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JOURNEY TO DIAGNOSIS WITH A RARE NEUROMETABOLIC DISEASE, CEREBROTENDINUS XANTOMATOSIS (VAN BOGÆRT DISEASE) AND CONCOMITANT PSYCHIATRIC SYMPTOMS

Hatice Ayça Kaloğlu[1] & Şerif Bora Nazli[2]

[1] Dışkapı Education and Training Hospital, Psychiatry Department, aycakaloglu@gmail.com
[2] Dışkapı Education and Training Hospital, Psychiatry Department, nserifbora@gmail.com, bosbora@yahoo.com

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INTRODUCTION

Cerebrotendinous Xanthomatous (CTX), also known as van Bogært–Scherer–Epstein disease or van Bogært disease, is a rare congenital lipid metabolism disorder with variable clinical presentation (Harris 1968).

Cerebrotendinous Xanthomatosis (CTX) is an autosomal recessive disease that most commonly progresses with tendon xanthomas, juvenile cataracts and chronic diarrhea. The synthesis of bile acids -*cholic acid and chenodeoxycholic acid*- is impaired due to mitochondrial sterol-27-hydroxylase enzyme deficiency, an enzyme involved in bile acid biosynthesis, Mitochondrial sterol-27-hydroxylase enzyme activity decreases as a result of CYP21A1 gene mutation in the 2nd chromosome (Cali et al 1991).

The cholestanol accumulation, which is a byproduct of bile acid synthesis pathway, is observed in many organs and tissues, including the CNS (Central nervous system) as a result of the deterioration of bile acid synthesis (Moghadasian 2004). Diffuse white matter pathology, demyelination and various neurological and psychiatric symptoms related to cholestanol accumulation in glial cell membranes can be observed as a result of cholestanol accumulation in the CNS. Cognitive deterioration may develop in patients (Panzenboeck et al 2007).

CASE REPORT

It was found that 40-year-old A.E., who had been followed without medication for the last 10 years with the diagnosis of "borderline intellectual functioning," had paranoid thoughts and sub-threshold depressive symptoms that started about 6 months ago. It was observed during the examination that the patient's mood was irritable. The patient did not cooperate with the interviewer, the speech of the patient was under pressure. It was learned according to the history taken from the patient's partner that the person had delusions of jealousy that fluctuated even during the day, and that the patient had a tendency to increase in forgetfulness in recent months. The patient was recommended low-dose antipsychotic treatment after the first examination.

It was understood in the second interview made 2 weeks later that the patient did not benefit from the medical treatment given. The suppressed speech and irritability continued, and the delusions of jealousy fluctuated throughout the day like a delirium. The developmental history of the patient was detailed. The case was not consanguineous, they were 2 siblings. The patient's sibling did not have a history of psychiatric and/or neurological disease. There was no remarkable feature in the early development history. There was no motor or language delay. It was learned that the patient had achieved below average in classes since primary school, had behavioral problems and distractibility from time to time, but had never applied to psychiatry for this reason. It was understood that the patient was diagnosed with "Borderline Intellectual Functioning" during adolescence. It was learned from the patient's close relatives that the patient had clumsiness since adolescence, but they did not dwell on it and that the patient was connected to his current mental retardation.

On the person's psychotic symptoms fluctuating during the day, forgetfulness that is not compatible with patient's age and vitamin levels

Plasma cholestanol level and gene analysis were requested from the person in cooperation with Neurology and Medical Genetics. The patient's plasma cholestanol level was measured and the result of the examination was 48 microgram/mL, the patient was consulted to the Genetics department in terms of CTX mutation when this high level was noticed.

The diagnosis of CTX was considered as a result of the necessary consultations due to the high cholestanol level and ultimately the gene mutation. There was a decrease in the complaints of absent-mindedness and

forgetfulness in the follow-ups within 1 month as a result of the standard CTX treatment. Paranoid thoughts have completely disappeared.

