

Case Report

Polyneuropathy from Thiamin Deficiency Associated with Thyrotoxicosis

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Polyneuropathy from thiamin deficiency can occur in persons who consume a diet consisting mainly of polished rice with low protein and thiamin content in the setting of excessive physical activity or hypermetabolic states. The authors report here a 17-year-old fisherman who presented with a 3-month history of symptoms and signs consistent with polyneuropathy. There were also clinical features of thyrotoxicosis which was confirmed by thyroid function test. His dietary intake consisted mainly of polished rice and fish both of which contain a small amount of thiamin. This could not cope with his hypermetabolic condition from thyrotoxicosis resulting in thiamin deficiency with polyneuropathy.

Keywords: Polyneuropathy, Thiamin, Thyrotoxicosis

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Polyneuropathy is one of the three types of nervous system involvement other than Wernicke's encephalopathy and Korsakoff syndrome in thiamin deficiency⁽¹⁾. The deficiency state has been linked to chronic malnutrition, consumption of polished rice and alcohol, parenteral nutrition, gastrectomy, gastric surgery for morbid obesity, excessive physical exercise and increased metabolic demand⁽¹⁻⁷⁾. Nevertheless, this disease state in association with thyrotoxicosis has seldom been specifically documented. The authors report here a case of chronic polyneuropathy from thiamin deficiency associated with thyrotoxicosis.

Case Report

A 17-year-old fisherman from Surin province presented with weakness of both legs for 3 months. Three months previously, he was unable to walk upstairs or stand up from sitting but could still walk by himself. One week later, he felt numb from the toes to both knees. Two months prior to admission, there was mild pain in his shoulder and the numbness developed

on the fingers on both sides. Later on, he developed weakness of his hands with difficulty in holding a pen and noticed that the muscles of the upper and lower extremities were wasted. He was still able to raise his arms then. One week before admission, he had hoarseness of voice. All of the symptoms gradually became so severe that he could not work any longer. He denied any history of drug abuse or exposure to toxic substances. He seldom had alcoholic drinks. His dietary intake consisted mainly of polished rice and some fish.

Physical examination revealed BP 130/70 mmHg, P 100/min, T 37 C, RR 18/min. He appeared alert and cooperative with profound sweating. He had exophthalmos and lid lag. The thyroid gland was diffusely enlarged with approximate weight of 40 g. No abnormality was found on examining the heart, lungs and abdomen. Neurological examination showed reactive pupils of 3 mm. in diameter and normal optic fundi. There was no nystagmus and the cranial nerves were all normal. The muscle tone was normal. There was mild wasting of forearm, thenar, hypothenar and leg muscles on both sides with symmetrical moderate weakness of both upper extremities being more marked distally. In the lower extremities, in contrast, the proximal muscles were weaker than the distal ones. The deep

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tendon reflexes were almost all absent except for depressed biceps jerks. The Babinski sign was absent. Pinprick sensation was impaired in gloves and stockings pattern from toes to knees and fingers on both sides. The straight leg raising test was negative. The joint position sense was intact.

Investigations showed abnormal thyroid function test: FT4 > 7.8 ng/dl (normal = 0.93-1.7), T3 421 ng/dl (normal = 58-159), TSH < 0.005 UIU/ml (normal = 0.1-3.7), negative thyroglobulin antibody, thyroid microsomal antibody 1:1,600 and low erythrocyte transketolase activity (ETKA = 62.5 IU, normal \geq 130.8 IU) with high thiamin pyrophosphate effect level (TPPE = 15 %, normal 0-14% according to Brin's guideline⁽⁸⁾). Nerve conduction study showed sensorimotor axonal polyneuropathy. Muscle sampling was not performed.

The diagnosis was thiamin deficiency polyneuropathy with thyrotoxicosis. He was treated with propylthiouracil and intravenous thiamin infusion. His muscle power began to improve after a few days. His sensory function slowly improved thereafter but hoarseness of voice remained unchanged after 10 days of admission. He was lost to follow up after discharge.

Discussion

From the clinical point of view, this patient definitely suffered from sensorimotor polyneuropathy. The pattern of his weakness was rather interesting in that it was more marked distally in the upper extremities but more so proximally in the lower extremities. In polyneuropathy from thiamin deficiency (beriberi), the disproportionate affection of muscle power may be striking. It usually takes the form of predominantly distal weakness but the proximal muscles are often affected as well and the weakness is often confined to the legs. In some patients, all the leg muscles are affected more or less equally and in a few, weakness appears to be most severe in the proximal muscles⁽⁹⁾. The numbness started in the toes spreading to the knees and gradually extended to the fingers. The progression of his sensory symptoms is consistent with axonal degeneration. Regarding the possible causes of polyneuropathy in this patient, polyneuropathy from thyrotoxicosis is very rare and he had no history of exposure to toxin or drug abuse. As regards his nutrition, his food intake consisted mainly of polished rice and fish. This occurred in the setting of hypermetabolic state from thyrotoxicosis. The clinical picture was compatible with polyneuropathy from thiamin deficiency. Laryngeal weakness leading to hoarseness of voice is a well-described complication in polyneuropathy from thiamin

