

# Amyloidosis with Multiple Myeloma Presenting with Acromegalic Features

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## ABSTRACT

Amyloidosis and multiple myeloma are included in the same spectrum of clonal plasma cell disorders. Amyloidosis can present with localized deposits or manifest as systemic disease involving multiple organs. Here we are reporting a case of an elderly female, having amyloidosis leading to facial disfigurement and neuropathy for many years and then presenting with concomitant multiple myeloma as an incidental diagnosis with no typical symptoms related to it at all.

**Key Words:** *Amyloidosis. Multiple myeloma. Monoclonal gammopathy of undetermined significance (MGUS). Smoldering multiple myeloma.*

## INTRODUCTION

Primary amyloidosis and multiple myeloma both involve clonal plasma cell proliferation.<sup>1</sup> In most cases with a monoclonal plasma cell disorder, whether multiple myeloma or Monoclonal Gammopathy of Undetermined Significance (MGUS), the monoclonal L chain secreted by the clone remains soluble in the bloodstream. However, in some patients, the immunoglobulin L chain or L-chain fragment lead to its deposition as amyloid because of its physicochemical characteristics. Thus, some patients with light chain-type amyloidosis meet the diagnostic criteria of multiple myeloma, whereas other patients can be considered as having MGUS in which the clonal immunoglobulin product is amyloidogenic.<sup>2</sup>

L chain - type amyloid deposits can involve any organ system. The most common organs involved are the kidneys, the heart, the gastrointestinal tract, the peripheral nerves, and the liver. In most cases, the deposits affect multiple organ systems. In a minority of cases, localized amyloid deposits, including amyloid masses (amyloidomas), may be found at various sites, even in the absence of systemic disease. Factors leading to the specific pattern of organ involvement in a particular patient are not clear.

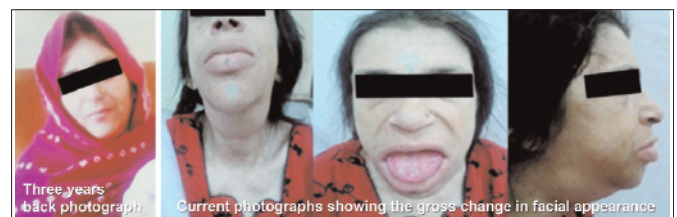
Here we report an elderly female presenting with acromegalic features who turned out to be a case of AL amyloidosis with multiple myeloma. There was an unusual presentation of 12 years history of AL amyloidosis limited to soft tissue giving an acromegaly-like appearance and presenting as asymptomatic

multiple myeloma. This has not yet been reported in literature.

## CASE REPORT

A 60 years female with no known co-morbidities, presented with 12 years history of pain and numbness in both hands gradually leading to hand deformities. For the last 3 years, she had noticed unusual enlargement of lower lip and tongue along with a painless swelling in the submandibular region. These disfigurements were not associated with headache or visual disturbances.

On examination, she was vitally stable, having an enlarged lower lip with prognathism, grossly enlarged tongue with teeth indentations on it and a large soft tissue swelling in the submandibular region (Figure 1). Both hands had fixed flexion deformities of proximal and distal interphalangeal joints and flattening of thenar and hypothenar eminences (Figure 2), with soft tissue



**Figure 1:** Current photographs showing the gross change in facial appearance.



**Figure 2:** Photographs showing flexion deformities along with wasting of small muscles of hands.

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*Received: December 13, 2013; Accepted: May 04, 2015.*



**Figure 3:** Photographs showing soft tissue swelling at the wrist joint.

swellings at both wrists (Figure 3). Fine-touch sensations were reduced on palms of both hands along with diminished reflexes in upper limbs. Rest of the systemic examination was normal. On the basis of these examination findings a provisional diagnosis of acromegaly with carpal tunnel syndrome was made and investigations were sent.

Her routine investigations were normal. Ultrasound of neck showed enlarged sub-mandibular glands. Skeletal X-rays of skull, hands and feet were done which did not show any feature related to acromegaly. MRI brain with pituitary cuts was normal. Serum TSH, growth hormone and IGF-1 were normal. Nerve conduction studies showed severe axonal type involvement of both median nerves, moderate involvement of both ulnar nerves and partial involvement of both radial nerves.

Keeping in view the soft tissue swelling, carpal tunnel syndrome, neuropathy and macroglossia, an alternate diagnosis of amyloidosis was made and rectal biopsy was done which showed apple green birefringence on polarization microscopy after Congo red staining confirming the diagnosis of amyloidosis. Further serum immunofixation showed IgG Kappa monoclonal gammopathy. Kappa light chain serum level was 14.10 gm / L (normal = 5.74 - 12.76) and serum IgG was 14.45 gm/L (normal = 6 - 15.6). Because of monoclonal gammopathy, bone marrow biopsy was done which showed 30% marrow infiltration with plasma cells suggesting multiple myeloma. Two tests, immunofixation and bone marrow plasmacytosis confirmed the diagnosis of multiple myeloma with no lytic lesions on skeletal survey and normal renal function tests.

Patient was then referred and enrolled with the oncology department for chemotherapy.

## DISCUSSION

Systemic amyloidosis are a group of complex diseases caused by tissue deposition of misfolded proteins that

result in progressive organ damage.<sup>3</sup> Light chain AL amyloidosis is the most common form of systemic amyloidosis. The amyloidogenic protein in AL amyloidosis is an IgG light chain or a fragment of a light chain that is produced by a clonal population of plasma cells in the bone marrow. The plasma cell burden in this disorder is low, typically 5 - 10%,<sup>4</sup> although in approximately 10 - 15% of patients, AL amyloidosis occurs in association with multiple myeloma.<sup>5</sup> When associated with multiple myeloma, it is accompanied with signs and symptoms of hypercalcemia, anemia, lytic lesions of bones and renal insufficiency. It has been reported that approximately 10% of patients with AL amyloidosis may have MM at the time of diagnosis.<sup>5</sup> It has also been reported that upto 30% of MM patients may have subclinical amyloid deposits in subcutaneous fat aspirate, bone marrow biopsy, or biopsies of other vital organs like heart, liver and kidneys.<sup>6</sup>

A concurrent diagnosis of AL amyloidosis requires fulfilling diagnostic criteria for both conditions. Presence of amyloidosis in multiple myeloma patients is usually associated with poor survival. The median survival time in these patients is assumed to be about 4 months and death usually occurs as a complication of amyloidosis effecting major organ systems.<sup>7</sup>

The unusual feature in this case is the long history of features of carpal tunnel compression along with soft tissue deposits in submandibular gland and tongue for about 8 years, though in literature a very aggressive disease with high mortality has been reported with co-existing myeloma and amyloidosis. Whether this patient had smoldering myeloma or MGUS to start with, can not be assumed. Smoldering multiple myeloma, which accounts for about 8% of the malignancy, resembles Monoclonal Gammopathy of Undetermined Significance (MGUS), but MGUS is far less likely to progress to active disease or amyloidosis at 20 years. Smoldering multiple myeloma has a 78% probability of progression, versus 21% for MGUS progressing to myeloma.<sup>8</sup> Chotzen discussed a case of limited amyloidosis to the skin which after 20 years progressed to systemic disease.<sup>9</sup> However, the patient's bone marrow examination did not reveal multiple myeloma. Wallis and Stough also reported a single case of systemic amyloidosis having 18 years survival.<sup>10</sup>

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