



## Hormones and Signaling

Elixir Hor. & Sig. 109 (2017) 48008-48010

Elixir  
ISSN: 2229-712X

### Macroamylasemia on multiple myeloma: A case report

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#### ARTICLE INFO

##### Article history:

Received: 13 June 2017;

Received in revised form:

4 August 2017;

Accepted: 17 August 2017;

##### Keywords

Macroamylasemia,  
Hyperamylaseemia,  
Multiple myeloma.

#### ABSTRACT

Hyperamylasemia caused by the ectopic production of amylase in multiple myeloma (MM) is rarely described in the literature. It may also correspond to a macroamylase, a complex immunoglobulin amylase. We report the rare case of a 61 years old patient with MM with Kappa light chains, who developed an accidental discovery hyperamylaseemia without symptoms of pancreatic or salivary disease. The patient developed an advanced acute kidney injury, with hypercalcemia, normochromic anemia, associated with diffuse bone pain and accidental discovery of an important hyperamylaseemia without symptoms of pancreatic or salivary disease. Electrophoresis and immunofixation of serum proteins demonstrate a Kappa light chain monoclonal peak. The sternal puncture reveals the presence of dysmorphic plasma cells estimated at 48%. Radiography of the skeleton shows skull geodes at the skull and diffuse demineralization. Abdominal CT does not show signs of pancreatic involvement. The diagnosis is a Kappa light chain MM associated with macroamylase. The patient is treated with the Cyclophosphamide-Dexamethasone-Thalidomide protocol and died of his disease after two months. The interest of this observation is to emphasize this benign biochemical anomaly in order to avoid complementary and / or therapeutic invasive investigations.

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#### I Introduction

The macroenzymes are responsible for apparent increases in serum activity of the corresponding enzyme. The practice of unnecessary and sometimes dangerous tests may result from their ignorance. Hyperamylasemia caused by ectopic amylase production in multiple myeloma (MM) is rarely described in the literature. This is most often a hyperamylasemia on amylase-secreting myeloma, in which case the level of amylase shows a reliable index of disease activity in patients with this type of myeloma [1]. It may also correspond to a macroamylase, a complex immunoglobulin amylase. We report the rare case of a patient with MM with Kappa light chains, in which accidentally discovered hyperamylasemia without symptoms of pancreatic or salivary disease.

#### II Observation

Mr LL, 61 years old, without any special medical history, is admitted to our department in October 2013 for an altered general condition since 1 month, a diffuse bone pain associated with anorexia and vomiting for 5 days without other transit disorders, evolving in a context of apyrexia and slimming. The clinical examination found a conscious patient, in fairly good general condition, dehydrated with blood pressure at 100 / 56mmHg and tachycardia at 95bpm; the palpation of the tibial and sternal bone crests was painful. The abdominal examination revealed a slight defenseless epigastric sensibility, the rest of the clinical examination is normal. The biological balance shows an advanced renal insufficiency (creatininemia = 1460  $\mu\text{mol} / \text{l}$ ), hypercalcemia at 143mg / l, normal normochromic anemia (hemoglobin = 7.8g / dl), hyperprotidemia at 82g / l with normal lipasemia and

hyperamylasemia at 3085 IU / l ((24-fold normal). On the urinary level, there is a decrease in urinary amylase at 6 IU / l (normal value ranges from 51 to 964 IU / l), a proteinuria at 3.2 g / 24h and an inactive urinary sediment.



Figure 1. Pepper pot skull.

Electrophoresis and immunofixation of serum and urinary proteins demonstrated a monoclonal IgA Kappa ( $\kappa$ ) peak. At the sternal puncture, the presence of dysmorphic plasma cells is estimated at 48%. Radiography of the skeleton shows 'punched out' lytic lesions. The diagnosis is a MM IgA- $\kappa$  chains.

The abdominal CT scan shows no signs of pancreatic involvement, there is no evidence of salivary or pancreatic involvement. Amylase urinary excretion is low (6 U / l / 24h) and the amylase / creatinine clearance ratio is 0.75 (normal value ranges from 1 to 3%). Thus, it was considered that the diagnosis of macroamylase was most likely.

The patient received rehydration and alkalization initially parenterally and then orally, he also received proton pump inhibitors and CDT protocol (Cyclophosphamide-Dexamethasone -Thalidomide) according to the following scheme.

Oral Cyclophosphamide: 500mg once per week for 6 weeks.

Oral Dexamethasone 40mg: 1tab /, four days / week for 4 weeks then once a week.

Thalidomide 100mg /day.

The evolution was marked by a short-term clinical and biological improvement (J5) with a serum creatinine at 664  $\mu\text{mol} / \text{l}$ , serum calcium at 96mg / l and total proteins at 72g / l. Two months later, the patient dies at home from his disease as part of a progressive alteration of the general state and acute dyspnea.

### III Discussion

Hyperamylasemia is a condition of elevated serum amylase activity, constantly accompanied by hyperamylasuria, and is mostly found in pancreatic (acute or chronic pancreatitis and cancer) and salivary glands diseases. However, other pathologies are often associated with hyperamylasemia, such as acidosis [2], alcoholism [3], dyslipidemia [4], acute or chronic hepatitis and cirrhosis [5].

In medical literature, many conditions of benign hyperamylasemia are also described, as familial hyperamylasemia [6], and macroamylasemia [7, 8], it corresponds to amylase polymers or macromolecules bound to immunoglobulins that were not filtered by the glomerulus due to their high molecular weight. The amylase - molecular weight of 55 000 daltons- is filtered and excreted by the kidney, which is not the case of the macroamylase whose molecular weight is approximately 210000 daltons [9,10].

Macroamylasemia has been described in patients with MM in 1881 [11]. It is characterized, unlike the other situations, by hyperamylasemia with weak or normal amylasuria; In this case the amylase ratio / creatinine clearance is useful because urinary excretion of amylase is also influenced by glomerular filtration rate (GFR).

Macroamylase is not a pathological entity, as no clinical symptoms are described [12]. It is found in approximately 0.4% of the general population [8,15] and, although it may occur in apparently individuals [8,10], a variety of pathological condition, such as malabsorption, cancer, liver disease and diabetes have been reported to be associated with macroamylasemia [7–9]. So, any patient with hyperamylasemia with low amylase/creatinine clearance ratio and normal GFR should be considered for the possibility of having macroamylasemia.

Sagrastani and al [16] reported a rare case of IgA- $\kappa$  multiple myeloma and macroamylasemia. In their case, hyperamylasemia was not present at the diagnosis of myeloma but appeared at the relapse of the disease, with an additional  $\gamma$ -chain oligoclonal component, suggesting a possible role of these chains in producing macroamylasemia. However, direct evidence for the binding of monoclonal immunoglobulins to amylase has not been available.

Therefore, macroamylasemia is regarded as another cause of hyperamylasemia associated with multiple myeloma.

In the second case, described by Machida and al [17], hyperamylasemia appeared to be caused by macroamylasemia resulting from a complex of amylase and monoclonal IgA- $\lambda$  produced by myeloma cells, which was identified by immunofixation analysis. This appears to be the first

demonstration of the amylase-binding activity of monoclonal immunoglobulins produced by myeloma cells.

In our case, the normal serum lipase and the absence of abdominal symptoms and pathological sonographic findings leads us to exclude pancreatic damage. Levy.P suggests the possibility of an elevation of pancreatic enzymes not exceeding 3-fold in the case of advanced RA [18]. In our patient, the massive elevation of amylase (24-fold normal) associated with low amylasuria (6 U/ l/24h) and decreased amylase/creatinine clearance ratio (0.75) allowed us to retain the diagnosis of macroamylase associated with IgA- $\kappa$  MM.

The coexistence of macroamylasemia with the oligoclonal component suggested that these chains, from their immunochemical features, may have bound amylase molecules, producing large-sized complexes not filtered by the glomeruli and thereby increasing amylase activity in serum.

The death of the patient did not allow us to follow the evolution of amylasemia after a possible modification of the oligoclonal component.

### IV Conclusion

To the best of our knowledge, this is the third described case of macroamylasemia associated with multiple myeloma. In our opinion, this case is interesting given the problem of differential diagnosis with hyperamylasemia due to other disorders and the interest of awareness of this association in order to avoid a variety of unnecessary diagnosis investigations and / or invasive therapeutics.

### V Conflicts of interest

The authors declare that they have no conflicts of interest in relation to this article.

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