Sullivan	
Chapter 20	BYPASS-OMA: Hypoglycemic Hyperinsulinemic Nesidioblastosis after Gastric Bypass Surgery – A Case Report and Review of the Literature.....	98
	Jessica Cao, Cindy Kim, Thatcher Huynh, Amanda Frugoli, Heidi Henson, Vera Valdez and Tricia Westhoff-Pankratz	
Chapter 21	Pembrolizumab in a Patient with Treatment-Naïve Unresectable BRAF-Mutation Negative Anaplastic Thyroid Cancer	104
	Fadi Nabhan, Elizabeth Kander, Rulong Shen, Amit Agrawal, Vineeth Sukrithan, Ye Zhou, Ashima Goyal, Katie Roll, Manisha Shah and Bhavana Konda	

Chapter 22	Prolactin-Secreting Leiomyoma Causing Hyperprolactinaemia Unresponsive to Dopamine Agonist Therapy and Resolution following Myomectomy.....	109
	Lucinda Barry, Selvan Pather, Ash Gargya and Anthony Marren	
Chapter 23	Lack of Catch-Up Growth with Growth Hormone Treatment in a Child Born Small for Gestational Age Leading to a Diagnosis of Noonan Syndrome with a Pathogenic <i>PTPN11</i> Variant	114
	Daniel J. Olivieri, Lauren J. Massingham, Jennifer L. Schwab and Jose Bernardo Quintos	
Chapter 24	Central Hyperthyroidism due to Thyroid-Stimulating Hormone-Secreting Pituitary Microadenoma in an Adolescent Boy: Case Report and Review of the Literature.....	120
	Le Hoang Bao, Nguyen Minh Duc, Phan Cong Chien, Thieu-Thi Tra My, Tran Viet Thang and Tran Quang Nam	
Chapter 25	Gonadoblastoma with Dysgerminoma Presenting as Virilizing Disorder in a Young Child with 46, XX Karyotype: A Case Report and Review of the Literature	127
	Prathamesh Chandrapattan, Amitabh Jena, Rashmi Patnayak, Swayamsidha Mangaraj, Sujata Naik and Saroj Panda	
Chapter 26	The Highs and Lows of an Unknown Pheochromocytoma in an Elderly Patient.....	133
	Christina N. DiMaria, Lorena I. Rasquin and Wikien A. Hung Pinto	
Chapter 27	Atypical Presentation of Testicular Adrenal Rest Tumor (TART) Leading to Bilateral Partial Orchiectomy in a 31-Year-Old Adult Revealing Primary Adrenal Insufficiency with <i>CYP11A1</i> Deficiency.....	136
	Cyril Garcia, Marie Dusaud, Paul Chiron, Mathilde Solle, Sika Nassouri, Lionel Groussin, Mathilde Sibony, Claire Goursaud, Florence Roucher Boulez Lyse Bordier	
Chapter 28	Attenuation of Autoimmune Phenomena in a Patient with Autoimmune Polyglandular Syndrome Type 1.....	141
	Jill D. Jacobson, Julia R. Broussard, Courtney Marsh and Brandon Newell	
Chapter 29	Acute Lymphoblastic Leukemia Presenting as Pituitary Apoplexy: A Case Report and Review of the Literature.....	146
	Rahul Gupta, Urmimala Bhattacharjee, K. S. Lekshmon, Shakun Chaudhary, Prashant Sharma, Aditya Jandial and Pinaki Dutta	
Chapter 30	Rare Association between Two Genetic Conditions: Turner Syndrome and Neurofibromatosis Type 1.....	151
	R. El Qadiry, K. Danaoui, H. Nassih, A. Bourrahout and I. Ait Sab	
Chapter 31	Pregnancy in a Transgender Male: A Case Report and Review of the Literature	155
	Ayesha Hassan, Jessica Perini, Amna Khan and Apoorva Iyer	
Chapter 32	Spontaneous Adrenal Hemorrhage with Mild Hypoadrenalism in a Patient Anticoagulated with Apixaban for Antiphospholipid Syndrome: A Case Report and Literature Review.....	158
	Jia Wei Tan, Anant Shukla, Jiun-Ruey Hu and Sachin K. Majumdar	
Chapter 33	Ectopic ACTH Syndrome Emerging 5 Years after the Diagnosis of Neuroendocrine Tumor.....	164
	Minghao Liu, Diane Hamele-Bena, John Ausiello and Gabrielle Page-Wilson	

