ELSEVIER

Article

Hypophosphatasia: the patient's and patient's family's point of view

L'hypophosphatasie vue par les malades et leurs familles

S. Ursprung

Président bénévole de l'association Hypophosphatasie Europe, 16, rue Barbanègre, 68330 Huningue, France

Available online at

ScienceDirect

www.sciencedirect.com

Summary

Today, public opinion and the French authorities are more aware of rare diseases, in particular due to the implementation of national plans for rare diseases (PNMR I: 2005-2008 and PNMR II: 2011-2016), the existence of national networks and the current organization of the reference expert centers for rare diseases. While the management of rare diseases is now better structured, it remains long for the patients to be diagnosed. It is not always easy for physicians to clearly identify one of the 7,000 rare diseases even though they increasingly ask themselves the question: is this a rare disease? A person diagnosed with a rare disease lives in a familial, social and professional environment that has not prepared him or her, suddenly or after years of uncertainty, for such an experience. It may be temptng to take refuge in isolation. The patient's pathway is a real challenge and include the recognition to his/her 'difference' and the right to benefit from the expert medical and social care. Patients affected with hypophosphatasia, a very rare bone and dental disease, are not exceptions to the rule, despite the dynamic support of Hypophosphatasie Europe, the first patient association, created in 2004. In twelve years, the overall understanding of hypophosphatasia has dramatically improved, including through the discovery of novel therapies. Yet, diagnostic errance, transition between childhood and adulthood and management and care of affected adults remain unsolved issues.

Résumé

Aujourd'hui, l'opinion publique et les instances de l'État sont sensibilisées aux maladies rares notamment grâce à la mise en œuvre des Plans nationaux de maladies rares (PNMR I : 2005-2008 et PNMR II : 2011-2016), à l'existence des filières nationales de santé et au maillage actuel des centres de référence et de compétence. Si la prise en charge de ces maladies s'avère mieux structurée, encore faut-il que les diagnostics soient correctement faits. Il n'est en effet pas toujours simple pour les médecins d'identifier l'une de ces 7 000 maladies, même s'ils ont de plus en plus le réflexe de se poser la question : Et si c'était une maladie rare ? La personne atteinte d'une maladie rare vit dans un environnement familial, social, professionnel qui ne la prédispose pas, du jour au lendemain ou après des années d'errance, à vivre une telle expérience. Sous réserve qu'elle sorte de l'isolement dans lequel elle est parfois tentée de se réfugier, s'engage alors pour elle un vrai parcours du combattant pour être reconnue dans sa « différence » et correctement prise en charge médicalement et socialement. Les malades atteints d'hypophosphatasie (HPP – maladie osseuse et dentaire très rare) ne font pas exception à la règle, même si l'action déterminée d'Hypophosphatasie Europe, première association de patients créée en 2004, a changé la donne. En 12 ans, la connaissance globale de l'HPP a beaucoup évolué. Pourtant, certains aspects comme l'errance diagnostique, la transition entre enfants et adultes et le suivi médical des adultes restent encore problématiques.

***Corresponding author.**
e-mail: steve.ursprung@gmail.com (S. Ursprung)

1. Introduction

In the lottery of life, fortunes vary. We do not all enjoy the same privileges. This applies to one's place of birth, social environment, family and parents from whom one inherits, one's ability to learn, etc. This also apples to one's genetic capital, with the difference that due to heredity or random, there is nothing an individual can do to change his genetic grounds. The risk of being affected by a rare disease is high and everyone is potentially concerned. Thus, when parent or adults begin to think that "something is not right", and when caregivers are confronted with clinical signs that they are unable to label or identify, they should be able to ask themselves: could this be a rare disease?

2. HPP: one rare disease among many

A disease is termed rare when it affects less than one person in 2,000, i.e., for France, less than 30,000 persons (definition based on the prevalence defined by the European regulations on orphan drugs). Currently, over 7,000 rare diseases have been identified. Five new rare diseases are reported in the medical literature each month. About 80% of them have a genetic cause. HPP is a very rare bone and dental genetic disease for which the prevalence of the severe forms ranges from 1/100,000 to 1/300,000. In France, for all forms of the disease taken together, we estimate that 80 to 100 persons suffer from the disease. The disease is due to a deficiency in, or inactivity of, the enzyme alkaline phosphatase (ALP). Six clinical presentations of the disease, depending on age at symptom onset, are arbritrarily designed. The disease affects all ages, on all continents worldwide, and affects men and women equally.

3. In quest of a diagnosis: the need to know

When the patient (or his/her family) realize that something is wrong, he naturally contacts his general practitioner or pediatrician, and then the various specialists to whom he is referred. The patient undergoes numerous tests and examinations, which, in the case of HPP, may not be productive, if one is not aware of what needs to be looked for. Diagnostic errance begins and may last several years. HPP, is still a disease that may be overlooked or confused with other diseases (osteogenesis imperfecta), when not erroneously considered a psychosomatic disease. Undoubtedly, the patient prefers to know, because knowing is understanding that "it's not all in his head". Knowing allows the patient to identify the enemy to be fought. Hence the importance of giving a name to his symptoms. Daniel, who was diagnosed very late (although he could have been diagnosed in childhood given the clinical signs he presented) witnesses:

"I have always lived with the disease, without realizing it. I thought I was a fragile person who couldn't stand pain. [...] Is it normal to be in such pain? And then, suddenly, you are told that you have a rare disease which is enormously painful. [...] Yes, even though it happened late, being diagnosed was very important to me. It was a satisfaction to know that I did indeed have a disease." Confirming Daniel's diagnosis also enabled the disease to be diagnosed in his twin brother and older sister, who were also unaware (or in denial?) of the disease.

Of course, there are also those who suffer without trying to understand. There are those who want to know and there are those who, once they know, have great difficulty accepting their condition although they are the first to express the fact that they had an intuition that something was wrong. Thus, Murielle, alerted by the fact that her baby, aged one year, swallowed a milk tooth while feeding from a bottle, immediately began searching, until the day the diagnosis was announced. She says: "When the disease was announced, I experienced a lot of emotion, a lot of anxiety, but it was over quickly. My husband and I had really had our heads in the sand. [...] We were scared, and then our fear turned into denial. We completely refused to accept the diagnosis for several months. Finally, the diagnosis was confirmed after another alkaline phosphatase assay after 2 years of uncertainty. It felt like a cold shower at the time, but I was also very ambivalent: I was reassured. It's horrible not knowing what to fight against. [...] We were offered little psychological support at that time and it's very regrettable. I felt I had been abandoned to my own resources. My dentist told me that my daughter was the first little patient with the disease that he had seen. That clearly shows how difficult it is to be aware of rare diseases. Because of their very rareness, healthcare professional may not be aware of them."

4. After the diagnosis, the need to understand (or not)

Thus, after a period of doubt and uncertainty, of variable duration, HPP is diagnosed and the diagnosis shatters all the patient's preconceptions. All patients say that there is a "before diagnosis" and an "after diagnosis". Since the disease is genetic, the first step is to identify the source of transmission, usually in the parents. A veritable tsunami sweeps them into a world of guilt, shame, fear and even resentment. This may weaken couples (or make them stronger) as they are forced to abandon their image of an "ideal, healthy child".

Similarly, family histories, which were previously taboo, may resurface with serious consequences, as Isabelle explains: