Drug-Induced Thyrotoxic Periodic Paralysis

Michael P Kane and Robert S Busch

OBJECTIVE: To report a case of iodine-induced (Jod–Basedow) hyperthyroidism leading to thyrotoxic periodic paralysis (TPP).

CASE SUMMARY: A 64-year-old white male, one day status-post-cardiac catheterization, presented to the local emergency department with profound weakness of his extremities and an inability to stand on his own. Pertinent laboratory test results included a potassium level of 3.0 mEq/L. Treatments of oral and intravenous potassium supplementation resulted in his complete recovery. Two days later he was diagnosed with hyperthyroidism and subsequently treated with nadolol 40 mg daily and methimazole 20 mg daily. At time of writing, the patient remained euthyroid, receiving no antithyroid medications. There had been no further reports of paralysis in the 6 years since his original presentation. The Naranjo probability scale indicated a probable relationship between the patient’s episode of TPP and his exposure to the iodinated contrast dye.

DISCUSSION: TPP is an uncommon manifestation in white patients with hyperthyroidism. Iodine-induced TPP is even more rare, with only 2 such cases reported as of November 2, 2005. In this case, Jod–Basedow hyperthyroidism was induced by the iodine-containing dye that the patient received during cardiac catheterization. Soon after the dye was administered, he developed TPP.

CONCLUSIONS: Clinicians should be aware not only of potential causes of drug-induced thyroid disease, but also of the potential for drug-induced hyperthyroidism leading to TPP. The diagnosis of TPP should be considered in patients presenting with acute onset of extremity weakness or paralysis and hypokalemia. Quick diagnosis and prompt treatment of TPP can prevent life-threatening complications of this treatable and curable disorder.

KEY WORDS: hypokalemia, drug-induced; Jod–Basedow; thyrotoxic periodic paralysis.


Thyrotoxic periodic paralysis (TPP) is an uncommon, potentially life-threatening endocrine emergency. It is a rare complication of hyperthyroidism and, while the pathophysiologic features of this disorder have not been entirely elucidated, it most likely involves a hyperthyroidism-related hypokalemia and muscle-weakening condition caused by a sudden shift of potassium into cells (as opposed to a depletion of total body potassium stores) and progressive depolarization of the resting membrane potential. Increased thyroid hormone levels change the plasma membrane permeability to sodium and potassium by increasing activity of sodium–potassium–adenosine triphosphatases, the number and activity of which increase in hyperthyroidism. In contrast to the high female predominance of hyperthyroidism, TPP occurs in a 20:1 male:female ratio. While TPP is not uncommon in individuals of Asian descent (~1.9% of thyrotoxic pts.), it is unusual in non-Asian patients, involving only 0.1–0.2% of hyperthyroid cases in North America, based on experience from the Mayo Clinic. Drug-induced hyperthyroidism resulting in TPP is even more rare.

Hypokalemia with associated weakness of the extremities, or even frank flaccid paralysis of the extremities and signs of hyperthyroidism are the characteristic features of the disease. Proximal muscles, especially of the lower extremities, are most commonly affected, though patients may present with respiratory failure, arrhythmias, or thyroid storm. In some instances, however, patients may not have obvious symptoms related to hyperthyroidism (silent hyperthyroidism) or the periodic paralysis may precede the symptoms of hyperthyroidism. As a result, clinicians may easily overlook this disease, even when life-threatening hypokalemia is present.
TPP should be recognized when it occurs because of its severe and potentially fatal complications, which are reversible with appropriate potassium replacement, β-blocker therapy, and correction of the hyperthyroid state. We report a case of a patient developing hyperthyroidism and subsequent TPP as a result of iodine exposure via a coronary catheterization.

