Case Report

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Surgical removal of multiple xanthomas in familial hypercholesterolemia: a case report

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Introduction: Xanthomas are skin swellings that are caused by the accumulation of cholesterol and lipids in the body. They are associated with lipid disorders, such as familial hypercholesterolemia (FH). FH is a rare genetic disorder, which is characterized mainly by high levels of low density lipoprotein cholesterol.

Case presentation: The authors report a case of an 11-year-old female who had multiple swellings all over the body with the largest measuring 7 × 4 × 3 cm in diameter. These lesions were gradually increasing in size since 4 years. She was being bullied by her school colleagues because of swellings appearance. Clinical examination revealed multiple yellowish masses on the patient's elbows, knees, and buttocks which were painless, firm, and nontender. Laboratory tests revealed elevated levels of serum cholesterol (512 mg/dl) and low density lipoprotein cholesterol (469.2 mg/dl). Masses ultrasound showed similar echogenicity to upper and lower extremities subcutaneous fat. Incisional biopsy microscopic images revealed clusters of foam cells. These findings led to a diagnosis of Homozygous FH and she underwent surgery to remove the xanthomas on her elbows.

Discussion: Xanthomas are small, yellowish skin swellings that form due to the presence of high lipids. As they are typically painless and small, this could lead to a late treatment or misdiagnosis. Drugs, lifestyle changes, and surgery represent treatment plan options.

Conclusion: Xanthomas can be the first indication of an underlying hypercholesterolemia problem and this case report highlights the importance of early diagnosis of Homozygous FH by providing the suitable management for this case in its early stages which can prevent developing serious complication.

Keywords: case report, familial hypercholesterolemia, lipid disorder, surgical intervention, xanthoma

Introduction

Xanthoma refers to exogenous mass arises on the skin within the tendon, connective tissue, and subcutaneous tissue[1,2]. It can be an important sign in clinical practice about underlying lipid metabolism disorder especially in patients with familial hypercholesterolemia[3]. With recurrence rate ranging from 25 to 39%[4]. FH is a genetic disorder, which can be inherited, featured by elevated levels of low density lipoprotein cholesterol, xanthomas and may develop symptoms of ischemic heart disease, vascular problems, or aortic stenosis[3].

HIGHLIGHTS

- Xanthoma can be misdiagnosed as a tumor.
- Xanthoma can be an early presentation for any underlying lipid disorder.
- Surgical removal of xanthoma combined with lipid lowering medication is effective.

Xanthoma can be classified into multiple categories like tuberous, tendinous, eruptive, disseminated, and planar xanthoma[5]. The most common type of xanthoma in FH patients is tendinous (40–50% of all patients) which can be defined as subcutaneous tumors located in tendons that are used for extension[3,6]. Tuberous xanthoma are less observed in clinical practice[7]. It can be seen in 10–15% of all FH patients and usually appears as a nodule in pressure areas as the extensor aspect of the elbows, knees and buttocks, and measuring less than 2 cm in diameter[3,6].

In recent years, there has been an increased interest in xanthoma according to the importance of early diagnosing any underlying lipid disorder, which leads to preventing the chance of developing complications[1]. We are reporting a case about a female who presented with xanthomas the largest measuring 7 × 4 × 3 cm which have been surgically removed. This case report was written using Surgical CAse REport criteria 2020[7].

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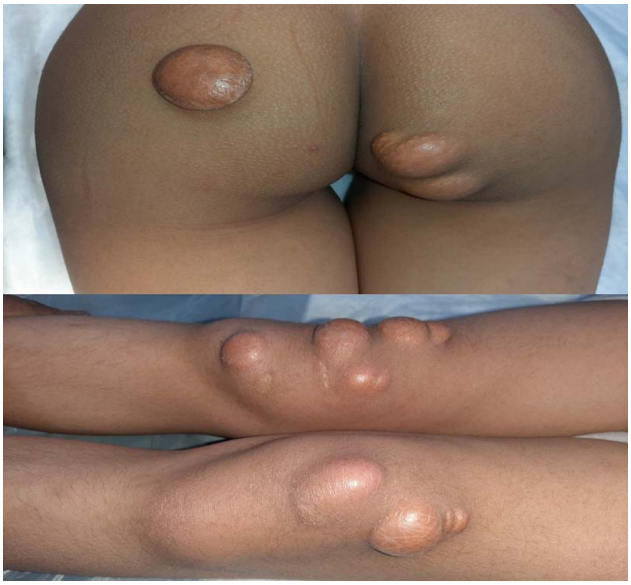

Figure 1. Multiple swellings over knees and buttocks.