deficiency (beriberi) and alcoholic neuropathy due to vocal cord paralysis from lesion of the vagus nerve⁽¹⁰⁾. However, the vocal cords of this patient were not examined by an ENT specialist. Blood transketolase activity and the TPPE is the most reliable index of the functional state of thiamin. The result of low erythrocyte transketolase activity and high thiamin pyrophosphate effect supported the diagnosis. Polyneuropathy from thiamin deficiency can occur in persons who consume a diet consisting mainly of polished rice with low protein content in the setting of excessive physical activity or hypermetabolic states. Thyrotoxicosis is thought to be the precipitating cause of thiamin deficiency in this case because this is a hypermetabolic condition requiring high energy supply. The creation of high energy phosphate needs thiamin pyrophosphate (TPP) as a coenzyme for transketolase to work properly⁽¹¹⁾. Usually, pork is the richest source of thiamin (0.69 mg / 100 g) whereas fish contains only 0.01-0.13 mg /100g⁽¹²⁾. While this amount of thiamin consumption may or may not meet the normal requirement, this could not cope with his hypermetabolic condition⁽¹³⁾. In addition, a recent study demonstrated that a reduction of intestinal thiamin absorption and transportation occurred in T3-induced thyrotoxicosis rats probably as a consequence of reduction in phosphorylation of thiamin to TPP due to a reduced pyrophosphokinase activity^(14,15). In cases of polyneuropathy from thiamin deficiency associated with thyrotoxicosis, the florid symptoms and signs of thyrotoxicosis may mask the more trivial clinical features of thiamin deficiency polyneuropathy in some cases and the diagnosis of the latter may be missed or delayed.

The most prominent feature in the pathology of peripheral nerves in beriberi has been shown to be axonal degeneration with large myelinated fibers being more affected than unmyelinated ones^(16,17). In general, the course of axonal polyneuropathy is usually rather chronic with slow recovery. However, reversible acute axonal polyneuropathy associated with Wernicke-Korsakoff syndrome has been reported⁽¹⁸⁾. These patients improved rapidly within two weeks in response to intravenous thiamin infusion similar to the presented patient whose muscle power began to improve after a few days of treatment. There are two possible pathophysiological mechanisms which can account for rapid recovery from axonopathy: 1) degeneration of motor nerve terminals and intramuscular nerves and 2) physiological conduction failure. The first possibility was suggested in a patient with acute motor axonal neuropathy (AMAN) who showed rapid recovery⁽¹⁹⁾. A

motor point biopsy in the presented patient revealed loss of motor nerve terminal in the neuromuscular junctions and extensive degeneration of myelinated axons of the intramuscular nerves in contrast to normal finding of the sural nerve biopsy. Rapid recovery may partly be due to regeneration of the distal motor nerves which can develop in a short time. However, in beriberi neuropathy, axonal degeneration was shown in the sural nerves but motor nerve terminals have not been studied. In a study of sural nerves in this condition, active regeneration of axons was extensive in patients receiving vitamin B⁽¹⁶⁾. It is possible that in beriberi, distal and more proximal nerves are all involved and recover in different time course. Several mechanisms can physiologically influence nerve conduction. Thiamin and thiamin pyrophosphatase are localized in the peripheral nerve membranes. The fact that thiamin phosphorylated derivatives are associated with the specific protein forming the sodium channel has led to the hypothesis that thiamin derivatives and more specifically thiamin triphosphate (TTP) play an important role in the control of sodium conductance at the axonal membranes⁽²⁰⁾. Moreover, dysfunction of the sodium channels at the nodes of Ranvier has been suggested to cause conduction slowing or physiological conduction block^(21,22). The authors speculate that nerve conduction may be readily improved by thiamin supplement resulting in rapid recovery.

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ภาวะปลายประสาทผิดปกติจากการขาดไทอามีนร่วมกับโรคต่อมไทรอยด์เป็นพิษ

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ภาวะปลายประสาทผิดปกติจากการขาดไทอามีนเกิดได้ในผู้ที่รับประทานข้าวสารที่ได้ผ่านการสีและอาหารที่มีปริมาณโปรตีนและไทอามีนต่ำ ร่วมกับการออกกำลังกายหนักๆหรือในภาวะที่มีการเผาผลาญพลังงานมากผิดปกติ ผู้นิพนธ์รายงานผู้ป่วยชายอายุ 17 ปี ชาวประมง มีอาการชาปลายมือปลายเท้าเป็นเวลา 3 เดือน ร่วมกับอาการแสดงที่เข้าได้กับความผิดปกติของปลายประสาทและต่อมไทรอยด์เป็นพิษด้วย ชาวประมงรายนี้รับประทานอาหารที่ประกอบด้วยข้าวขัดสีและปลาเป็นส่วนมาก ซึ่งมีปริมาณไทอามีนต่ำทั้งคู่ ประกอบกับผู้ป่วยมีการเผาผลาญพลังงานมากผิดปกติจากโรคต่อมไทรอยด์เป็นพิษ ทำให้เกิดภาวะขาดไทอามีนร่วมกับภาวะปลายประสาทผิดปกติ