Case Report

Stabilisation of Laryngeal AL Amyloidosis with Long Term Curcumin Therapy

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1. Introduction

Immunoglobulin light chain amyloidosis (AL) along with multiple myeloma (MM), smoldering myeloma (SMM), and monoclonal gammopathy of undetermined significance (MGUS) represent a spectrum of plasma cell dyscrasias (PCDs) [1]. AL is a rare and serious disorder characterized by the deposition of amyloid fibrils in different tissues with a mortality rate of more than 80% within 2 years of diagnosis, particularly if associated with renal or cardiac involvement [2, 3]. AL may coexist with any of the PCDs. It has been reported that up to 30% of MM patients may have subclinical amyloid deposits. In the case of SMM, no treatment will be directed against the plasma cell clone, potentially allowing for unbridled progression of the AL. The subtype of amyloidosis called AL is the most heterogeneous form of the disease, consistent with the fibril protein being unique in each patient. Virtually any organ system excluding the brain can be affected and in almost any combination.

Curcuma longa or turmeric is a tropical plant native to southern and southeastern tropical Asia. It is a perennial herb belonging to the ginger family. The most active component in turmeric is curcumin [4]. Numerous reports suggest that curcumin has chemopreventive and chemotherapeutic effects. Curcumin has been shown to inhibit the proliferation of a wide variety of tumor cells, including multiple myeloma cells through the downregulation of IL-6 and NF-κB [5]. Studies by Golombick et al. [6–9] have found that curcumin decreases paraprotein load, bone turnover, free light chains, and % plasma cells in the bone marrow of some MGUS and smoldering myeloma patients. In addition to the beneficial effects noted above, it has been suggested that curcumin may have beneficial effects on diseases characterized by the formation of aggregated fibrillar protein deposits [10]. Curcumin has strong affinity for fibrillar amyloid proteins and is already used to stain in vitro tissue sections from individuals affected with neurodegenerative disease such as Alzheimer’s and Parkinson’s disease [11].

Based on the demonstrable effects of curcumin in MGUS and SMM, we administered curcumin to a patient with IgG lambda smoldering myeloma with supraglottic AL amyloidosis. In this case report we demonstrate the beneficial
effects of curcumin on the size of his laryngeal amyloid deposit after five years of therapy.

2. Case Presentation

A 72-year-old male patient presented to the Haematology Clinic in 2006 for evaluation of laryngeal amyloidosis, secondary to smoldering myeloma. This was incidentally discovered by Doppler studies after being investigated for a cerebrovascular event. He denied symptoms of dysphagia or dysphonia. His comorbidities included spinal canal stenosis due to osteoarthritis, diet controlled diabetes, and hypertension. He had no history of fever, weight loss, recurrent infections, or skeletal events. Direct laryngoscopy confirmed an expansion of the supraglottis without evidence of soft tissue invasion or fixation to the prevertebral tissue. This involved mostly the region of the aryepiglottic fold and extended down to the false vocal fold on the right side causing effacement of the right pyriform fossa (Figure 1). It was submucosal without ulceration. Vocal cord mobility was normal and there was no evidence of lymphadenopathy. Biopsies confirmed the diagnosis of amyloidosis, as an AL type (Figure 2). A diagnosis of SMM was established by bone marrow dyscrasia (18% plasma cell infiltration, IgG lambda) and an elevated plasma paraprotein (14 g/L) but a negative 24-hour urine Bence Jones protein. The B2 microglobulin (2.2 mg/L), EUC, and calcium levels were normal. A skeletal survey, and chest, abdomen, and pelvic CT scan excluded lytic and soft tissue lesions. Antimyeloma therapy was not initiated as he was otherwise asymptomatic.

In 2008, repeat laryngoscopy demonstrated progressive disease. There was a significant increase in the prominence of the right thyroid cartilage and supraglottic swelling. The plasma paraproteinemia (14 g/L) and free light chain ratio remained stable and the 24-hour urine Bence Jones Protein remained negative. A repeat bone marrow biopsy revealed persistent plasmacytosis (18%) and negative Congo red stains for amyloidosis. In June 2008 the patient had three courses of melphalan (8 mg daily for 4 days) and dexamethasone (12 mg daily for 4 days) chemotherapy which resulted in an improvement in his paraproteinemia (6 g/L). He declined further chemotherapy due to dexamethasone-related weight gain and secondary diabetes and melphalan-related gastrointestinal side effects and cytopenias. In 2009, he developed worsening in back pain and was found to have CT evidence of a sacral lytic lesion. He was treated with localised external beam radiation therapy for pain control but with no systemic therapy.