Case presentation

An 11-year-old girl presented with multiple yellowish masses all over the body which have been gradually increasing in size since ~4 years. The masses were asymptomatic and her main complaint was cosmetic because she was being bullied by her school colleagues. The total number of these lesions was fifteen ranged in size from $3\times2\times1$ cm to $7\times4\times3$ cm and were spread as following (six on the elbows, three on the buttocks, six on the knees) (Fig. 1). Clinical examination showed painless, firm, nontender, soft inconsistency, and mobile swellings which had well-defined edges. The masses did not meet the criteria of lipoma or multiple lipomatosis. Patient was not taking any medication and did not undergo any surgery. It was revealed that her father was diagnosed with hyperlipidemia and had a history of ischemic heart disease. Ultrasound of the swellings showed multiple similar well-defined heterogeneous subcutaneous focal lesions with similar echogenicity to the subcutaneous fat seen upper and lower extremities with no calcification or cystic changes likely familiar multiple lipomatosis. Patient was sent for an incisional biopsy of the masses in elbow and buttocks. Specimens microscopic image revealed skin covered tissue showing large dermal aggregates of foam cells, also known as lipid-laden macrophages, that extended to the subcutis with admixed smaller population of multinucleated giant cells (Fig. 2). Fibroblastic proliferation and increased collagen deposition were also seen. The pathological report with clinical manifestation were consistent tuberous xanthomas that was confirmed by her lipid profile which revealed elevated serum cholesterol and low density lipoprotein (LDL). The results were as following: serum cholesterol 512 mg/dl (reference range, up to 200 mg/dl), LDL 469.2 mg/dl (reference range, less than 130 mg/dl), high density lipoprotein 32 mg/dl (reference range, 45–65 mg/dl) whereas very low density lipoprotein was 10.8 mg/dl (reference range for female, 25–50 mg/dl). Based on the findings and clinical features, patient was diagnosed with HoFh and multiple xanthomas according to The Simon Broome Register Diagnostic Criteria. Genetic analysis for Apo A, Apo B, and LDL receptors was not done due to low social economic status. The patient underwent surgery by performing elliptical incisions in an oval shape with appropriate edges, and the masses were completely excised (Fig. 3). The wound was

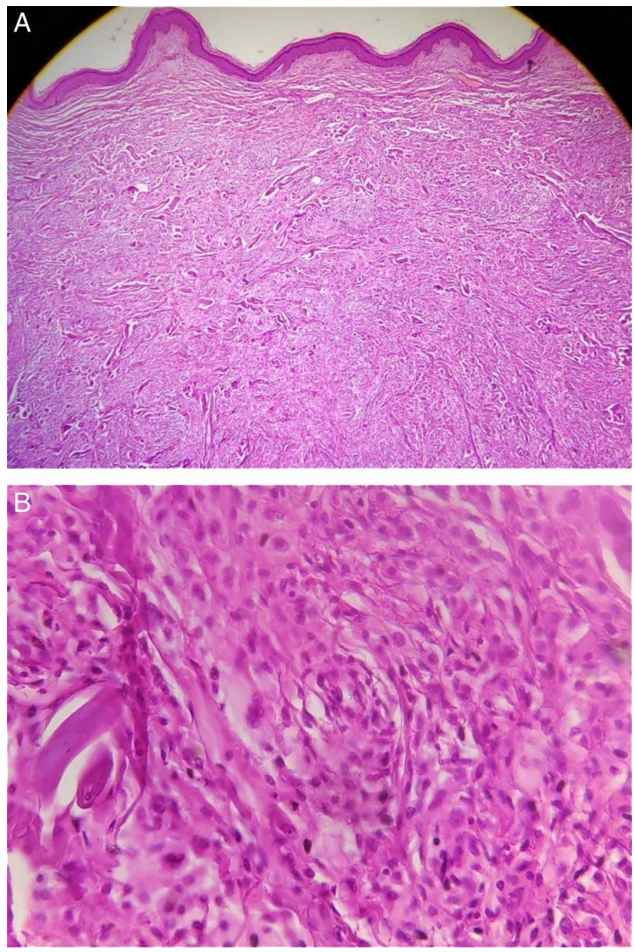

Figure 2. (A) Section shows skin tissue with unremarkable epidermis. There is diffuse infiltrate by foamy macrophages (xanthoma cells) involving dermis and extending to subcutis. (B) The xanthoma cells have an eccentric nucleus and abundant foamy cytoplasm. There is no significant cytological atypia or increased mitosis.

