Palmar Xanthoma—An Indicator of a More Sinister Problem

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Received: 18 May 2009 / Accepted: 21 May 2009 / Published online: 22 September 2009
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Abstract Multiple palmar xanthomas may often be seen first by the hand surgeon. One such case presented to us in the hand clinic. Further investigations revealed the presence of a more sinister metabolic problem of type III hyperlipoproteinemia. We discuss the details of this case and review relevant literature on the subject.

Keywords Xanthoma · Hyperlipoproteinemia · Hypercholesterolemia

Introduction

We would like to present a case of multiple palmar xanthomas that was first seen by us in the hand clinic. Further investigations revealed the presence of a more sinister metabolic problem. We discuss the details of this case. In addition, relevant literature on the subject has been reviewed.

Case Report

A 47-year-old African-American gentleman was referred to our hand surgery clinic with complaints of multiple palmar lesions that had been present for over a year. The lesions were progressively increasing in number and size but were

otherwise asymptomatic. No significant past medical history was present. Family history included a diagnosis of coronary artery disease in his father. Initial evaluation revealed multiple yellowish maculo-papular lesions over volar aspects of both hands (Fig. 1). The lesions were non-tender with no ulcerations. Our initial clinical diagnosis was that of multiple palmar xanthomas. No similar lesions were found elsewhere on the body. Examination of the eyelids did not reveal any xanthelasma palpebrarum.

To confirm our clinical suspicion of palmar xanthomas, we performed an excision biopsy of one of the lesions. Histopathology confirmed the diagnosis of cutaneous xanthomas and revealed the presence of “foamy macrophages” (Figs. 2 and 3). Blood biochemical studies were subsequently ordered. A lipid panel examination revealed hypertriglyceridemia, 737 mg/dl ($N=0-149$ mg/dl), hypercholesterolemia, 949 ($N=125-200$ mg/dl), and high cholesterol to high density lipoprotein ratio of 29.66 ($N<5$). DNA analysis for any low density lipoprotein receptor gene mutation was not done due to its high cost. Further studies revealed a normal fasting blood sugar of 103 mg/dl. However, the level of hemoglobin A1C was high, 6.1 ($N<6\%$). Thyroid function and liver functions were normal. A final diagnosis of hypercholesterolemia and hypertriglyceridemia (type III hyperlipoproteinemia) was made, and the patient was started on fenofibrate. The patient is currently being followed by his primary care physician and, at the time of writing of this report, did not show any worsening of the palmar xanthomas.

Disclaimer No benefits, financial or otherwise, have been or will be received for this study.

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Discussion

Xanthomas are lesions characterized by accumulations of lipid-laden macrophages. They are commonly associated

Figure 1 Clinical picture showing numerous yellowish maculopapular lesions on the patient's palms.

with all types of hyperlipidemia. However, type III hyperlipidemia is particularly known to be associated with palmar xanthomas and has a proclivity to the development of premature atherosclerosis.

This form of hyperlipoproteinemia which is also known variously as remnant hyperlipidemia, dysbetalipoproteinemia, or “broad beta disease” is characterized by the accumulation of beta-very low density lipoprotein (VLDL). This in turn leads to an elevation of both triglyceride and cholesterol levels [5]. It is a rare form of genetically influenced hyperlipidemia and predisposes the affected patients to a higher risk of cardiovascular diseases.

Xanthomas develop primarily due to lipid leakage from the vasculature into surrounding tissues, where macrophages phagocytize these lipids. Accumulation of lipids in the macrophages leads to formation of “foamy macrophages” [3]. At least seven different types of xanthomas have been identified. These include xanthelasma palpebrarum (the most common type and can be associated with any

Figure 2 Low power micrograph showing the entire circumscribed lesion (black arrows) with overlying skin (white arrows).

Figure 3 High power micrograph showing multiple “foamy macrophages”.

type of hyperlipoproteinemia), eruptive xanthomas (type I, IV, or V hyperlipoproteinemia), planar xanthomas (type III hyperlipoproteinemia), tuberous xanthomas (type II and III hyperlipoproteinemia), tendinous xanthomas (common in type II hyperlipoproteinemia), xanthoma disseminatum, and verruciform xanthoma. The last two varieties occur in normolipemic patients.

Planar xanthomas are mostly macular and rarely elevated lesions. They can occur at any site. They can also be associated with secondary hyperlipidemia, especially in cholestasis [2]. They may be associated with monoclonal gammopathy and hyperlipidemia, particularly hypertriglyceridemia. Generalized planar xanthomas can cover large areas of the face, the neck, and the thorax. Planar xanthomas in the palm are commonly referred as xanthoma striatum palmare (XSP). XSP is a rare but important sign of type III hyperlipoproteinemia. Although XSP is considered pathognomonic of type III hyperlipoproteinemia, Hsu et al. suggested that primary biliary cirrhosis should be considered in the differential diagnosis, especially with elevated liver function tests. Other reported conditions associated with XPS are pancreatic insufficiency and multiple myeloma. A hypothesis for the formation of planar xanthomas in the palm was proposed by Walton et al. following an experimental study on rabbits. This study suggested that minor trauma in pressure loading areas (foot pad in rabbits and hands in human beings) leads to increased vascular permeability, increased leakage of lipids, and eventual planar xanthoma formation [1].

Type III hyperlipoproteinemia is characterized by the accumulation of beta-VLDL, which is manifested by increases in both triglyceride and cholesterol levels in the plasma. A genetic basis for this disorder is well established. Various mutations of apoprotein E impair its ability to bind to the beta-VLDL receptor. A majority of patients are

homozygous for the apoprotein E2 variant. We did not perform these investigations in our patient due to the high cost involved. We, however, did refer the patient back to his primary care physician for further follow-up. Type III hyperlipidemia is associated with coronary heart disease and diabetes mellitus in young patients. Asymptomatic palmar xanthomas can lead to early diagnosis of this potentially lethal disease. Early medical intervention in the form of antihyperlipidemic drugs and dietary modification can lead to improved life expectancy.

Less than 20 cases of patients with palmar xanthomas have been reported so far in the English literature. They can be an early and sometimes only clinical sign of the underlying pernicious condition, i.e., type III hyperlipoproteinemia [6]. As seen in this case, the patient presented primarily with palmar masses and was hence referred to us for initial evaluation. Biopsy of the lesions confirmed our initial suspicion of palmar xanthomas, and subsequently, the underlying hyperlipoproteinemia was diagnosed. Failure to diagnose and initiate treatment for hyperlipoproteinemia could potentially have led to serious cardiac morbidity at a later date [4]. Our experience serves to

reiterate the importance of recognizing the fact that palmar xanthomas may first present to a hand surgeon, and it is imperative to remember that it may serve as an indicator of a more sinister underlying problem.

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