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Case Report: Young Onset Stroke from Familial Hypercholesterolemia

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Abstract

Introduction: Familial hypercholesterolemia (FH) is a medical condition that leads to extremely high levels of low-density lipoprotein (LDL) cholesterol, increasing the risk of ischemic heart disease, including myocardial infarction. However, the link between FH and ischemic stroke is still debatable. In this case, we report a young adult female who had FH and high levels of LDL and suffered from an early-onset ischemic stroke. **Case Presentation**: A 38-year-old female presented with acute numbness and weakness in her right limb, as well as speech difficulty. She had no history of hypertension, migraine, or diabetes, but did have a history of eyelid xanthoma. The results of the neurological examination confirmed a slightly gradual response, a mild weakness in her right limb, and a slightly reduced response to touch and pain. Laboratory tests showed very high cholesterol and LDL levels, as well as an increased CRP level. Radiological examination via a CT scan revealed lesions within the left frontotemporal region. The patient was prescribed dual antiplatelet therapy and vascular risk factor medication, and after 6 days of treatment, was discharged to go home.

Conclusion: We present a case of ischemic stroke in a young patient with clinically diagnosed FH, highlighting the possibility of FH in those with early-onset cerebrovascular disease.

Keywords: cerebrovascular disease, familial hypercholesterolemia, ischemic stroke, low-density lipoprotein cholesterol

Introduction

Stroke in younger people has a greater impact on their quality of life compared to stroke in older people. Typically, strokes that occur before the age of 45 are considered as young-onset strokes.[1] In young adults, the number of ischemic stroke cases continues to increase over time, which has occurred along with the change of lifestyle in the younger population. Compared with elderly patients, young ischemic stroke patients have a greatly expansive of risk factors. These risk factors are related to specific ages, like pregnancy and the use of birth control pills. The behavioral-linked risk factors encompass obesity, minimal physical activity, immoderate intake of alcohol, and smoking.[1,2]

A previous research study revealed that individuals who experienced a stroke at a young age frequently exhibited certain risk factors including dyslipidemia (52.7%), smoking (47.3%), hypertension (39.3%), and patent foramen ovale (PFO, 32.8%). In general, narrow blood vessel blockages were uncommon, and they were all linked with high blood pressure. Most people with these blockages had other risk factors.[3] More studies have shown that among young adults with stroke, blockage-caused stroke was more common than hemorrhage-caused stroke was more common than hemorrhage-caused stroke. The risk factors for stroke in this young adult group were HIV infection, excessive waist-to-hip fat ratio, and sickle cell disease[4].

Familial hypercholesterolemia (FH) is a qualification for adequate treatment of their high risk of ischemic stroke. According to the clinical criteria, 11.5% of acute ischemic stroke or transient ischemic attack patients had potential familial hypercholesterolemia.[5] A recent review and meta-analysis study of adults with Familial Hypercholesterolemia revealed that individuals with the condition, as clinically diagnosed, included an elevated risk of ischemic stroke.[6] Until now, there are only a small number of case reports about familial hypercholesterolemia and its relation to the risk of stroke in younger adults. We present a case of an ischemic stroke with an early onset that was clinically identified as Familial Hypercholesterolaemia (FH) in a young female patient.

Case report

A 38-year-old woman came to our emergency department unit with sudden numbness and weakness in her right limbs and also difficulty speaking. She had no history of high blood pressure, migraine, or diabetes. The patient had a history of eyelid xanthoma. When we asked about her family's health history, she mentioned that her mother had a sudden cardiac arrest and died at the age of 50 years. The patient reported that her parents and sibling had hyperlipidemia but noted no history of CAD. Examination revealed sluggishness, mild weakness in her right limb, and a slightly reduced response to pain and touch. Furthermore, we observed increased cholesterol levels exceeding 200 mg/dl (228 mg/dl) and LDL levels beyond100 mg/dl (237.3 mg/dl), elevated triglyceride levels surpassing 150 mg/dl (336.6 mg/dl), and increased in CRP level (9.78 mg/dl). Cardiac constellation exposes no signs and symptoms of Atrial Fibrillation (AF). ECG and also Echocardiography showed no indication of Patent Foramen Ovale (PFO). Chest x-rays were performed with the results were within normal range.

