INTRODUCTION

Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic condition in which there is an anomaly in the production of a monoclonal immunoglobulin (McIg), resulting in excess levels in blood or urine of abnormally high levels of an immunochemical type of Ig reflecting lymphoplasmacytic proliferation. Indeed, only production by strictly identical cells, monoclonal cells (1), can justify the presence of Ig with strictly identical properties. Detection of this McIg is most often achieved using protein electrophoresis, with a characteristic narrow band in the d-globulin zone (1). Protein electrophoresis makes it possible to identify McIg corresponding type of heavy (G, A, M, D, E) or light (k, l) chain and provides information about the magnitude of the monoclonal peak. The diagnosis of MGUS is made after documentation of a
peak of McIg by protein electrophoresis (< 30 g/L), in the absence of any clinical signs of malignant haemopathy, autoimmune disease or viral infection such as HIV or hepatitis C. In rare cases, an isolated monoclonal light chain can be detected, and, in the absence of renal failure, can be detected in the urine only (Bence-Jones protein). This warrants performing blood and urine immuno-electrophoresis, for the detection of an McIg (2).

Most MGUS are benign forms that require no treatment, but close monitoring is necessary due to the non-negligible risk of progression to overt malignant disease. Monoclonal gammopathy of undetermined significance can transition to multiple myeloma (3, 4), which is a malignant haemopathy characterized by clonal impairment and excessive production of medullary plasmocytes, which are responsible for production of McIg. The predictive factors of progression to malignant disease remain poorly documented, and are most often associated with deregulation of the medullary microenvironment function, responsible for efficacious haematopoiesis and homeostatic balance in the bone tissue. For this reason, MGUS can be considered as a pre-cancerous state. The magnitude of the McIg peak at the time of diagnosis, and the Ig isotype are predictors of progression to malignant disease.

Clinical and biological context

Epidemiology

Monoclonal gammopathy of undetermined significance is an asymptomatic condition in which there is abnormal production of an McIg, with resulting excess levels found in the blood and/or urine. This deregulation of the globulinaemia represents a pathological situation in which there is overproduction of McIg by malignant plasma cells. The diagnosis of MGUS is based on demonstration of a peak of McIg on protein electrophoresis in the absence of any clinical signs of lymphoid haematological neoplastic disorders (1). The magnitude of the monoclonal peak at the time of the diagnosis, and the isotype are predictive factors of transition to malignant disease. The majority of MGUS are benign forms that require no treatment. However, regular monitoring is required for all MGUS (5).

Monoclonal gammopathy of undetermined significance primarily affects elderly subjects, and prevalence increases with age [1–2% among subjects aged 50 to 60 years, ~ 5% of patients aged 60 to 75 years, and 10% of subjects over 80 years of age] (6). Seventy per cent of McIg are IgG (d heavy chains), 15% are IgA (a heavy chains), and 15% are IgM (m heavy chains); biclonal gammopathies are exceptional. The light chain type is k in 60% of subjects, and l in 40%. As for multiple myeloma, MGUS is twice as frequent in subjects of African American or mixed race origin. Prevalence is higher in men than in women. The risk of progression of MGUS to multiple myeloma is approximately 1% per year. The epidemiology of McIg in haematological hospital wards is over-represented since malignant pathologies are frequently observed in this context. Monoclonal gammopathy of undetermined significance can also develop into other lymphoproliferative disorders such as lymphoma (2).

This disease is all the more serious in patients with early onset, or with late diagnosis (elderly patients). A minimum of biological examinations is necessary in asymptomatic patients to rule out a latent myeloma (5). Clinical history taking should look for bone pain or recurrent infection. Once the diagnosis of MGUS is confirmed, the patient should be informed about the need for a clinical plus biological check-up twice a year, in view of the risk of transition to malignant disease. Rare occurrences of very rapid development to malignancy call for re-evaluation in case of the sudden appearance of clinical symptoms. The role of obesity should also be considered as a potential risk factor associated with the development of MGUS.

Aetiologic context

The presence of McIg reflects proliferation of clonal plasma cells. Although this monoclonal status may correspond to malignant cell proliferation [multiple myeloma, Waldenstrom macroglobulinaemia, chronic lymphoid leukaemia, non-Hodgkin’s lymphoma, myelodysplastic syndrome] (7), it is frequent that extensive investigations fail to find any sign of these diseases. However, long-term monitoring of the so-called benign gammopathy brought to light a risk of transition to malignant disease of approximately 1% per year. This led to the introduction of the term MGUS, in order to take into consideration the potential risk of deterioration, however small that risk may be (2).

The occurrence of MGUS could be linked to several factors such as environmental factors, viral factors, pathophysiological predisposition, genetic or epigenetic predispositions.

Environmental factors: Exposure to chemicals, particularly pesticides, could contribute to the transition from MGUS to malignant disease (8, 9), especially in elderly patients who have been chronically exposed to such risk factors throughout their lives. Pesticides remain a major public health challenge as they could be related to the occurrence of epigenetic deregulation, and secondarily, to the occurrence of certain types of cancer. According to the regional federation for defence against harmful organisms, potentially toxic chemical agents include molecules used in banana plantations that have been recently been banned, weedkillers (Karmex®, Ouragan®, R-Bix®), fungicides (Baycor®), nematicides and insecticides (Rugby 10G+®), weedkillers used in sugar plantations, also recently banned, Calliherbe®, Dico Pur CL®, Karmex®, Novflex®, Flo80®, Velpar S®, Asulox®, Weedone®. In a French West Indies Caribbean area, such as Martinique, the ten most widely sold active substances were weedkillers (glyphosate, glufosinate ammonium, asulame, 2, 4-d, s-metolachlore, diquat), nematicides (oxamyl, fosthiazate) and fungicides
In view of the genetic specificities of the Caribbean populations, the insular and environmental context, it will be interesting to determine by a cross-sectional aetiological study, the incidence and prevalence of MGUS in one country in the Caribbean, since no such study has been performed to date. The medium-term objective is to determine the biological parameters that can determine which patients will remain asymptomatic and which will go on to develop malignant disease.

The study of MGUS in the French West Indies area for the first time, according to the French West Indies cancers registries, will be a real new challenge and motivated by the need to understand the development of the precancerous state, and it should be based on diagnosis, epidemiological data, aetiological factors, and clinical follow-up.

The expected findings and their potential repercussions would have major public health interest, and should form the basis for the first time in the Caribbean, a wider prognostic study to determine risk factors for MGUS that are associated with a pre-malignant disease state, in order to support the hypothesis of a possible geographic distribution of these blood disorders linked to environmental exposure to pesticides.

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