Case Report

A 64-year-old white male presented to the local emergency department (ED) with extreme weakness of his lower extremities and an inability to walk or stand without support. There was no history of trauma, fever, gastrointestinal illness, palpitations, tremor, heat intolerance, myalgias, or known ingestion of toxins. His past medical history was significant for an appendectomy 40 years ago, atherosclerotic heart disease, type 2 diabetes mellitus diagnosed 6 months previously, and a cardiac catheterization that he had undergone one day prior to presentation. The patient had had no known drug allergies, and medications at presentation included pravastatin 20 mg at bedtime, aspirin 325 mg daily, and vitamin C 500 mg daily. He had been started on a sulfonylurea soon after his diagnosis of diabetes mellitus, but this had been discontinued shortly thereafter following a hypoglycemic episode.

During a primary care routine follow-up visit, the patient had reported a burning sensation in his throat after exertion, which was also associated with some breathlessness. A stress test conducted at that time was positive. Subsequent cardiac catheterization showed 30–50% diffuse intimal lesions, none of which was felt to be angioplastable at that time. During the catheterization, the patient received 80 mL of the contrast agent MD 76 (diatrizoate meglumine 66%, diatrizoate sodium 10%), which contains 370 mg/mL of iodine.

The patient awoke at 0130 the morning following his cardiac catheterization with profound weakness of his extremities, resulting in difficulty raising his arms and legs. He then became so weak that he could not lift himself off the bed. The patient noted that he drank a quart of orange juice before coming to the hospital and actually felt much better by the time he arrived at the ED.

Upon ED arrival he was able to move his arms and legs against gravity but not against resistance. Physical examination revealed heart rate 99 beats/min, blood pressure 134/80 mm Hg, respiratory rate, 18 breaths/min, and temperature 36.3 °C. There were no tremors, palpitations, or goiter. The patient was alert and oriented to person, place, and time. Sensation to light touch and pinprick were normal; the cranial nerves were intact. Systemic examination was also normal. He had no gastrointestinal symptoms.

Laboratory studies revealed hypokalemia (potassium 3.0 mEq/L) and a glucose level of 214 mg/dL. Results of a complete blood cell count, as well as renal and liver function tests, were within normal limits. An electrocardiogram revealed sinus tachycardia. An electrolyte panel obtained during a routine primary-care follow-up visit 17 days prior to ED admission listed a potassium level of 4.8 mEq/L. In the ED, the patient received 50 mEq of potassium chloride orally and an infusion of 1 L of NaCl 0.45% with 40 mEq of potassium chloride at a rate of 125 mL/h. The patient was able to move his upper extremities within 30 minutes of therapy initiation and all extremities within 3 hours. He received no insulin or insulin secretagogue therapy during his ED stay. The patient was discharged from the ED later that day with a referral to an endocrinologist and weight 71 kg (body mass index 24.5). His thyroid gland was palpable, with normal size and configuration and no appreciable nodules. Neurologic examination revealed normal sensory appreciation and motor function. Deep tendon reflexes were symmetrical and not hinged, and cranial nerves were intact. There was no tremulousness of outstretched hands. Signs and symptoms of thyrotoxicosis, such as weight loss, diaphoresis, palpitations, or mild diffuse goiter, were absent.

Biochemical testing demonstrated a potassium level of 4.5 mEq/L, normal magnesium and calcium levels, hemoglobin A1C 6.6%, thyroid stimulating hormone level 0.01 µIU/mL (reference range 0.4–4.0), unbound thyroxine level 3.3 pmo/L (0.8–1.9), total thyroxine level 13.3 µg/dL (5.2–12.5), triiodothyronine level 204 ng/dL (82–179), thyroid-stimulating immunoglobulin level 200% (0–130), antithyroglobulin antibody titer 20.0 IU/mL (0–40) and antithyroid peroxidase antibody titer 28.5 IU/mL (0–35). Radioactive iodine uptake scanning was not performed given the patient’s earlier iodine exposure via cardiac catheterization. Based on history, physical findings, and biochemical testing, a diagnosis of TPP was made.

Therapy was initiated with nadolol 40 mg daily and methimazole 20 mg daily. The patient became clinically and biochemically euthyroid within one month, with therapies subsequently tapered and discontinued after 3 months. He remained euthyroid at time of writing and had reported no further episodes of paralysis after 6 years of follow-up.

