Dr. Ian J. Barbash (Medicine): A 37-year-old man was admitted to this hospital because of muscle pain and weakness. The patient had been well until the evening before admission, when mild diffuse myalgias developed. He awoke in the morning with diffuse muscle cramps and intense pain in his legs (he rated the pain at 10 on a scale of 1 to 10, with 10 indicating the most severe pain). On arising to go to the bathroom, he felt unsteady and had difficulty walking. After he returned to bed, diffuse muscle pain persisted, with weakness in his arms and legs and numbness in his legs; he was unable to arise again. He called family members and was brought to the emergency department at this hospital.

The patient reported that he had had similar but much less severe pain intermittently for the past month, not associated with weakness and primarily in his upper thighs, after prolonged periods of rest. The pain occurred several times a week, most often at night, occasionally awakened him, and resolved spontaneously after a few minutes. He reported weight loss of 3.2 kg during the previous month, occasional blurred vision during the previous year, intermittent left wrist pain, and a slight tremor. Six weeks before admission, he had fever, sore throat, and decreased appetite; a chest radiograph revealed patchy opacities in the upper lobe of the right lung, features consistent with possible pneumonia; his symptoms improved after azithromycin was administered. A diagnosis of gynecomastia had been made approximately 3 months earlier, when he presented with left breast tenderness and a palpable mass (4 cm by 3.5 cm) under the areola; mammography subsequently revealed bilateral subareolar densities (greater on the left breast than on the right breast) that were consistent with gynecomastia. The patient also had androgenetic alopecia and seborrheic dermatitis. He reportedly had been treated for tuberculosis 17 years earlier. His diet was high in carbohydrates; he reported eating 10 slices of pizza for dinner the night before admission. Medications included finasteride and clobetasol shampoo. He had no known allergies. He was born in Colombia, had lived in the United States for about 17 years, and had visited Colombia 6 months before admission. He drank alcohol infrequently, did not smoke or use illicit drugs, and reported no paint sniffing or exposure to toluene. He lived with his brother, worked in a restaurant, was single, and had been sexually active in the past, with women
only. His mother had had diabetes mellitus and hypercholesterolemia and died of bladder cancer, his father had hypertension, and a cousin and a niece had thyroid disease; the patient was not sure of the exact diagnoses. There was no history of autoimmune disease.

On examination, the blood pressure was 166/72 mm Hg, the pulse 100 beats per minute, the temperature 37.3°C, the respiratory rate 16 breaths per minute, the oxygen saturation 99% while the patient was breathing ambient air, and the weight 66.2 kg. The patient was unable to stand; strength in the muscles of flexion and extension measured 3 out of 5 at the hips and knees and 4 out of 5 at the ankles and elbows. Hand grip measured 4+ out of 5. Ankle, knee, and brachioradialis reflexes were absent. The remainder of the examination was normal.

Results of a complete blood count were normal, as were blood levels of urea nitrogen, calcium, magnesium, total protein, albumin, globulin, total and direct bilirubin, creatine kinase, and aspartate aminotransferase. Serum toxicologic screening was negative; other test results are shown in Table 1. An electrocardiogram showed sinus rhythm at a rate of 96 beats per minute, with nonspecific ST-segment and T-wave changes. A urinalysis was normal.

Potassium chloride (120 mmol, total) was administered orally and intravenously, with resolution of weakness. An intravenous catheter was placed in the internal jugular vein. A chest radiograph was normal. Test results of urine solutes and osmolality, from a specimen obtained 3.5 hours after presentation, are shown in Table 1. The patient was admitted to the hospital.

Additional diagnostic tests were performed.

**Differential Diagnosis**

Dr. Eugene P. Rhee: This 37-year-old man presented with a 1-month history of intermittent leg pain, culminating in an episode of profound weakness. The predominantly proximal deficits in muscle power and the lack of deep-tendon reflexes are consistent with a severe myopathy. Although a variety of inflammatory, infectious, toxic metabolic, and autoimmune processes can result in acute myopathy, this patient’s symptoms are readily attributable to his marked hypokalemia, which was

