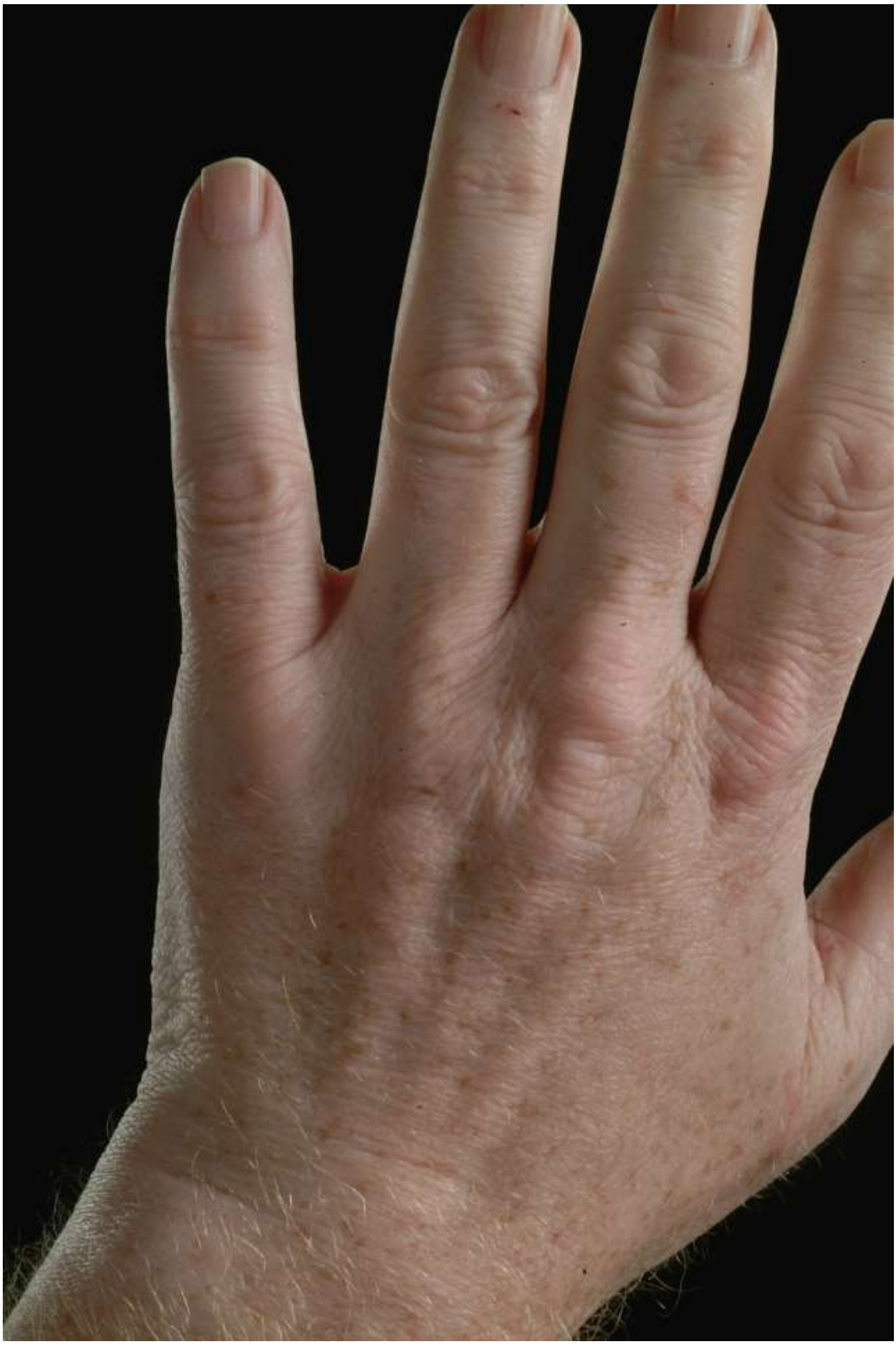
A man with nodules on the back of his hands

M. G. Zayed[1]
ORCID identifier: 0000-0001-9816-983X

S.C. Bain[1,2]
0000-0001-8519-4964
[1]Swansea University Medical School, Swansea and [2]Swansea Bay University Health Board, Singleton Hospital, Swansea, UK



A 43-year-old man was admitted with central chest pain and ECG changes suggesting an acute coronary syndrome. On review, he had firm non-tender nodules on the dorsum of both hands. These had been present for several years and his mother's hands had a similar appearance.

Questions:

1. What is the physical sign shown and what is the likely diagnosis?
2. What are the causes, complications and prognosis of this condition?
3. How is this condition diagnosed and is there a role for screening?

Answers and learning points:

Question 1

This image shows xanthoma of the extensor tendons of the hands. The Achilles tendon can also be affected. It occurs secondary to prolonged hypercholesterolaemia where lipids infiltrate the tendon and the surrounding sheath leading to irregular thickening [1]. It is most commonly seen in familial hypercholesterolaemia (FH), but can be found in other rare hereditary disorders such as sitosterolemia and cerebrotendinous xanthomatosis [2].

Question 2

FH is the most common dominantly inherited genetic disorder [3]. It is typically caused by mutations affecting function of the low-density lipoprotein (LDL) receptor, resulting in markedly raised LDL-cholesterol levels from birth [4]. Up to 50% of untreated men and 30% of untreated women will have a myocardial infarction by the age of 50 and 60 years respectively [5,6]. Effective cholesterol lowering therapy has greatly improved the prognosis [7].

Question 3

Only a minority of people with FH have clinical signs. FH should be suspected in people with a total cholesterol above 7.5 mmol/L (and/or LDL-cholesterol over 4.9 mmol/L) and a history of ischaemic heart disease (IHD) before the age of 60 or a family history of IHD in first degree relatives under the age of 60 (or second degree relatives under the age of 50) [8]. Genetic testing is available in parts of the UK, however, not all causative mutations are known and so a negative test does not refute the clinical diagnosis. NICE recommends using the Dutch Lipid Clinic Network Criteria (DLCNC), or Simon Broome criteria to make a diagnosis of FH in primary care [9].

Despite the life-threatening complications and the availability of effective treatment, FH remains massively underdiagnosed [10]. Several screening tools have been considered in different settings including primary care, paediatrics, coronary care units and biochemistry laboratories. In Wales there is a programme of 'cascade screening' with FH specialist nurses attached to lipid clinics using cholesterol testing and, when appropriate, genetic testing to follow up relatives of index cases with possible or definite FH. This is supplemented by specialist paediatric lipid clinics to manage children of people with FH.

Learning points

1. Tendon xanthoma are most commonly caused by FH.
2. FH is still massively underdiagnosed.

References:

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