Bilateral Achilles Tendon Enlargement

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Abstract

Cerebrotendinous xanthomatosis is a rare, autosomal-recessive, lipid-storage disease with accumulation of cholestanol in most tissues, particularly within the Achilles tendons. It has been characterized both clinically and biochemically, and recently from the molecular biological aspect as well. Juvenile cataract, childhood diarrhea, mental retardation, cerebellar ataxia, and tendon xanthomas are the most prominent features of this disease. Bilateral symmetrical firm masses of Achilles tendons may be the first symptom the patient recognizes because it can jeopardize his or her ability to walk. However, the treatment strategies for tendon tumors vary.

In a recent case, we diagnosed the disease properly, according to the clinical manifestations and the radiological and laboratory examinations. The genetic mutation was characterized by analyzing sterol 27-hydroxylase from the patient’s family (located on nucleotide 599) and led to a nonsense mutation. It is a unique type of mutation that has never been reported to our knowledge. Tendon lesions are characterized by the loss of muscle fibers and accumulation of lipid products. To help the patient regain the strength of the Achilles tendon and walking abilities, a large area of tendon tumor was excised, followed by reconstruction with a tibialis posterior allograft, which is the second strongest tendon in the foot and ankle. Although the use of this type of graft is uncommon, the final result was satisfactory. At the 10-month follow-up examination, the patient could walk easily without pain. This case report suggests that the surgical procedure will provide an alternative for the repair of large-area degenerative Achilles tendons.

Figure: T1-weighted sagittal MRI of the right ankle and Achilles tendon.

Drs Huang, Miao, Yang, and Tao have no relevant financial relationships to disclose.

The authors thank Drs Ye Zhao-ming, Li Wei-xu, and Lin Nong for their help with the surgical and treatment strategies; Dr Jian-chen Xu and Prof Ming Qi at the Center for Genetic & Genomic Medicine, Zhejiang University, for their help in providing technical assistance of genetic analysis; and Dr Jing-hong Xu for help with the pathological diagnosis.

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doi: 10.3928/01477447-20111021-28
Cerebrotendinous xanthomatosis is a rare, autosomal-recessive, lipid-storage disease caused by mutations in the mitochondrial enzyme, sterol 27-hydroxylase (CYP27A1) gene. The biochemical pathogenesis of cerebrotendinous xanthomatosis is linked to increased levels of plasma and tissue cholestanol and defective bile acid synthesis. Thus, the diagnosis of cerebrotendinous xanthomatosis is based on typical symptoms, elevated serum cholestanol, deficiency of sterol 27-hydroxylase, and xanthomatous cells in xanthomas.

This article describes an extremely rare case of bilateral Achilles tendon xanthomas along with neurological changes, which may be only the second case ever reported on the Chinese mainland. We performed surgery on a right-side Achilles tendon tumor. A wide degenerative area of the tendon was resected, and the tibialis posterior tendon was harvested and transferred to reconstruct motion function. This surgical procedure was unique and provided an alternative for the repair of large-area degenerative Achilles tendon.

**Case Report**

A 38-year-old man presented with a slow and progressive enlargement of tendinous nodules over a 2-year period. The disease had progressively worsened over the prior 6 months. He reported claudication and clumsy movement. After admission, we found that he presented with mental retardation, hypomnesia, and tremors. He had no history of head injury or trauma. His family stated that his intelligence was normal in the past, but reported that his character had recently become irascible.

On physical examination, symmetrical, firm masses with an average diameter between 8 and 10 cm were noted on the bilaterally posterior aspect of the legs above the calcaneus. The mass on the right side was larger than that on the left. A neurological evaluation revealed positive Babinski reflex and signs of cerebellar dysfunction including dysdiadochokinesia and a failed heel–knee–toe test. Fundoscopic examination revealed no cataract.

Laboratory tests revealed a normal and complete hemogram and normal levels of serum cholesterol, triglycerides, and other lipoproteins in the patient. Enzyme-linked immunosorbent assay analysis of blood samples showed that the patient’s cholestanol level was 0.049 mmol/L, which is higher than the normal range (<0.015 mmol/L). However, the cholestanol level was normal in the patient’s parents and his son, at 0.0018, 0.0045, and 0.0021, respectively.

Magnetic resonance imaging (MRI) analysis of both ankles revealed bilateral enlarged Achilles tendons showing hypointensity on T1-weighted and T2-weighted images and proton-density fat-suppressed images (Figure 1). A brain MRI revealed symmetrical abnormal signal intensity characterized by hypointense T1-weighted and hyperintense T2-weighted echo images on both the anterior mesencephalon-posterior limb of the internal capsule and the deep cerebellar white matter. The crus cerebri was also involved, showing a diffuse reticulated appearance. The cerebellar sulcal was enlarged, which indicated cerebellar atrophy (Figure 2). Based on the clinical manifestations and radiological and laboratory examinations, we diagnosed this patient as having cerebrotendinous xanthomatosis.

Because the tendon tumor on the right side was larger than on the left and was...
the main cause of his claudication, a planned wide excision and reconstruction were performed on the right Achilles tendon tumor during the first stage of the operation. A 10-cm longitudinal skin incision was made in the middle of the tumor. The tumor presented within the Achilles tendon as a yellow, firm, hypertrophic neoplasm. Approximately 3×1 cm of soft tissue was resected from the mass for frozen biopsy (Figure 3). The tumor was resected 1.5 cm above the macroscopically palpable margin. The left tibialis posterior tendon was identified in the medial side and located under the medial malleolus. It was resected from the navicular bone and weaved through the Achilles tendon ends.