The Naranjo probability scale indicated a probable relationship between the patient’s episode of TPP and his exposure to the iodinated contrast dye, which, as of November 2, 2005, represents the first published case of contrast-induced TPP.

Discussion

Thyrotoxic periodic paralysis is a rare complication of hyperthyroidism, occurring most commonly in Asian males. In the US, the most common causes of hyperthyroidism are Grave’s disease, uninodular or multinodular goiters, and iodine-induced (Jod–Basedow) disease. This case is of particular interest due to the existence of Jod–Basedow leading to TPP in the same individual. The Jod–Basedow phenomenon occurs in patients unable to induce the Wolff–Chaikoff block, a normal protective mechanism that, in the presence of excess iodine, inhibits organification and subsequent excessive thyroid hormone synthesis. Iodine-containing medications known to cause hyperthyroidism include amiodarone, radiographic contrast dyes (eg, ipodate, iopanoic acid, diatrizoate), iodinated glycerol, and kelp supplements. The incidence of thyroid disease induced by iodine-containing drugs ranges from 1% to 22%.

Iodine-induced TPP is very rare, with only 2 cases identified upon review of the literature. A 34-year-old man presented to the ED with sudden lower extremity weakness, heat intolerance, tremors, and weight loss. The serum potassium level was 2.2 mEq/L at admission. Lower extremity weakness resolved immediately after potassium replacement therapy. The patient had received amiodarone, which contains 37.5% by weight iodine, for several months. Another report described a 37-year-old white male who developed TPP after exposure to saturated solution of potassium iodide (SSKI). The patient was euthy-
roid with a thyroid nodule and developed symptoms after 6 weeks of receiving SSKI 5 drops twice daily and levothyroxine 0.3 mg daily in an attempt to suppress his goiter. Typical of the Jod–Basedow phenomenon, the patient’s symptoms improved and finally resolved without specific antithyroidal therapy.

In addition to the 2 reports above, Akar et al.18 reported TPP in a Turkish male 10 days after receiving 10 mCi of radioactive iodine (131I). Rather than a direct effect of 131I serving as a substrate for additional thyroid hormone synthesis, the recurrence of TPP in this case was most likely due to a transient rise in thyroid hormone levels as a consequence of thyroid ablation (radiation thyroiditis). The iodinated contrast dye our patient received with his coronary catheterization (29.6 g of iodine) is believed to have caused his hyperthyroidism. Jod–Basedow hyperthyroidism is self-limiting, with correction of the hyperthyroid state occurring after dissipation of the iodine exposure. In our patient, methimazole was tapered and discontinued after 3 months of therapy.

Treatment of TPP consists of correction of hyperthyroidism and administration of potassium during the acute episode. Nonselective β-blocker therapy is also a typical standard of therapy as potassium replacement can result in rebound hyperkalemia.19,20 Prophylactic use of potassium supplements between paralytic attacks is not recommended,12 as recurrent episodes have not been consistently prevented by prophylactic potassium.21 The use of spironolactone, though not uniformly effective in all patients, may be effective in preventing paralysis in some patients.21 Muscle paralysis recovery usually occurs in reverse order of the appearance of the paralysis.22 Long-term therapy with definite control of hyperthyroidism (ie, induction of a euthyroid state) prevents recurrent episodes of paralytic attacks as long as the patient remains euthyroid.12,21,22

Conclusions

Clinicians should be aware not only of potential causes of drug-induced thyroid disease, but also of the potential of drug-induced hyperthyroidism leading to TPP. The diagnosis of TPP should be considered in patients presenting with acute onset of extremity weakness or paralysis and hypokalemia. Early diagnosis, including the monitoring of thyroid function, and prompt treatment of TPP can prevent life-threatening complications of this treatable and curable disorder.

References


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EXTRACTO

OBJETIVO: Describir un caso de hipertiroidismo inducido por yodo (Jod–Basedow) que resultó en una parálisis tirotoxica temporal (TPP, por sus siglas en inglés).

