Bilateral xanthomas of tendoachilles in a slow learner adolescent - A rare case report of van bogaert scherer epstein disease

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SUMMARY

Van Bogaert Scherer Epstein Disease is a rare autosomal recessive condition involving abnormal deposition of cholesterol and cholestanol in various parts of body, various clinical symptoms manifest on different age group, significantly neurological impairment in late presentation. We are reporting a slow learner young lady presented with bilateral painless ankle swelling, our initial clinical impression were torn Achilles tendon or Haglund's deformity. On further detail history taking, it leads us towards this disease and confirmed with biopsy. A proper history taking and assessment can easily diagnose this condition, early treatment can perhaps change the fate of these unfortunate patients.

INTRODUCTION

Van Bogaert Scherer Epstein Disease also known as cerebrotendinous xanthomatosis (CTX) is a rare inherited autosomal recessive condition, which is due to abnormal deposition of cholesterol and cholestanol in various parts of the body - especially the brain, lungs and Achilles tendon.[1] The condition is highly under diagnosed.

The disease starts with chronic diarrhoea and cataract during childhood, develops swelling over tendoachilles in adolescent. Significant neurologic impairment includes seizures, dementia, and cerebellar and extrapyramidal dysfunction, typically beginning in the third decade of life and progressing until death, often in the sixth decade of life if the condition goes untreated.

Early recognition of the disease with appropriate treatment can prevent the progression of disease which can lead to dependence in activities of daily living.

CASE REPORT

We are reporting an 18 years old young lady, who is a slow learner, not on proper peadiatric follow up. The case was presented to us with complaint of swelling over back of bilateral ankle for 8 years, progressively increasing in size, otherwise no pain and still ambulating well. On examination, firm swelling measuring 3x2cm, posterior aspect of bilateral ankle, attached to Achilles tendon and non-tender. (Figure 1)

Our first impression was bilateral torn Achilles tendon or Haglund's deformity. On further history taking, we found that patient was unable to solve simple mathematic equation and has history of undergone cataract surgery at the age of 11. Our clinical diagnosis was then towards cerebrotendinous xanthomatosis. Unfortunately, serum cholestanol test is not available in Malaysia. Thus, a Tru-cut biopsy was done and HPE reported as birefringent crystals with foamy cytoplasm and multinucleated giant cells with high concentration of cholestanol. Therefore, the diagnosis of cerebrotendinous xanthomatosis was confirmed.

Otherwise there is no history of chronic diarrhoea in childhood, no history of seizure and no consanguineous marriage of her parents. Patient's liver function and lipid profile were within normal range. No abnormal finding in her abdomen ultrasound.

The ideal medication therapy should be chenodeoxycholic acid, but we have replaced it with ursodeoxycholic acid, also a synthetic bile acid, as chenodeoxycholic acid is not available in our hospital. We were lucky that her disease was not at the full blown stage yet and she is still currently under medical follow up with close neuromuscular monitoring.

DISCUSSION

CTX is inherited in an autosomal recessive manner, associated with mutations in the CYP27A1 gene, located on chromosome 2q33-qter, resulting in primary enzymatic defect of mitochondrial sterol 27-hydroxylase, a primary enzyme required for bile acid synthesis from cholesterol.[2] Defects in this enzyme leads to disrupted chenodeoxycholic acid (CDCA) synthesis, an important bile acid. Due to low level of CDCA, feedback regulation on cholesterol 7-alpha-hydroxylase, which is the rate-limiting step in bile acid synthesis, is disrupted. Therefore, bile acid precursors, 7-alpha-hydroxy-4-cholesten-3-one, forms cholestanol and accumulate in the brain, muscle, blood vessels, eye, and tendon results in a degenerative process.

The presenting symptoms usually begin with chronic diarrhoea in childhood, infantile hepatitis with jaundice, and juvenile cataracts as cholestanol accumulates in lens. Xanthomas usually develop in the second decades of life on the Achilles tendons, patella, elbow and hand tendons.

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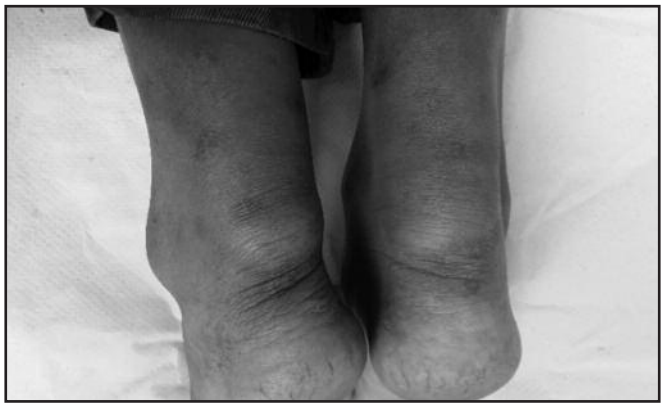

Fig. 1: Bilateral Xanthomas of Tendoachilles.

Furthermore, atherosclerosis may lead to stroke, and musculoskeletal xanthomas can cause motor and joint restriction.[3] Most of the patients have low intelligence quotient. In the third decades of life, CNS involvement becomes significant, resulting in seizure and cerebellar ataxia.

Diagnosis of CTX is made based on the combination of detailed history taking, clinical manifestation with specialized tests, including biochemical blood test and genetic screening. However if these specialized tests are not available, then biopsy should be taken in order not to miss this treatable disease. Both the serum cholestanol level and the cholesterol-to-cholestanol ratio are raise. The cholesterol-to-cholestanol ratio is a better indicator of disease than cholestanol level alone. Genetic test is to identify pathogenic variants in CYP27A1. Histopathology of the tendon mass biopsy will show accumulation of xanthoma cells and multiple dispersed lipid crystal clefts. MRI and CT scanning may show diffuse atrophy of the brain, as well as focal lesions, rarely xanthomata in the cerebellum, basal ganglia, and cerebrum. Imaging of spinal cord is usually normal.[4]

Treatments include replacement therapy involving administration of bile acids such as CDCA, ursodeoxycholic acid (UDCA), cholic acid, or taurocholic acid. Compared to administration of UDCA or taurocholic acid, CDCA treatment (750 mg/d) is the therapy of choice for treating the neurological and non-neurological symptoms of CTX, but cholic acid is also efficient for non-neurological symptoms.[5]

CONCLUSION

Cerebrotendinous Xanthomatosis is rare but treatable disease and often misdiagnosed. A proper history taking and assessment can easily recognize this condition, so that early treatment can be initiated and prevent further progression and may reverse the disease manifestation.

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