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### Table 1. Laboratory Data.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range, Adults†</th>
<th>On Admission</th>
<th>14.5 Hr after Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium (mmol/liter)</td>
<td>135–145</td>
<td>141</td>
<td>137</td>
</tr>
<tr>
<td>Potassium (mmol/liter)</td>
<td>3.4–4.8</td>
<td>1.9</td>
<td>4.1</td>
</tr>
<tr>
<td>Chloride (mmol/liter)</td>
<td>100–108</td>
<td>107</td>
<td>104</td>
</tr>
<tr>
<td>Carbon dioxide (mmol/liter)</td>
<td>23.0–31.9</td>
<td>23.2</td>
<td>26.2</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.60–1.50</td>
<td>0.43</td>
<td>0.91</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>70–110</td>
<td>113</td>
<td>111</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>2.6–4.5</td>
<td>1.2</td>
<td>4.4</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/liter)</td>
<td>45–115</td>
<td>129</td>
<td>192</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/liter)</td>
<td>10–55</td>
<td>63</td>
<td>78</td>
</tr>
<tr>
<td><strong>Urine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium (mmol/liter)</td>
<td>Not defined</td>
<td>96</td>
<td>180</td>
</tr>
<tr>
<td>Potassium (mmol/liter)</td>
<td>Not defined</td>
<td>9.5</td>
<td>39.1</td>
</tr>
<tr>
<td>Osmolality (mOsm/kg of water)</td>
<td>Not defined</td>
<td>726</td>
<td>210</td>
</tr>
</tbody>
</table>

* To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for phosphorus to millimoles per liter, multiply by 0.3229.
† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.
confirmed by the rapid resolution of weakness after supplementation with potassium chloride. Thus, I will focus my discussion on the possible causes of hypokalemia. Ideally, the correct diagnosis will also explain other distinctive features of the case, including the patient's weight loss and bilateral gynecomastia.

CAUSES OF HYPOKALEMIA

Potassium is the most abundant cation in the body. Because of active potassium uptake by the sodium–potassium pump (Na⁺/K⁺-ATPase) across cell membranes, approximately 98% of total-body potassium is intracellular. The remaining 2%, approximately 60 mmol of potassium, constitutes the extracellular pool. Typical potassium intake on a Western diet is 50 to 100 mmol per day; therefore, robust mechanisms are needed to prevent dangerous increases in the potassium level in the extracellular fluid, in the short term and over time. Sudden increases can be prevented by increased cellular uptake by means of the Na⁺/K⁺-ATPase, a process that is stimulated by insulin and catecholamines. This transeellular shift does not result in the net removal of potassium from the body. Instead, the kidneys maintain long-term potassium balance, excreting approximately 90% of ingested potassium; the rest is secreted through the gastrointestinal tract and skin. Although potassium is freely filtered at the glomerulus, it undergoes extensive reabsorption in the proximal tubule and loop of Henle. Thus, net urinary excretion of potassium relies on secretion in the distal nephron, a process that is augmented by aldosterone.

Because the kidneys are able to reduce urinary potassium excretion to less than 20 mmol per day, hypokalemia due solely to inadequate intake is uncommon. Instead, the major causes of chronic hypokalemia are related to excessive potassium loss. In such cases, the clinician's challenge is to differentiate renal from nonrenal potassium wasting. When hypokalemia is sudden in onset, the clinician must also consider whether transeellular potassium shift, and not total-body potassium depletion, is responsible for the patient's presentation. Since 98% of total-body potassium is intracellular, relatively small changes in its distribution can cause clinically significant changes in the potassium level in the extracellular fluid.

RENER POTASSIUM LOSS

This patient was hypertensive at presentation, albeit in the context of acute stress. Persistent arterial hypertension can be an important clue when distinguishing aldosterone-mediated from non–aldosterone-mediated renal potassium wasting.