Chapter 34	Acute Secondary Adrenal Insufficiency Misdiagnosed as Acute Cholecystitis.....	169
	Moslem Sedaghattalab and Amir Hossein Doustimotlagh	
Chapter 35	The Utility of Immunohistochemistry in Differentiating Metastatic Primary Squamous Cell Carcinoma of the Thyroid from a Primary Lung Squamous Cell Carcinoma.....	172
	Nern Hoong Kao, Chien Sheng Tan and Adrian Jit Hin Koh	
Chapter 36	Nonmosaic Isodicentric Y Chromosome: A Rare Cause of Azoospermia – From Genetics to Clinical Practice.....	176
	Jolijn Van Cauwenberghe, Sigri Beckers and Peter Coremans	
Chapter 37	Clinical Features and Outcomes of Dipeptidyl Peptidase-4 Inhibitor-Associated Bullous Pemphigoid (DPP4i-Associated BP) in Thai Patients.....	181
	Yotsapon Thewjitcharoen, Ekgaluck Wanothayaroj, Chattip Thammawiwat, Sriurai Porramatikul, Chuleekorn Vorayingyong, Soontaree Nakasatien, Sirinate Krittiyawong, Kumutnart Chanprapaph and Thep Himathongkam	
Chapter 38	Denosumab-Induced Hypocalcemia after Billroth II Gastric Bypass Surgery.....	187
	Abigail M. Schmucker, Dina E. Green and Philip M. Montemuro	
Chapter 39	Successful Treatment of Tumor-Induced Osteomalacia by Multidisciplinary Therapy with Radiation to Intracranial Fibromyxoid Tumor.....	191
	Mariangela Massacesi, Francesco Micciché, Mario Rigante, Gianluigi Petrone, Elisabetta Lepre, Maria Antonietta Gambacorta and Vincenzo Valentini	
Chapter 40	ARMC5 Primary Bilateral Macronodular Adrenal Hyperplasia Associated with a Meningioma: A Family Report.....	196
	M. J. Ferreira, J. Pedro, D. Salazar, C. Costa, J. Aragão Rodrigues, M. M. Costa, A. Grangeia, J. L. Castedo and D. Carvalho	
Chapter 41	PES Syndrome Presenting as Severe Hyponatremia in an Asymptomatic Septuagenarian.....	201
	Rahul Pansare and Sangeetha Nanthabalan	
Chapter 42	Autosomal Dominant Hypophosphatemic Rickets Presenting in a Phenotypically Normal Adult Female.....	205
	Hala Mualla, Su Ah Bae and Abid Yaqub	
Chapter 43	Diabetic Ketoacidosis Revealing a Severe Hypertriglyceridemia and Acute Pancreatitis in Type 1 Diabetes Mellitus.....	210
	Fatima Zahra Zaher, Imane Boubagura, Sana Rafi, Ghizlane Elmghari and Nawal Elansari	
Chapter 44	Persistent vs Recurrent Cushing's Disease Diagnosed Four Weeks Postpartum.....	214
	Leena Shah, Emily V. Nosova, Joshua B. Bederson and Khadeen Christi Cheesman	
Chapter 45	Diagnostic Challenges in Ovarian Hyperthecosis: Clinical Presentation with Subdiagnostic Testosterone Levels.....	218
	Sanket Shah, Callie Torres and Naser Gharaibeh	

