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# IgA Multiple Myeloma, Revealed by Isolated Nephrotic Syndrome in a 36 Years Old Patient

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**Abstract**

Multiple Myeloma (MM) or Kahler's disease is a malignant plasmocytic infiltration of the bone marrow; these plasma cells secrete a complete or not immunoglobulin (Ig) and various cytokines. The average age of onset is beyond 65 years old, very rare before 40, and never concerns the child. In general, bones lesions frequently dominate the clinical picture, and it's rarely revealed by other signs. Some studies have examined the impact of age on the different aspects of MM, and the prognostic factors according to age groups. This case is about a 36-year-old man diagnosed with an IgA multiple myeloma, revealed by isolated nephrotic syndrome due to primary renal amyloidosis, without any other clinical or biological sign. We present through this particular observation, the clinical aspect, the radiological and biological characteristics as well as the evolution of this pathology in the young subject, compared to older patients.

**Keywords**: Myeloma; Young subject; IgA; Nephrotic syndrome.

## Introduction:

MM is characterized by a monoclonal proliferation of plasma cells that invade the bone marrow and secrete a monoclonal immunoglobulin [1]. It is a rare disease that accounts for about 80% of malignant monoclonal gammopathies and 15% of malignant hemopathies. This affection preferentially affects subjects over 65 years of age with a frequency peak between 67 and 70 years [2]. Bone manifestations dominate the clinical picture. The singularity of this observation involves several aspects: the very young age of the patient, the revelation by isolated nephrotic syndrome announcing a primitive kidney amyloidosis, and the absence of any other clinical or biological sign, including bone lesions.

## Observation:

S.D, age 36 years old, followed for relapse of pulmonary tuberculosis initially treated in 1992, admitted in nephrology department of the Mohamed VI University Hospital for the diagnostic and therapeutic management of edematous syndrome that appeared 10 days before.

On clinical examination, the patient was conscious, in good general condition, presenting as only symptom a generalized edema. The rest of the examination was normal. An initial biological

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assessment was requested, hemogram and assay of urea, creatinine, albumin and 24H proteinuria were performed, showing the following results: hemoglobin at 13.6g/dl (N=13-18 g/dl), leukocytes at 4510/mm3 (N=4000-10000/$mm^3$), platelets at 266000/IU (N=150 000-450 000 /$mm^3$); urea at 0.18 g/l (N=0,15-0,45 g/l) and creatinine at 5.77 mg/l (N=7-13 mg/l); however proteinuria was at 5,89 g/24h (N<0,5 g/24h) and albumin at 20,1g/L (N=40-50 g/l). A renal biopsy puncture was therefore indicated and revealed primary renal amyloidosis. Serum protein electrophoresis revealed hypoalbuminemia, hyper alpha2 globulinemia, hyper beta2 globulinemia, with a non-homogeneous zone of gamma globulins *(Figure 1)*. The immune-electrophoresis of serum proteins showed a monoclonal band of IgA Kappa type (*Figure 2*), and the urinary proteins immunofixation showed traces of albumin, a huge Ig monoclonal peak and a lack of light chains (*Figure 3*). An additional assessment was carried out: the standard radiographs of the hole body skeleton were all normal, the myelogram study revealed a 25% plasmocytosis with signs of dystrophy (*Figure 4*), the serum calcium was normal at 86.42 mg / L (N=86-104 g/dl), so was the LDH at 342 UI/l (N=190-400 UI/l), and the Beta 2 microglobulins; viral serologies were also negative. Unfortunately, the immunophenotyping could not be performed in our context. At the end of this assessment, the diagnosis of IgA multiple myeloma associated to primary renal amyloidosis (AL) was confirmed. The patient was transferred to the clinical hematology department for therapeutic care.

**Discussion:**

Multiple myeloma (MM) is a malignant hemopathy characterized by clonal proliferation of plasma cells invading the hematopoietic bone marrow [1]. It accounts for about 15% of hematologic cancers, which ranks second in order of frequency after lymphoma. In France, the annual incidence is 5 to 6 / 100,000 inhabitants, or approximately 3,000 new cases diagnosed each year [1]. In general, the incidence increases rapidly with age, and men are more often affected than women [1,2]. In highly medicalized countries, there is no recent increase in incidence, but the impact of MM in terms of public health will increase in the years to come, due to the aging of the population. The median age is 72, but is reduced to 65 in the hospital series [1]. The occurrence in adolescents and young adults remains exceptional [1,2]. Our patient was 36, a very young age for multiple myeloma.