Aldosterone-Mediated Renal Potassium Wasting

Primary aldosteronism, as with an aldosterone-producing adenoma (Conn's syndrome) or adrenal hyperplasia, can cause hypokalemia and hypertension. An aldosterone-producing adrenocortical carcinoma could further explain the patient's weight loss and gynecomastia (if the tumor also secreted estradiol). If the patient were found to have an elevated renin level in addition to an elevated aldosterone level, secondary causes of hyperaldosteronism would need to be considered (e.g., a renin-secreting tumor or renal-artery stenosis). The absence of a concomitant metabolic alkalosis does not rule out a diagnosis of hyperaldosteronism. Hypercortisolemia can also present with hypokalemia and hypertension. Cortisol has a high affinity for the mineralocorticoid receptor but is normally prevented from binding because of rapid metabolism by 11β-hydroxysteroid dehydrogenase (11β-HSD). Chronic licorice intoxication can mimic hyperaldosteronism, because glycyr rhetic acid, a component of licorice, inhibits 11β-HSD, allowing endogenous cortisol to activate mineralocorticoid receptors. Alternatively, very high cortisol levels can exceed the metabolic capacity of 11β-HSD, allowing cortisol to exert aldosterone-like effects on potassium balance and blood pressure. This patient's weight loss would seem to argue against Cushing's syndrome but could be consistent with an ectopic corticotropin-producing lung tumor (perhaps misinterpreted as pneumonia on his recent chest images). The patient's medications include clobetasol shampoo, a topical glucocorticoid. Cushing's syndrome resulting from topical glucocorticoids has been reported in adults, although typically in those with inflammatory skin conditions such as psoriasis. Finally, several genetic disorders, including glucocorticoid-remediable aldosteronism, congenital adrenal hyperplasia, 11β-HSD deficiency, and Liddle's syndrome, can cause hypokalemia and hypertension by increasing the levels of aldosterone or by mimicking its activity; however, these
diagnoses are all unlikely given the patient’s age and family history.

Non–Aldosterone-Mediated Renal Potassium Wasting

If the patient is not persistently hypertensive, non–aldosterone-mediated causes of renal potassium wasting would need to be considered. Diuretic agents, for example, are the most common cause of hypokalemia.

Intrinsic disorders that cause potassium wasting (e.g., Bartter’s syndrome and Gitelman’s syndrome) mimic the effects of diuretics but are manifested in childhood or adolescence. Some causes of renal tubular acidosis are associated with hypokalemia, but this patient’s bicarbonate level is normal. This also argues against surreptitious glue-sniffing or toluene intoxication, which the case history explicitly excludes; toluene is metabolized to hippuric acid, leading to acidaemia, and the rapid renal excretion of hippurate anions can result in obligate potassium wasting.

Urine Studies

In the absence of known diuretic use, assessment of urine potassium excretion is critical for establishing renal potassium wasting. Urine potassium loss of 20 mmol or more over a 24-hour period in a patient with hypokalemia indicates ongoing, excessive renal potassium secretion. When a 24-hour urine collection is impractical, a spot urine sample that reveals a potassium level of 15 mmol or more per liter is suggestive of an excessive renal potassium loss. Conversely, a urinary potassium loss of less than 20 mmol in 24 hours or a spot urine potassium level of less than 15 mmol per liter indicates previous renal potassium loss (e.g., prior use of diuretics), nonrenal potassium loss, or transcellular potassium shift (Fig. 1). This patient’s spot urine potassium level was 9.5 mmol per liter, mandating consideration of nonrenal causes of hypokalemia. It is important to recognize, however, that relatively low spot levels of urinary potassium can be consistent with renal potassium wasting if urine volumes are high; this is an important caveat, because hypokalemia can cause polyuria.

Nonrenal Potassium Loss

There is no history of heat exposure or prolonged exertion to support cutaneous losses as the cause of this patient’s hypokalemia. Diarrhea severe enough to cause this degree of hypokalemia would be associated with a metabolic acidosis due to concomitant bicarbonate loss. In contrast, excessive vomiting can cause hypokalemia and a metabolic alkalosis. Much of the potassium loss in patients with excessive vomiting, however, is through urination, as a result of potassium excretion alongside bicarbonate and because of the secondary hyperaldosteronism that results from volume contraction. This patient’s case history does not support either diarrhea or vomiting as the cause of his hypokalemia.

Transcellular Shift

Although any cause of severe hypokalemia can result in marked muscle weakness, most cases associated with acute paralysis are due to transcellular shift, rather than net potassium loss. This patient’s history of recurrent, transient episodes of muscle weakness, ranging from mild weakness to complete paralysis, is highly suggestive of acute swings in the transcellular distribution of potassium. On rare occasions, transcellular shift resulting from exogenous stimuli can result in severe hypokalemia. For example, abuse of an adrenergic agent such as pseudoephedrine could have caused the patient’s hypokalemia through catecholamine-induced stimulation of the transmembrane Na+/K+-ATPase; such abuse could also have caused the hypertension, tachycardia, and tremor. Barium intoxication is another rare cause of hypokalemic paralysis resulting from the transcellular shift of potassium. More commonly, however, a transcellular shift that results in hypokalemic paralysis represents a diagnosis of either familial hypokalemic periodic paralysis or thyrotoxic periodic paralysis (TPP).