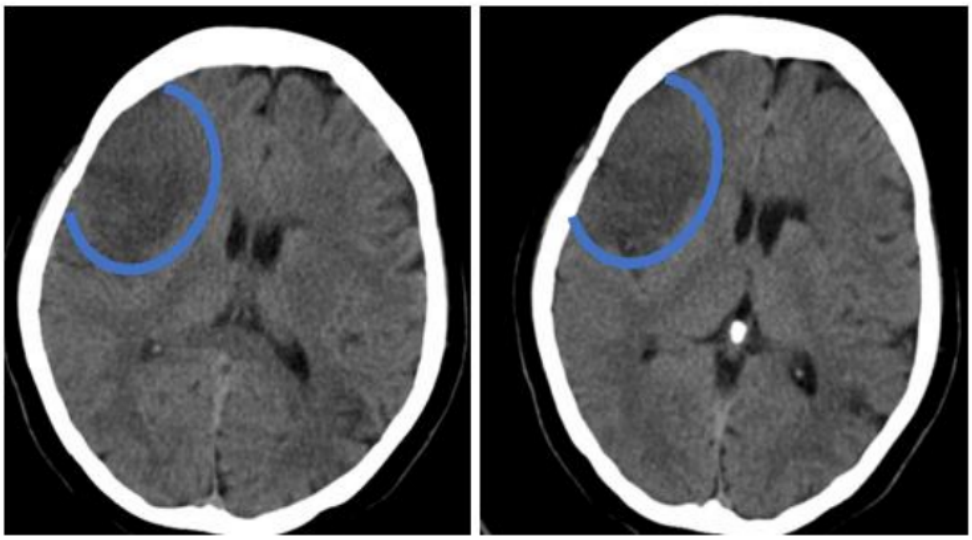

FIGURE 1. An ischemic was found in the left frontotemporal region based on the plain brain CT scan

Table 1. Clinical Criteria from the Dutch Lipid Clinical Network for the Diagnosis of Heterozygous Familial Hypercholesterolaemia [12,13]

Family history	Score
• 1st degree relative with premature coronary heart disease	1
or	
• 1st degree relative with verified LDL cholesterol >95th percentile by age and gender for country	1
• 1st degree relative with tendon xanthoma and/or arcus cornealis	2
or Children <18 years with verified LDL cholesterol >95th percentile by age and gender for country	2
Clinical history	
1. Premature coronary heart disease	2
2. Premature cerebral or peripheral vascular disease	1
Physical examination	
1. Tendon xanthoma	6
2. Arcus cornealis <45 years	4
LDL cholesterol	
1. >8.5 mmol/l	8
2. 6.5–8.4 mmol/l	5
3. 5.0–6.4 mmol/l	3
4. 4.0–4.9 mmol/l	1
DNA analysis	
1. Causative mutation in *LDLR*, *APOB* or *PCSK9*	8
Clinical diagnosis	
Definite FH	>8
Probable FH	6–8
Possible FH	3–5
Unlikely FH	<3

Based on the Clinical Criteria for Diagnosis of Heterozygous Familial Hypercholesterolaemia by the Dutch Lipid Clinic Network, this patient presents with several indicators: a first-degree relative (women ≤60 years) who has premature coronary heart disease, a first-degree relative with xanthoma and/or arcus corneal (specifically, a history of eyelid xanthoma), premature cerebral or peripheral vascular disease, LDL cholesterol level exceeding 8.5 mmol/l (LDL-cholesterol 13.18 mmol/l), and clinical diagnosis definite HF (score >8).

The patient was admitted to the hospital and received necessary medical care to support their recovery, which consisted of a loading dose of 300 mg of clopidogrel, followed by a maintenance dose of 75 mg of clopidogrel. The patient was prescribed a dual anti-platelet regimen, which included a low dose of aspirin (80 mg), along with

Atorvastatin 40 mg daily and basal insulin. The patient was also administered Anemolat (40 mg). To address the remaining functional deficits, rehabilitation through physiotherapy was provided. After six days of treatment, the patient's disability had improved to a minor level (MRS 2), and she was discharged from the hospital.