The etiology of multiple myeloma is still unknown, environmental factors such as exposure to toxins (pesticides, herbicides, fertilizers, dyes, petroleum and petroleum products) and especially ionizing radiation are risk factors. A link with the HHV-8 herpes virus is possible. Also, there are rare family and conjugal cases, arguing for the importance of environmental and genetic factors, and a higher frequency among Afro-americans [1,2]. Our patient here was a farmer by profession, and worked with his father since his childhood, which argues for early and prolonged exposure to pesticides, herbicides and fertilizers.

Before the onset of MM, there may be a precancerous clinical condition called monoclonal gammapathy of undetermined significance (monoclonal gammapathy of undetermined significance or MGUS). These benign mono-clonal gammopathies are much more common than

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myeloma cases since 1% of the population over 50 is concerned [2]. They are characterized by: the presence of a mono immunoglobulin serum clone; a lower level of plasma cells in the bone marrow compared to MM; and absence of bone lesions. The urinary proteins of Bence Jones, which are often found in the case of a MM, are absent in this situation [2]. The precise mechanism of transformation from benign monoclonal gammopathy to MM is not clearly identified. Secondary genetic modifications (RAS / p53 mutations, secondary translocations ...), changes in the microenvironment of the bone marrow (angiogenesis process), or the role of cytokines are often evoked [2]. Patients with monoclonal gammopathy of undetermined significance have an annual risk of progression to myeloma or other malignancies of 1%, with progression lasting several decades [2]. Our patient may have had an MGUS before his MM, given the absence of bone involvement at the time of diagnostic as well as the absence of Bence Jones proteinuria, but this cannot be proven.

Studies have shown that the initial clinical manifestations of MM do not differ between young and old [3]. In contrast, some studies have found a slightly higher incidence of bone pain and lacunary osteolytic lesions at the beginning of MM in the elderly. In fact, the frequency of vertebral and nonvertebral fractures and abnormalities associating osteolytic lesions and diffuse bone hypertransparency was greater in the elderly [4]. This is explained by the weakness of the bone structure in the elderly, due to, among other things, senile osteoporosis to different degrees. For example, Umeda et al. found significant difference in the elderly on the association of lytic lesions and osteoporosis (63.5% vs. 28.3%) ($p < 0.001$) [4]. Althought, some different series of literature did not reveal any significant difference between the young and the elderly subjects concerning the frequency and localization of osteolytic lesions during MM [4].

Ben Ghorbel and al. showed that kidney failure was more common in young people [5]. Primary renal amyloidosis is associated with MM in 10 to 15% of cases [1, 5], but the percentage of its association with MM according to age, or at the time of diagnosis, or as a way of revealing the disease was not revealed in the literature, and will therefore require more research, at least statistical. Ben Ghorbel and al. also showed that the IgA isotype was more frequent in the elderly (39.3%), and the light chains were more frequent in the young subjects [5]. A recent tunisian study did not reveal any difference in the nature of the monoclonal component. This result has been confirmed in most studies [4, 6], as in the San Miguel and al. and Snozek and al. studies, where IgG was the most common immunoglobulin in both age groups (62%), followed by IgA (26%) and light chains (8%) [5, 7, 8]. The tunisian study also noted a higher proportion of MM with urinary light chains in young people, which is consistent with previous literature data [5, 8].

Other studies revealed that biological parameters in terms of means or percentages do not differ between young and elderly patients [4]. But the difference was the prognostic value of each bioassay [4, 5, 8]. A small percentage of young patients experienced hypoalbuminemia, elevated LDH and sedimentation rate. Older patients, on the other hand, have a higher percentage of poor prognostic factors [4]. According to the tunisian study, the biological data can be divided into three categories. In the first category, albumin and serum calcium have a more pronounced prognostic role in the elderly, whereas serum creatinine and platelet levels have a greater

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prognostic role in patients under 65, thus defining the second category [4]. The third category, which successively groups hemoglobin levels, LDH levels, CRP and quantitative and qualitative data for the myelogram, does not differ from the prognostic point of view between the two age categories [4]. Our patient did not show any bone pain and his x-rays showed no image of osteolysis, his renal function was normal, and presented a monoclonal peak of IgA immunoglobulin, without detection of light chains, and no biological bad pronostic risk factors, witch makes it a very singular case.

H.Sahli and al. showed a higher proportion of younger patients in stage III of Durie and Salmon classification, reflecting a higher tumor burden in patients under 65 years of age. These results are similar to those of Ben Ghorbel et al. and Bouatay et al. [4, 5, 6]. The high proportion of stage patients is not correlated with survival in both age groups. Indeed, in several studies using age as a single survival variable, young subjects had prolonged survival compared to older patients [4, 8]. This can be explained by at least two factors. The first factor is therapeutic: intensive treatment is possible with a higher frequency of complete remission in young patients. The second factor is the frequency of co morbidities in the elderly. The teams of Corso et al. and Riccardi et al. studied the influence of age and clinical stage of MM and noted better survival in young and early-stage patients [4]. It thus appears that age is the most important prognostic factor between the MM of the young subject and that of the elderly subject, despite a greater tumor mass in young patients [4].

