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EDITORIAL

Familial hypercholesterolaemia: a look toward the East

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Article Chlebus et al., see p. 960

There are very few genetic diseases that have been so well described as heterozygous familial hypercholesterolaemia [1–3]. However, this disease "advances undercover," and it is only after several cardiovascular episodes [4, 5] that the question of the genetic origin of this metabolic disease is raised.

The cardiologist is nevertheless in the front line. It is indeed the cardiologist who must suspect the diagnosis when a premature coronary artery disease occurs in a patient with high levels of low-density lipoprotein cholesterol (LDL-C) [6, 7]. A rapid family history suggests the diagnosis, and certainty is provided by a battery of clinical arguments or by genetic diagnosis.

Nevertheless, it rapidly became apparent that hypercholesterolaemia in the broad sense covers two different nosologic entities. On the one hand, polygenic hypercholesterolaemia corresponds to complex interactions between nutrition and certain genetic polymorphisms that contribute to the development of the disease [8]. On the other hand, heterozygous familial hypercholesterolaemia corresponds to a monogenic disease involving exposure to LDL-C from birth.

The majority of studies show that only 10% of patients who are carriers of familial hypercholesterolaemia are diagnosed [9]. This is because familial hypercholesterolaemia is a disease that progresses slowly from birth and in which cholesterol deposits build up insidiously in the arteries. The first diagnosis is thus generally an acute coronary syndrome or an effort angina. If the cardiologist does not pay particular attention to the family history, genetic hypercholesterolaemia blends in with all the pure and mixed hypercholesterolaemias that are encountered daily in intensive care units.

At the present time, the prevalence of heterozygous familial hypercholesterolaemia is 1 in 200 or 1 in 250 [1]. It is by far the most common genetic abnormality in medicine, well ahead of cystic fibrosis, the prevalence of which in the general population is 10 times lower. The clinical diagnosis is easily made when extravascular cholesterol deposits are present, such as tendon xanthomas, xanthelasmas, and premature corneal arcus in persons aged under 45 years. Presently, such extravascular deposits are less frequent because patients with hypercholesterolaemia are treated earlier than in the past. For this reason, clinical scores have been developed to facilitate screening for this genetic condition. The most popular of these diagnostic scores is the Dutch Lipid Clinic Network score (Dutch score), which combines a family history of cholesterol and of premature cardiovascular disease, and a personal clinical history of extravascular deposits and premature cardiovascular disease as well as LDL-C levels before starting drug therapy [10]. The presence of a mutation of course confirms the diagnosis.

In other words, LDL-C level is not in itself sufficient to predict the presence of premature coronary artery disease, but it justifies the search for a mutation in daily practice in order to limit as much as possible the risk of accelerated atherosclerosis [11].

To convince physicians of the usefulness of screening, the study of Chlebus et al. [12] is essential. In a sample of 2812 adults, the authors applied a Dutch score of six or above. Based on the calculated prevalence in their sample, Chlebus et al. [12] estimated at 136,300 the number of adult carriers of familial hypercholesterolaemia in Poland. Familial hypercholesterolaemia is diagnosed in only 25% of patients. Only 32.8% of patients who are carriers of familial hypercholesterolaemia receive high-dose statins, and about 60% of patients treated with high-dose statins have LDL-C level ≥ 4.1 mmol/L. Because Poland is a country of high coronary risk [13], these findings justify nation-wide screening for familial hypercholesterolaemia.

In conclusion, heterozygous familial hypercholesterolaemia is the most common genetic disease in medicine. Familial hypercholesterolaemia is the most demonstrative example

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of accelerated coronary atherosclerosis. The disease raises no problem of clinical diagnosis, nevertheless it is diagnosed late when cardiovascular complications occur, such as acute coronary syndrome. Precise genetic diagnosis is available and enables optimal assessment of coronary risk. At the present time, the mission of the cardiologists in Eastern Europe [12, 14], as well as in the West [2, 10, 11], is to detect in the stream of patients those whose LDL-C is highest and who deserve particular attention with regard to diagnosis, prognosis, and treatment.

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