In 2009, the patient commenced curcumin therapy at a dose of 1500 mg per day, gradually increasing to 3600 mg per day. By October 2010, the supraglottic swelling had decreased in size. In March and October 2011, the patient underwent video assessment of the larynx and no progressive disease was evident. The patient has remained extremely well apart from chronic arthritic pain. MRI scans excluded new or progressive skeletal disease, particularly his sacrum. Serial haematological and otolaryngeal investigation, performed annually from 2010 to 2014, has demonstrated stable disease. The biomarkers performed over a 5-year period on curcumin therapy are outlined in Table 1.

3. Discussion

The amyloidoses are a group of diseases that have in common the extracellular deposition of pathologic, insoluble fibrils in various tissues and organs. The fibrils have a characteristic \( \beta \)-pleated sheet configuration. Many different proteins can form amyloid fibrils, and the types of amyloidosis are classified on the basis of the amyloidogenic protein as well as by the distribution of amyloid deposits being either systemic or localized [12]. In the systemic form, the amyloidogenic protein is produced at a site that is distant from the site of deposition. In contrast, in localized disease, the amyloidogenic protein is produced at the site of deposition.

Light chain (AL) amyloidosis is the most common type of systemic amyloidosis and appears to be more common than previously thought [2, 13]. The amyloidogenic protein in AL amyloidosis is an Ig light chain or a fragment of a light chain that is produced by a clonal population of plasma cells in the bone marrow. Plasma cell burden in this disorder varies and is typically 5 to 10% [3] and in approximately 10 to 15% of patients, AL amyloidosis occurs in association with multiple
Table 1: Haematological and biochemical data performed at first visit (February 2006) and at 3 months (2009) after commencing curcumin therapy and thereafter annually (2010–2014).

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<tr>
<td>Bone marrow biopsy (% plasma cells)</td>
<td>18</td>
<td>2</td>
<td>5</td>
<td>&lt;2</td>
<td>&lt;2</td>
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<tr>
<td>Paraprotein (g/L)</td>
<td>14</td>
<td>6</td>
<td>1</td>
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<tr>
<td>Free light chain ratio (0.3–1.7)</td>
<td>1.7</td>
<td>1.3</td>
<td>0.81</td>
<td>0.68</td>
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<tr>
<td>Lambda FLC (&lt;26.3 mg/L)</td>
<td>9</td>
<td>4</td>
<td>37</td>
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<tr>
<td>Kappa FLC (&lt;19.4 mg/L)</td>
<td>15</td>
<td>5</td>
<td>30</td>
<td>27</td>
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<tr>
<td>Globulin (22–38 g/L)</td>
<td>29</td>
<td>23</td>
<td>30</td>
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<tr>
<td>Calcium (mmol/L)</td>
<td>2.32</td>
<td>2.34</td>
<td>2.46</td>
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<td>Ig G (&lt;6.2–14.4 g/L)</td>
<td>20</td>
<td></td>
<td>9.5</td>
<td>9.5</td>
<td>9.4</td>
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<td>Ig M (&lt;0.48–3.04 g/L)</td>
<td>0.71</td>
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<td>0.85</td>
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<td>Ig A (0.6–3.96 g/L)</td>
<td>1.63</td>
<td>1.68</td>
<td>1.42</td>
<td>1.35</td>
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<td>Haemoglobin (128–175 g/L)</td>
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<td>120</td>
<td>139</td>
<td>135</td>
<td>136</td>
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<td>WCC (4.0–11.0 × 10⁹/L)</td>
<td>6</td>
<td>3.2</td>
<td>4.3</td>
<td>6.8</td>
<td>6.1</td>
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<td>Platelets (150–450 × 10⁹/L)</td>
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<td>114</td>
<td>164</td>
<td>171</td>
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<td>LDH (u/L)</td>
<td>167</td>
<td>163</td>
<td>133</td>
<td>142</td>
<td>140</td>
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<td>B2 microglobulin (g/L)</td>
<td>2.2</td>
<td>2.5</td>
<td>3.1</td>
<td>3.4</td>
<td>3.7</td>
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<td>Serum creatinine (60–120 μmol/L)</td>
<td>109</td>
<td>135</td>
<td>127</td>
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<td>eGFR (&gt;89 mL/min)</td>
<td>57</td>
<td>45</td>
<td>46</td>
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<tr>
<td>u-creat (8.8–17.6 mmol/L)</td>
<td>10.3</td>
<td>8.1</td>
<td>6.6</td>
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<tr>
<td>u-prot (0.01–0.20 mg/day)</td>
<td>0.15</td>
<td>0.06</td>
<td>0.05</td>
<td>0.07</td>
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* After 3 months of curcumin therapy.

"u-creat" refers to urinary creatinine and "u-prot" refers to urinary-protein.
curcumin in patients with plasma cell dyscrasias [6–9]. We recommend further evaluation of curcumin in patients with primary AL amyloidosis.

**Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this paper.

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**References**