DISCUSSION

The mean age at diagnosis has been reported as 35 for CTX. Early diagnosis is important in terms of providing treatment without tissue damage (Nie et a 2014). The disease is usually easily recognized in the group of young patients with chronic diarrhea, cataracts, tendon xanthomas and amnesia in the history (Mignarri et al 2012). There have been very few reports of a Cerebrotendinous Xanthomatosis patient diagnosed on the basis of a psychiatric picture although psychiatric symptoms are observed in the clinical follow-up of CTX patients. As far as we know, no such notification has been made from our country.

Psychiatric symptoms in CTX vary. There may be a delay in making the diagnosis, since the psychiatric conditions that may be associated with the disease have not been detailed yet. Psychiatric symptoms expected to be seen in the disease may be as behavioral impairment, personality disorders, mood disorders, psychotic disorders, and dementia-related psychopathology. Fraidakis examined 13 CTX cases in his case series review published in 2013 and stated that 6 of the cases had a psychiatric symptom in the process. Organic dementia was present in half of the 6 cases, and early psychiatric findings such as decreased intellectual capacity and mild cognitive retardation were observed in only 2 patients. Again, behavioral disorders that started in adolescence were reported in these 2 cases, as in our case (Fraidakis 2013). He emphasized in another review that CTX may be the cause of childhood mental retardation (Bjorkhem 2013).

Early recognition of this slowly progressing and fatal disease is very important; because both psychiatric and neurological symptoms respond to chenodeoxycholic acid treatment. The earlier the treatment is started, the faster the progression of the disease is stopped (Berginer et al 1988). Chenodeoxycholic acid is the primary treatment in the treatment *of cerebrotendinous* xanthomatosis, it prevents the accumulation of cholestanol in the tissue. Early detection of CTX is crucial for the use of chenodeoxycholic acid as a specific treatment. Chenodeoxycholic acid therapy has the potential to both alleviate symptomatology and improve prognosis by slowing neurodegeneration and disease progression, thus preventing or even reversing psychiatric symptoms (Bonnot et al 2010).

In the treatment of two siblings with CTX-related attention deficit and hyperactivity disorder (ADHD) and oppositional defiant disorder who also had mild cognitive retardation, both siblings were treated with chenodeoxycholic acid, and their psychiatric symptoms were reported to subside and their mild cognitive decline recover (Bonnot et al 2010). In our case, cognitive symptoms such as forgetfulness and absent-mindedness and paranoid delusions improved with 250 mg chenodeoxycholic acid treatment 3 times a day. This highlights the need for early diagnosis and treatment of the disease before irreversible neurological lesions occur.

Although there are a few case reports that psychiatric symptoms may also occur in the course of CTX, more studies and publications are needed in terms of the importance of *early diagnosis* in the course of treatment. To the best of our knowledge, this article we sent is a case report emphasizing the definition of CTX, based on the psychiatric symptoms that were first sent from our country.

When the existing literature is examined; it appears that most cases of cerebrotendinous xanthomatous are diagnosed by recognition of xanthomas. The purpose of reporting this case is to keep in mind that psychiatric symptoms with atypical course may also be associated with a neurological or metabolic picture, even without xanthomas or diarrhea suggestive of lipid storage disease and similar symptoms suggestive of a metabolic picture.

This case report was written to raise awareness among psychiatrists about a disease, which can be destructive. We hope to raise awareness among psychiatrists about this treatable inherited metabolic disorder by reporting this case.

CONCLUSION

Cerebrotendinous Xanthomatous (CTX), also known as van Bogært–Scherer–Epstein disease or van Bogært disease, is a rare congenital lipid metabolism disorder with variable clinical presentation .This case report was written to raise awareness among psychiatrists about a disease, which can be destructive. We hope to raise awareness among psychiatrists about this treatable inherited metabolic disorder by reporting this case. Early recognition of this slowly progressing and fatal disease is very important; because both psychiatric and neurological symptoms respond to chenodeoxycholic acid treatment.

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Correspondence:
Şerif Bora Nazli
Dışkapı Education and Training Hospital
Psychiatry Department
nserifbora@gmail.com, bosbora@yahoo.com