Clinically, attacks of familial hypokalemic periodic paralysis and TPP are indistinguishable and are characterized by aches in the proximal muscles, cramping, and weakness that can progress to paralysis; hypokalemia is a hallmark of both presentations (Table 2). In both cases, attacks can be precipitated by carbohydrate-heavy meals (e.g., multiple slices of pizza) because of insulin’s stimulatory effects on the Na+/K+-ATPase. Attacks also occur during periods of rest, particularly after strenuous exercise, as potassium released during activity is reabsorbed by skeletal muscle. Other overlapping characteristics, all features of the current case, include a male predominance, normal acid–base status, and a low phosphorus level (also due to transcellular shift).

Familial hypokalemic periodic paralysis is an autosomal dominant genetic disorder due to mutations in ion channels of the skeletal-muscle sar-
colemma, including the α₁ subunit of the dihydropyridine-sensitive calcium channel¹⁹ and the sodium channel SCN4A.²⁰ TPP is generally viewed as an acquired disorder, defined by the presence of hyperthyroidism (of any cause), although signs and symptoms of excess thyroid hormone may be subtle or even absent at presentation. The pathogenesis of TPP remains unclear, but thyroid hormone is known to increase the expression and activity of the Na⁺/K⁺–ATPase, perhaps unmasking an underlying predisposition for an increased transcellular shift of potassium in selected persons.²¹,²² Recently, some patients with TPP have been shown to harbor a mutation in the inwardly rectifying potassium channel Kir2.6 that alters muscle-membrane excitability but is not sufficient to produce symptoms in the euthyroid state.²³

Since familial hypokalemic periodic paralysis is usually manifested in patients who are less than 20 years of age, this patient's presentation is more characteristic of TPP, with disease onset between the ages of 20 and 50 years. More important, this patient has several cardinal features of hyperthyroidism. These are systolic hypertension with a wide pulse pressure, tachycardia, tremor, and weight loss. Furthermore, gynecomastia is a well-recognized complication of hyperthyroidism attributable to a relative increase in circulating free estradiol²³; the antiandrogenic effects of the finasteride that the patient was taking may have amplified this hormonal perturbation. Because hypokalemic paralysis rarely affects bulbar muscles, the patient's blurred vision raises the possibility of Graves' ophthalmopathy. The pneumonia 6 weeks before admission is not so neatly accounted for by the diagnosis of TPP. Perhaps the patient received an iodinated contrast agent during his evaluation, thus triggering the release of

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Figure 1. Algorithm for the Differential Diagnosis of Hypokalemia.

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Hypokalemia

Urinary K⁺ excretion ≥20 mmol/24 hr

Ongoing renal K⁺ loss

Check blood pressure

Hypertensive

Hyperaldosteronism
  Primary
    Adrenal adenoma, hyperplasia, carcinoma
  Secondary
    Renin-secreting tumor, renal-artery stenosis
  Glucocorticoid excess
    Cushing's syndrome, congenital adrenal hyperplasia
  Genetic disorders
    Glucocorticoid-remediable aldosteronism
    11β-Hydroxysteroid dehydrogenase deficiency
    Liddle's syndrome

Urinary K⁺ excretion <20 mmol/24 hr

Hypotensive or normotensive

Diuretics
  Vomiting
  Renal tubular acidosis
  Diabetic ketoacidosis
  Hypomagnesemia
  Bartter's syndrome
  Gitelman's syndrome

Prior renal K⁺ loss
  Prior diuretics or vomiting
  Nonrenal K⁺ loss
  Diarrhea, laxatives, K⁺-binding resin
  Excessive sweating
  Transcellular K⁺ shift
  Drugs (e.g., insulin, β₂-adrenergic agonists, barium)
  Acute cell proliferation (e.g., vitamin B₁₂ treatment of pernicious anemia, refeeding syndrome, acute leukemia)
  Andersen–Tawil syndrome
  Familial hypokalemic periodic paralysis
  Thyrotoxic periodic paralysis