RESUMEN DEL CASO: Un hombre blanco de 64 años se presentó a la sala de urgencias local un día después de una cateterización cardíaca quejándose de debilidad intensa en las extremidades e incapacidad para ponerse de pie por sí mismo. Los análisis de laboratorio pertinentes incluían niveles de potasio de 3.0 mEq/L. El tratamiento con suplementos de potasio oral e intravenoso produjo una recuperación completa. Dos días más tarde, el paciente se diagnosticó de...
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hipertiroidismo y, subsecuente, fue tratado con 40 mg de nadolol y 20 mg de metimazol diarios. Actualmente, el paciente permanece eutiroideo sin tomar los medicamentos antitiroides. Desde que ocurrió el episodio original hace más de 6 años, no ha habido nuevos episodios de parálisis. De acuerdo con el algoritmo de causalidad de reacciones adversas a medicamentos de Naranjo, la relación entre el episodio de TPP y la exposición al contraste yodado es probable.

DISCUSIÓN: La TPP es una manifestación poco común en pacientes caucásicos con hipertiroidismo. La TPP inducida por yodo es todavía más rara; sólo se habían notificado 2 casos previamente. En este caso, el hipertiroidismo Jod–Basedow fue inducido por el contraste yodado que el paciente recibió durante la cateterización cardíaca. Al poco tiempo, el paciente desarrolló TPP.

CONCLUSIONES: Los médicos deben estar alerta, no tan sólo a las posibles causas de enfermedad tiroides inducida por medicamentos, sino también al potencial de que el hipertiroidismo inducido por medicamentos resulte en TPP. Dicho diagnóstico debe considerarse en pacientes que presentan síntomas agudos de debilidad o parálisis en las extremidades e hipocalcemia. Un diagnóstico y tratamiento precoces de la TPP puede prevenir complicaciones que atenten contra la vida causadas por este alteración tratable y curable.

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RÉSUMÉ
OBJECTIF: Rapporter un cas d’hyperthyroïdie induit par l’iodine (Jod–Basedow) conduisant à une paralysie périodique thyrotoxique (PPT).

RÉSUMÉ DU CAS: Un homme caucasién âgé de 64 ans s’est présenté à la salle d’urgence 24 heures suivant une procédure cardiaque et se plaignait de faiblesses extrêmes aux extrémités et à l’incapacité de se tenir debout. Les laboratoires indiquaient un niveau de potassium à 3 mEq/L. Un traitement avec du potassium par voie orale et intra-veineuse a permis le rétablissement complet du patient. Deux jours après, il était diagnostiqué avec de l’hyperthyroïdie et traité subséquemment avec du nadolol 40 mg une fois par jour et avec du méthimazole 20 mg une fois par jour. Le patient est présentement euthyroïdien sans thérapie médicamenteuse. Il n’a pas eu de symptômes de paralysie depuis l’épisode initial. L’algorithme d’imputabilité de Naranjo a indiqué une relation probable entre l’épisode de paralysie et l’agent de contraste avec l’iode.

DISCUSSION: La PPT est une manifestation peu commune chez les patients caucasiens avec de l’hyperthyroïdie. La PPT induite par l’iode est encore plus rare avec seulement 2 autres cas rapportés précédemment. Dans ce cas, l’hyperthyroïdie de Jod–Basedow a été induit par un agent contrastant à l’iode que le patient avait reçu durant sa procédure cardiaque. Le patient a développé la PPT peu de temps après.

CONCLUSIONS: Les cliniciens devraient être informés non seulement des maladies thyroïdiennes causées par des médicaments, mais aussi des médicaments pouvant induire de l’hypothyroïdie menant à la PPT. Le diagnostic de la PPT devrait être considéré chez des patients une faiblesse ou paralysie extrême et subite ainsi qu’une hypokaliémie. Le diagnostic rapide et un traitement immédiat de la PPT peuvent prévenir des complications de cette maladie traitable.

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