Permissions

List of Contributors

Index

Acute Renal Failure Secondary to Inadvertent Propylene Glycol Overdose with Single-Day High-Dose Vitamin D (Stosstherapy)

David H. Jelley ¹, Deborah Zayneb Mohamad Ali ², and Michelle Condren ³

¹*Pediatric Department, University of Oklahoma School of Community Medicine, Tulsa, 4444 E 41st St., Tulsa, OK 74135, 918-619-4803, USA*

²*Pediatric Department, University of Oklahoma School of Community Medicine, Tulsa, 4502 E 41st St, Tulsa, OK 74135, 918-660-3400, USA*

³*University of Oklahoma College of Pharmacy, Pediatric Department, University of Oklahoma School of Community Medicine, Tulsa, 4502 E. 41st St, Tulsa, OK 74135, 918-660-3578, USA*

Correspondence should be addressed to David H. Jelley; david-jelley@ouhsc.edu

Academic Editor: Hyunsik Kang

Globally, there has been increasing attention paid to vitamin D deficiency and its treatment. Vitamin D stosstherapy with high-dose ergocalciferol in a single day is reemerging as a potential treatment option. We present an as yet unreported complication of acute renal injury due to propylene glycol toxicity in a 7-month infant treated with vitamin D stosstherapy. The product label for the vitamin D used for this patient states it is dissolved in propylene glycol (PG), but the amount is not listed on this or other US ergocalciferol liquid products that contain PG. Caution should be used when considering vitamin D stosstherapy with liquid ergocalciferol products available in the United States.

1. Introduction

Vitamin D is essential for calcium homeostasis and bone health and is obtained from sun exposure, vitamin supplements, and foods fortified with vitamin D including dairy products, infant formula, and breakfast cereals. Once foods were fortified, nutritional or vitamin D deficiency was thought to be a disease of the past, yet it remains common. While mild vitamin D deficiency is generally asymptomatic in children, more severe deficiency can result in rickets with or without hypocalcemia. Treatment includes vitamin D supplementation plus adequate nutritional intake of calcium. Stosstherapy, or single-day high dose vitamin D therapy, has been used since the 1930s and may be warranted when patients present with acute conditions secondary to low vitamin D requiring more rapid resolution of deficiency, or when there are concerns about compliance with daily therapy. Stosstherapy has been reported to be a safe and effective method of treatment [1]; however, concerns have been raised regarding the markedly elevated vitamin D levels which occur with this form of treatment. Furthermore,

unintended consequences related to other molecules in the drug formulation may occur; in this case propylene glycol results in acute renal failure following vitamin D stosstherapy in an infant with nutritional rickets.

2. Case

A previously healthy 7-month-old African-American male presented to the ER in late winter after a generalized tonic-clonic seizure. There was no history of trauma or febrile illness. He was exclusively breastfed but had only received a multivitamin supplement for the first three months of life. Physical exam revealed a postictal infant with short stature, length = 64 cm (<5th percentile) and weight of 9.2 kg (75th percentile). Neurologic exam demonstrated brisk patellar reflexes, and the remainder of his physical exam was unremarkable. Initial labs showed severe hypocalcemia with total serum calcium = 5.9 mg/dl (normal range 8.5-10.9 mg/dl) and ionized calcium = .67 mmol/L (normal range 1.18-1.29 mmol/L). He was treated with IV calcium, after which serum calcium levels rose slightly but remained significantly

TABLE 1: Serial laboratory values from admission through six-week followup appointment.