Hypertensive

Hyperaldosteronism
  Primary
    Adrenal adenoma, hyperplasia, carcinoma
  Secondary
    Renin-secreting tumor, renal-artery stenosis
  Glucocorticoid excess
    Cushing's syndrome, congenital adrenal hyperplasia
  Genetic disorders
    Glucocorticoid-remediable aldosteronism
    11β-Hydroxysteroid dehydrogenase deficiency
    Liddle's syndrome

Diuretics
  Vomiting
  Renal tubular acidosis
  Diabetic ketoacidosis
  Hypomagnesemia
  Bartter’s syndrome
  Gitelman’s syndrome

Hypotensive or normotensive

Prior renal K⁺ loss
  Prior diuretics or vomiting
  Nonrenal K⁺ loss
  Diarrhea, laxatives, K⁺-binding resin
  Excessive sweating
  Transcellular K⁺ shift
  Drugs (e.g., insulin, β₂-adrenergic agonists, barium)
  Acute cell proliferation (e.g., vitamin B₁₂ treatment of pernicious anemia, refeeding syndrome, acute leukemia)
  Andersen–Tawil syndrome
  Familial hypokalemic periodic paralysis
  Thyrotoxic periodic paralysis

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thyroid hormone from an underlying multinodular goiter. Alternatively, oropharyngeal dysmotility caused by hyperthyroidism may have resulted in aspiration.24

**Summary**
Numerous features of this case are consistent with a diagnosis of TPP, including episodic weakness with acute paralysis, hypokalemia with low levels of urinary potassium, and evidence of hyperthyroidism. Although the incidence of TPP is highest among Asians, it has been reported in other ethnic groups, including Hispanics.25-29 Early diagnosis is critical because definitive treatment of hyperthyroidism is curative. In the short term, potassium chloride supplementation is warranted to prevent life-threatening cardiac arrhythmias or respiratory failure. However, because patients with TPP do not have a net deficit in total-body potassium, overly aggressive repletion can be complicated by rebound hyperkalemia.30 This patient had a normal potassium level 14.5 hours after presentation. I suspect that a diagnosis of TPP was confirmed soon thereafter by biochemical evidence of hyperthyroidism.

*Dr. Eric S. Rosenberg* (Pathology): Dr. Barbash, would you tell us what the team was thinking when they first saw this patient?

*Dr. Barbash:* The team’s differential diagnosis was similar to Dr. Rhee’s; for the reasons he discussed, the leading diagnosis on admission was TPP.

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**Clinical Diagnosis**
Thyrotoxic periodic paralysis.

**Dr. Eugene P. Rhee’s Diagnosis**
Thyrotoxic periodic paralysis.

**Pathological Discussion**

*Dr. Anand S. Dighe:* Blood drawn when the patient was in the emergency room showed a very low thyrotropin level, at 0.01 μU per milliliter (reference range, 0.4 to 5.0). Results of thyroid tests showed an elevated free thyroxine (T4) level (3.4 ng per deciliter [43.8 pmol per liter]; reference range, 0.9 to 1.8 ng per deciliter [11.6 to 23.2 pmol per liter]) and an elevated total triiodothyronine level (307 ng per deciliter [4.7 nmol per liter]; reference range, 60 to 181 ng per deciliter [0.9 to 2.8 nmol per liter]). These levels were consistent with hyperthyroidism, and the patient was assessed for autoimmune thyroid disease by measurement of autoantibodies directed against the following thyroid antigens: thyroid peroxidase, thyroglobulin, and the thyrotropin receptor. The level of antithyroid-peroxidase antibodies was greatly elevated (>1000 IU per milliliter; reference interval, <35), and the level of antithyroglobulin antibodies was not elevated (<20 IU per milliliter; reference interval <40). The precise role of antithyroid-peroxidase and antithyroglobulin anti-

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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Familial Hypokalemic Periodic Paralysis</th>
<th>Thyrotoxic Periodic Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthyroidism</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Inheritance</td>
<td>Autosomal dominant (reduced penetrance among women)</td>
<td>Sporadic*</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>&lt;20</td>
<td>20–50</td>
</tr>
<tr>
<td>Racial predominance</td>
<td>White</td>
<td>Asian</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low urinary potassium excretion</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Normal acid–base status</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Provoked by high carbohydrate intake or strenuous exercise</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Some persons with thyrotoxic periodic paralysis have been shown to have a mutation in Kir2.6, an inwardly rectifying potassium channel.16

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**Table 2. Characteristics of Familial Hypokalemic Periodic Paralysis and Thyrotoxic Periodic Paralysis.**
bodies in the pathogenesis of autoimmune thyroid disease remains unclear, but these antibodies may represent epiphenomena, being markers of the thyroiditis common to many forms of autoimmune thyroid disease, such as Graves’ disease and Hashimoto’s thyroiditis.