After shaping, the tibialis posterior tendon was fixed to the calcaneus using a 5.0-mm corkscrew (AR-1920NSF; Arthrex, Naples, Florida). The proximal tendinous part of the allograft was sutured end-to-end to the proximal part of the Achilles tendon to reconstruct the defect. The excised mass measured 14.5×5.5×3.0 cm. Histology examination of the frozen and paraffin sections revealed multiple foam cells surrounded by macrophages within the dense connective tissue of the tendon, which was suggestive of xanthomas (Figure 4).

The ankle was immobilized in a plaster cast for 60 days. After removing the plaster cast, the patient was allowed to begin weight-bearing standing and progressive walking. After 10 months, he could walk smoothly without pain. Only the longitudinal arch of the foot transformed a little flat due to tibialis posterior dysfunction. The shape of the heel and the scar healed well. The patient was satisfied with the first surgery and subsequently underwent the identical procedure for the contralateral side with similar success at the 10-month follow-up.

Because cerebrotendinous xanthomatosis is an autosomal-recessive genetic disease, we detected CYP27A1 gene mutation based on DNA taken from the blood samples of the patient, his parents, and his son with their consent. The sequencing results demonstrated a heterozygous nonsense mutation of C to T transition at nucleotide 599 in the patient, which made the protein product truncated and nonfunctional (191Q->Q/X) (Figure 5). The patient’s father was also a carrier of a recessive heterozygous mutation of C to T at nucleotide 599. In the patient’s mother, the expected mutation of C to T transition at nucleotide 599 in CYP27A1 gene was not detected, suggesting the existence of other types of mutations, such as the deletion beyond the detection range (approximately 8%) or a transcription regulation domain mutation.

**DISCUSSION**

Because cerebrotendinous xanthomatosis is a rare disease and its symptoms...
vary, some cases that exhibit atypical manifestations or have slight neurological disorders, such as those in our patient, may be misdiagnosed as foot and ankle tumors. Musculoskeletal tumors of the foot and ankle are uncommon, and their diagnosis and treatment are difficult.

Approximately one-third of all benign lesions are ganglions. Plantar fibromatosis is the second most common soft tissue lesion, followed by epidermal inclusion cysts, lipomas, rheumatoid nodules, and tendon sheath giant cell tumors. Xanthoma, neurofibromatosis, and hemangiomas are rare. For malignant bone lesions of the foot and ankle, marginal en bloc resection or amputation may be an appropriate treatment. Therefore, accurate diagnosis and preoperative evaluation are important. Our case was discussed at a soft tissue tumor multidisciplinary meeting, and the final decision was made to perform surgical excision and reconstruction.

Several procedures have been used for the treatment of chronic degeneration of Achilles tendons. The majority of repair and reconstruction procedures include autogenous tissue transfers or heterogeneous homologous grafts. However, the latter was not commonly used because of limited suitable donor material sources and high complication rates of immunological rejection and infection. Among autogenous tendon transfer, methods such as peroneus brevis transfer and flexor hallucis longus transfer are commonly used. V-Y tendon alignment with plantaris weavon, gastrocnemius free turnndown flaps, multiple strips of fascia lata, flexor digitorum longus transfer, and bone-tendon-bone autograft harvested from the knee extensor mechanism were also therapy options. For most orthopedic surgeons, a tendon defect >5 to 6 cm, treated with use of a tendon graft alone or combined with a V-Y tendon alignment, is an easier and more convenient surgical procedure.

In our case, the reconstruction of the resected Achilles tendon could not be managed as well as in the procedures mentioned above. After removal of the xanthoma, there was a 15-cm defect in the Achilles tendon, which was too extensive to be reconstructed satisfactorily using those methods. For regaining the strength of the Achilles tendon and walking abilities, we decided to undertake reconstruction using posterior tibialis autograft, which is the second strongest tendon in the foot and ankle, and attach it using a corkscrew into the calcaneus. It is well known that procedures that combine pathological tissue excision, end-to-end anastomosis, and reinforcement of anastomosis are the best approach for Achilles tendon repair. The repair technique used in our case meets each of the necessary criteria. However, the use of this type of graft is uncommon because of possible donor-site morbidity and postoperative functional disorders.

A slight sign of flat foot was observed in the right foot due to tibialis posterior dysfunction. Although a certain amount of loss in inversion and plantarflexion strength is expected after a tibialis posterior transfer, we found no objective plantarflexion weakness or subjective functional compromise of ankle function. Advantages of tibialis posterior include improved length of the tendon and strength of the muscle than that of other transfer candidates, especially in treatment of the excision and reconstruction of large tumors of the Achilles tendon.

Cerebrotendinous xanthomatosis is a rare disease that has been reported in approximately 200 people worldwide. Until now, CYP27A1 was the only gene that has mutations implicated in cerebrotendinous xanthomatosis. Although 37 different mutations have been described in CYP27 gene in patients with cerebrotendinous xanthomatosis, the heterozygote nonsense mutation (191Gln to TAG stop condon) identified in our patient has never been reported to our knowledge. Currently, 6 other cases of cerebrotendinous xanthomatosis have been reported in the Chinese population. Our case is the first reported nonsense mutation of CYP27A1 in a Chinese patient.

Chenodeoxycholic acid is the drug of choice for treatment of cerebrotendinous xanthomatosis patients. Recent studies suggest that the combined treatment of chenodeoxycholic acid and hydroxymethylglutaryl-coenzymeA reductase inhibitors is a rational approach. Thus, we treated our patient with chenodeoxycholic acid (300 mg per day) and simvastatin (20 mg per day), but we did not observe an obvious improvement of the neurological symptoms. We postulate that the treatment is only effective if initiated at the first sign of symptoms (cataracts, diarrhea, and mild neurologic abnormalities) because once xanthomas appear, it is usually too late to obtain satisfactory results.
REFERENCES