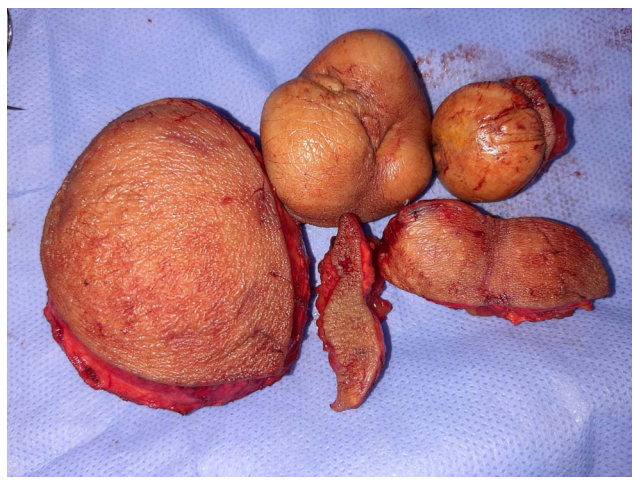

Figure 3. Surgically removed xanthomas from the elbows.

closed using primary closure and she was discharged in the same day. She was asked to do X-ray, echocardiography, and knee ultrasound and advised to follow up after 1 month. In addition, the family was referred to cardiologist and endocrinologist to do a screening for familial hyperlipidemia and to prescribe prophylaxis medication as they are at high risk for developing coronary heart disease. She did not show for the follow up appointment and we lost contact with the patient family.

Discussion

Xanthomas in literature are palpable masses in the skin, which have infiltrates of cholesterol, triglycerides, phospholipids, cholesterol esters, and lipid-laden foamy macrophages due to the increased lipid levels[3,6]. These lesions are not tumors but rather a presentation that can indicate underlying lipoprotein metabolic disorders and most common types of xanthomas are associated with disorders of lipid metabolism[5,6]. Xanthomas are usually noted in the second decade of life and the most common sites they manifest are the tendons that are subjected to mechanical stress like patellar tendon[1,8]. Whereas tuberous xanthoma is asymptomatic swelling, which can be seen clinically as flat or elevated nodules located over joints skin, where the most common joints are elbows, knees, and fingers joints[2]. As previously noted tuberous xanthoma usually measures less than 2 cm in diameter therefore the presentation of our patient with $7 \times 4 \times 3$ tuberous xanthoma is atypical. Children rarely develop xanthomas, but when they do, they should raise suspicions about underlying lipid disorder[9]. A previous case reported by Narasimahan *et al.*, about a 14-year-old girl presented with progressive breathlessness and multiple skin nodules which had been gradually increasing in size since 3 years and through further investigations she was diagnosed with left ventricular hypertrophy and aortic stenosis. The underlying cause behind these manifestations was Homozygous FH and the masses were defined as xanthomas[5]. Regarding the xanthomas, they typically regress by the treatment of the underlying cause, but in some cases surgical treatment can be a solution if there was a limitation in movement or cosmetic concerns as it is in our case[3]. Another study reported a case of 23-year-old male had discomfort and pain in the elbows and buttocks due to the presence of large tendinous and tuberous xanthoma, the largest measuring $6 \times 5 \times 5$ cm and $7 \times 5 \times 4$ cm, and have been surgically excised[1]. However, certain studies have reported that there is a significant risk of xanthoma recurrence following surgical removal[10]. Therefore, the most effective treatment for numerous and large tendinous and tuberous xanthomas seems to be a combination of local surgery excision combined with cholesterol lowering medication after the operation[1]. To stop or delay the onset of coronary heart disease, a very aggressive cholesterol lowering strategy should immediately be started[9]. It has been reported that medical management using HMG-CoA reductase inhibitors such as atorvastatin would reduce the size of the xanthomas[3]. In addition, statins may be able to soften xanthomas and reduce the possibility of recurrence[11]. In the United States, two novel agents have been approved as supplemental therapies for HoFH in patient aged between 12 and 18[9]. According to recent guidelines, patients with FH should limit their total calorie intake and consume fat less than 3% of their dietary intake[1]. Treatment options include lifestyle modifications, diet restriction, medication therapy, invasive procedures such as permanent lipid apheresis and, as a last solution, liver transplantation[1].

Conclusion

In summary, we presented the case of an 11-year-old female with multiple xanthomas who underwent surgery and was referred to an endocrinologist, highlighting the importance of early detection of underlying lipid disorders and emphasizing early correction of the lipid profile. By treating underlying lipid abnormalities early, major complications like atherosclerosis or cardiovascular disease can be avoided[1].

Ethical approval

Not applicable.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

A.M.S. and M.A.O.: did the surgery and were responsible of project administration, supervision, and revision; M.A.T., A.M., and Y.Z.F.: wrote the manuscript.

Conflicts of interest disclosure

The author declares no conflicts of interest.

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