The presence of thyrotropin-receptor antibodies was assessed with the thyroid-stimulating immunoglobulin (TSI) bioassay. With the TSI assay, the patient’s serum can be examined for the presence of antibodies capable of activating the thyrotropin-receptor signaling pathway. Results of sensitive TSI assays show that virtually all patients with active, untreated Graves’ hyperthyroidism have an elevated TSI index (the ratio of the stimulating activity of the patient to that of the control subject).21 This patient’s TSI index was 2.7 (reference value, ≤1.3). The elevated TSI index, the high thyroid hormone level, and the very low thyrotropin level are consistent with a diagnosis of Graves’ disease. However, on rare occasions, patients with Hashimoto’s thyroiditis may present with an initial hyperthyroid phase that has a similar laboratory presentation to that of Graves’ disease, including, in some cases, an elevated TSI index.22 The clinical course, histologic examination, presence of the extrathyroidal features of Graves’ disease (ophthalmopathy and dermopathy), and radioiodine-uptake scans may all provide useful information in distinguishing between these two diagnoses.

Dr. Rosenberg: Dr. Barbash, would you tell us your team’s initial approach?

Dr. Barbash: The patient did not receive any further potassium supplementation. He was started on methimazole and metoprolol on the advice of the inpatient endocrinology team. After the potassium level had remained normal for several days, he was discharged from the hospital. Shortly thereafter, a technetium-99m pertechnetate scan of the thyroid was obtained at an outpatient facility associated with this hospital. Dr. Scott will review the images.

Dr. James A. Scott: The technetium-pertechnetate scan (Fig. 2) showed an enlarged thyroid with diffusely increased uptake of the pertechnetate (twice the upper limit of the normal range), features consistent with Graves’ disease.

Dr. Rosenberg: Dr. Barbash, would you describe the rest of the patient’s course?

Dr. Barbash: Repeat thyroid-function tests performed approximately 3 weeks later revealed a free T₄ level of 1.1 ng per deciliter (14.2 pmol per liter), and his endocrinologist decreased his dose of methimazole. Two months later, the free T₄ level was low and the thyrotropin level was elevated, so thyroid hormone–replacement therapy was begun. Recently, laboratory studies revealed normal free T₄ and thyrotropin levels. The patient was admitted without a primary care doctor, so I, as his admitting intern, became his primary care physician. I have seen him in the clinic several times, and it is rewarding to have found a readily fixable problem and reassuring to know that the patient can proceed to live a normal life. His endocrinologist plans to perform radioactive iodine ablation soon.

Dr. Rosenberg: Are there questions for our discussants?

A Physician: How do you control the symptoms in the familial cases?

Dr. Rhee: Avoiding triggers, such as prolonged exercise and meals that are high in carbohydrates, can be helpful. Nonselective beta-blockers can prevent catecholamine-induced activation of the Na⁺/K⁺–ATPase, and for reasons that are unclear, acetazolamide may also be effective in reducing episodes of paralysis. Unfortunately, familial hypokalemic periodic paralysis, unlike TPP, is associated with a progressive myopathy, despite these preventive measures.

Dr. Lloyd Axelrod (Endocrinology): It is worth noting that the patient’s potassium level and symptoms were corrected with only 120 mmol of...
When the potassium level is below 2 mmol per liter in the most common forms of hypokalemia, the total-body deficit is 400 or 500 mmol. Commonly, 40 or 80 mmol of potassium will raise the potassium level transiently, but hours or days later, it will plummet again as that potassium is redistributed into the intracellular pool. The fact that 120 mmol of potassium was sufficient in this patient supports the diagnosis of TPP, indicating that the hypokalemia was due to transcellular potassium shift rather than total-body depletion.

REFERENCES