Discussion

We report a case of a young adult female who experienced an ischemic stroke. She had no history of hypertension, migraine, oral contraceptive use, and congenital heart disease. Her LDL was at a very high level and the presence of xanthoma indicated the familial hypercholesterolemia. The connection between FH and ischemic cerebrovascular disease is still debated. According to the DLCN Criteria, the patient was diagnosed with familial hypercholesterolemia, and her clinical symptoms were consistent with those typically seen in ischemic stroke cases.

Earlier studies demonstrate that in patients with FH, stroke transpires more occasionally than CAD. For two-thirds of individuals who likely have FH and those who may have a condition, their first symptom is often stroke or TIA. (6,7) To identify younger individuals who may have the condition, or had a stroke, it would be prudent to include Familial Hypercholesterolemia screening as part of standard medical testing. (7) Furthermore, for FH patients with stroke at an early age, a combative treatment is recommended. (8)

Nowadays, FH is mostly concealed and under treatment universally. Only 10% of people affected by FH receive proper diagnosis and treatment due to insufficient public and medical understanding. (9) Familial Hypercholesterolemia (FH) can be diagnosed clinically by identifying high levels of LDL-C in the plasma, a family history of hypercholesterolemia, instances of premature ASCVD, and the presence of tendon xanthomas. Unfortunately, only 10% of those affected by FH receive proper diagnosis and treatment due to insufficient public and medical understanding of the condition. (10) Generally, adult patients have a level of LDL-C higher than 4.9 mmol/l; however, some patients and their relatives may have lower cholesterol levels, particularly if they are younger. (11,12) The presence of tendon xanthomas is an indicator of a heightened risk of cardiovascular issues, as they serve as the pathognomonic for the underlying disease.

For approximately <20 % of FH individuals with a functional mutation, Xanthoma can be evident. Despite the absence of visible Xanthomas, the diagnosis of Xanthoma is not eliminated. (11)

In the diagnosis of FH, three different clinical criteria have been expanded. The MedPed program only considers lipid levels and not clinical symptoms or genetic testing. The criteria for Inclusion Criteria (IC) according to The Simon Broome Register incorporates tendon xanthomas, lipid levels, family history of hypercholesterolemia, premature ASCVD, and also the identification of a functional mutation through genetic testing. (11,12) The Dutch Lipid Clinic Network criteria is a widely used tool for diagnosing Familial Hypercholesterolemia (FH). It involves a scoring system based on factors such as LDL-C levels, the appearance of arcus corneal and tendon xanthomas, hypercholesterolemia premature CVD in the family, and positive genetic testing. A total score of 8 or above typically leads to a confirmed diagnosis of FH using this tool (12).

In individuals with FH, appropriate management is crucial for preventing cardiovascular disease/stroke. International guidelines suggest optimal LDL-C goals to reduce lipid levels. For adults, the target is less than 100 mg/dL (<2.6 mmol/L) for adults with coronary heart disease or diabetes, it is less than 70 mg/dL (<1.5 mmol/L); and for children it is less than 135 mg/dL (<3.5 mmol/L). Alternatively, a 50% reduction in LDL-C levels is recommended. The traditional treatments for familial hypercholesterolemia (FH) include statins, which are 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors, ezetimibe, which is a medication that selectively hinders the transport of cholesterol and phytosterol in the mucosa of the small intestine, and apheresis. In addition, Evolocumab, a medication that acts as a PCSK9 inhibitor, is used to reduce plasma LDL-C levels in individuals with homozygous FH and severe heterozygous FH. This medication has shown good tolerance and efficacy. (13,14). Due to consistently improving and advancing research, there is a promising outlook for more effective and efficient treatment options for patients suffering from FH shortly (14).

Conclusion

We report a case of a young individual who had an ischemic stroke. The patient was clinically diagnosed with Familial Hypercholesterolaemia (FH). This case suggests that

FH should be considered as a potential cause in patients who experience cerebrovascular disease at a young age.

Conflict of interest

The authors declare no conflict of interest

Ethics

Verbal informed consent has been obtained from the patient. No identification of the patient's identity.

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