	Admission Feb 11	Post Stosstherapy Feb 14	Discharge Feb 18	Outpatient followup March 28	Normal Values
Calcium	5.9	7.0	9.8	10.2	8.0-10.5 mg/dL
Ionized calcium	0.67	0.88	1.18		1.18-1.29 mmol/L
Phosphorus	5.3	5.6	6.0		3.8-6.2 mg/dL
Magnesium	2.1	2.2	1.6		1.7-2.9 mg/dL
Vitamin D	<4	112	350	86	30-100 ng/ml
Alkaline phosphatase	876	905	746	307	150-420 U/L
PTH	404.8	582.3	40	40	7.2-111.9 pg/mL
Creatinine	0.41	3.00	0.41	.45	0.20-0.73 mg/dL
CO ₂	17	14	26	21	20-24 mmol/L

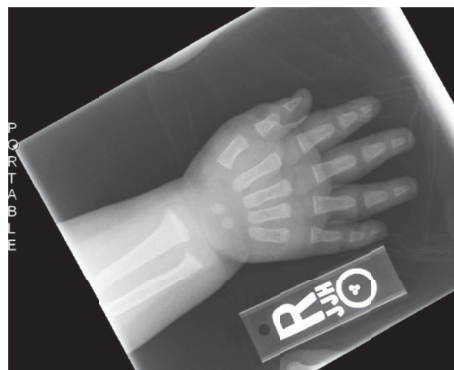


FIGURE 1: Classic rachitic changes of the wrist: fraying and widening at the radial and ulnar metaphyses.

below the normal range. Subsequent evaluation showed an undetectable 25-hydroxy vitamin D level of less than 4 ng/ml, with elevated parathyroid hormone and alkaline phosphatase levels (Table 1). Skeletal survey showed rachitic changes (Figure 1).

The patient was diagnosed with nutritional rickets and was administered vitamin D stosstherapy treatment with ergocalciferol (Virtus Pharmaceuticals, ergocalciferol oral solution, USP, 8,000 international units per mL) 100,000 international units given orally every 2 hours for a total of 600,000 international units over 12 hours. By the last dose, the patient had become lethargic and urine output was decreased from 2.1 cc/kg/hr before treatment to .7 cc/kg/hr after treatment. Labs revealed acute renal failure, metabolic acidosis, and hyperkalemia. Creatinine level rose from .41 mg/dl pretreatment to 3.0 mg/dl following stosstherapy over a 36-hour timespan. He was treated with fluid resuscitation, diuretics, sodium polystyrene sulfonate, bicarbonate, and continued IV calcium. Renal function and calcium levels normalized, and serum creatinine returned to baseline of .41 mg/dl and total calcium = 9.8 mg/dl. The patient was discharged home after 4 days on oral vitamin D and calcium supplementation.

3. Discussion

To our knowledge, this is the first reported case of renal failure due to vitamin D stosstherapy. Derived from the

German word stossen, meaning “to push”, stosstherapy consists of high-dose (600,000 units) ergocalciferol given over a single day. Use of this therapy for rickets was first reported over 75 years ago and is now regaining popularity [1–4]. For decades all infants in the German Democratic Republic (GDR) received 600,000 units ergocalciferol every 3 months for the first 18 months of life. While a significant percentage of these infants had elevated vitamin D levels and hypercalcemia, none were reported to have suffered renal injury or nephrocalcinosis [3, 5]. While renal failure has been associated with chronic vitamin D toxicity when dosed on a daily or weekly basis, we found no reports associated with single day stosstherapy [6].

Post hoc analysis of the ergocalciferol preparation carried by our hospital found that the side panel states it is dissolved in propylene glycol (PG), but the amount is not listed on this or other US ergocalciferol liquid products that contain PG. Further investigation revealed that the above product contains 103.6 g/100 mL of propylene glycol. The infant received 600,000 units of vitamin D₂, equivalent to 75 mL of solution or 77.7 g of propylene glycol. According to the World Health Organization, this far exceeds the maximum tolerable amount of 25 mg/kg/day (or 227.5 mg for the baby in this event). In fact, the baby was exposed to 340 times the maximum amount [7]. Propylene glycol is a clear, colorless, odorless, and tasteless product used as a stabilizer, thickener, and texturizer. When given in large doses, drugs containing PG induce metabolic acidosis and reversible acute