## Conclusion

MM is a hematological malignancy that its incidence increases with age. The importance of bone syndrome in the literature may be due to rheumatological recruitment bias, since patients are most often elderly and consult first in rheumatology for bone pain. In general, patients aged less than 65 years had a large tumor mass but more favorable prognostic factors. It appears that age is the most important prognostic factor. Cytogenetic studies are needed to draw more relevant conclusions [9, 10].

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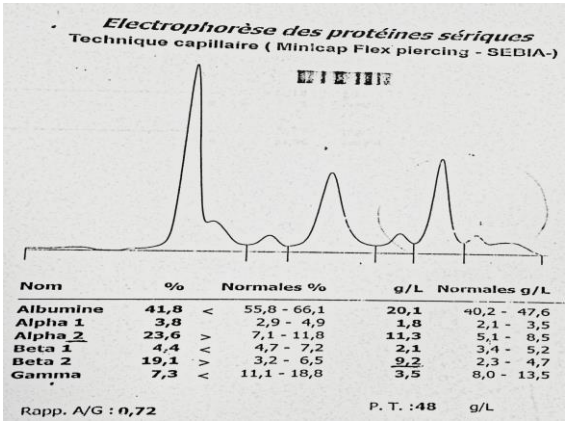


Figure 1: Serum proteins electrophoresis revealing hypoalbuminemia, hyper alpha2 globulinemia, hyper beta2 globulinemia, with a non-homogeneous zone of gamma globulins.

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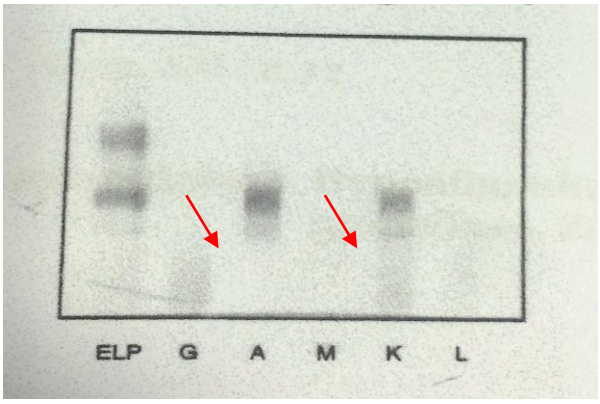


Figure 2: Serum proteins immuno-electrophoresis showing a monoclonal band of IgA Kappa type.

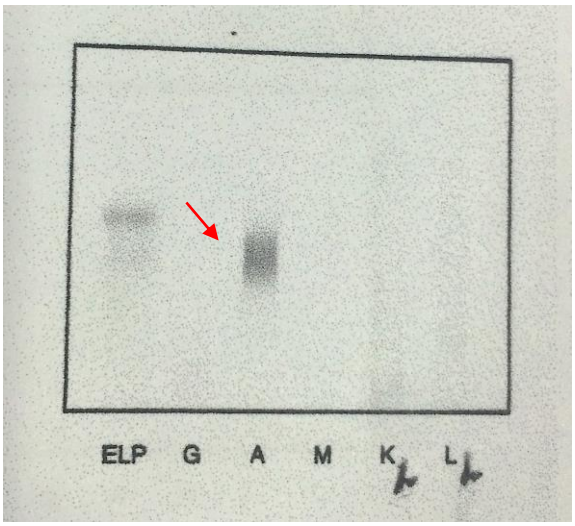


Figure 3: Urinary proteins immunofixation showing a huge Ig monoclonal peak and a lack of light chains

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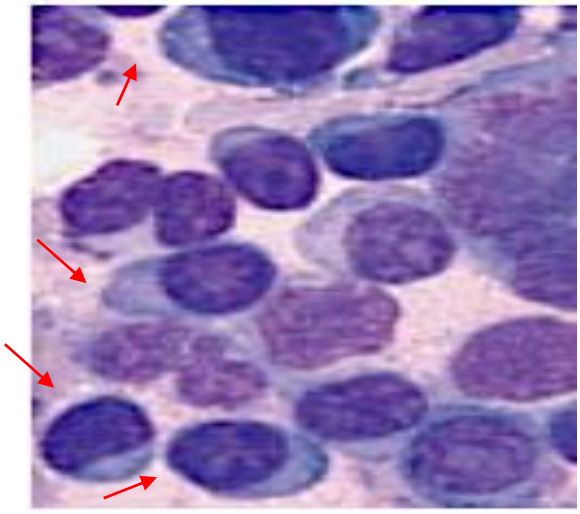

Figure 4: Photograph of the patient's medullary smear (G x 500) showing infiltration by dystrophic plasma cells.