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Letter to the Editor

A rare case of primary systemic amyloidosis of the neck with massive cervical lymph node involvement: A case report and review of the literature

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ABSTRACT

Amyloidosis is a term applied to a diverse group of disorders that share the deposition of amyloid protein in various extracellular tissues. Systemic amyloidosis may involve almost any organ system in the body including regions in the head and neck; however, neck lymph node involvement is rare, with only five previous cases reported. We present the case of a primary systemic AL amyloidosis with hepatic, cervical, retroperitoneal, axillary and inguinal lymphnode localizations, unresponsive to medical therapy and treated with a surgical approach followed by autologous bone marrow transplantation. We review the pertinent literature with exclusive attention to the otorhinolaryngologic aspect.

1. Introduction

We present a case of systemic amyloidosis with massive cervical localization, treated with medical and surgical therapy. Cervical lymph nodes are rarely affected by amyloidosis, which is defined as an extracellular deposition of a fibrillary protein known as amyloid and provided with unique ultrastructural, X-ray diffraction, and biochemical properties, found in various tissues and organs [1].

We report an extensive literature review focused on cervical lymph node involvement; we also discuss the histopathologic characteristics and the various clinical features of primary amyloidosis with emphasis on its otolaryngologic manifestations.

2. Materials and methods

A 53-year-old woman was presented to the Department of Otolaryngology—Head Neck Surgery at the University of Pisa (Italy) with a history of progressive, massive enlargement of the neck lymph nodes, associated with fatigue, weight loss, and light headedness, lasting eight months. She was a non-smoker and her past medical history was unremarkable, except for chronic, non-active hepatitis C.

On physical examination (Fig. 1a), an impressive, poorly mobile cervical adenopathy was noted extending bilaterally from her mastoids to her clavicles, mainly affecting the submandibular lymph nodes. She also showed a bilateral increase of the submandibular, laterocervical and supraclavear lymph nodes; at palpation, the mass was firm, not mobile and painless. The larynx and the trachea were not displaced; endolaryngeal examination was normal. Cranial nerve examination revealed no deficits. Pulmonary and cardiovascular examinations were within normal limits, while examination of the abdomen revealed an enlarged liver extending 4 cm below the right costal margin at the midclavicular line; splenomegaly was not noted. The patient also demonstrated bilateral axillary and inguinal lymphadenopathy.

Initial laboratory evaluation revealed a full blood count and erythrocyte sedimentation rate (ESR), serum calcium, renal and liver function all within normal limits. Serum and urine protein electrophoresis demonstrated monoclonal lambda light chains. Electrocardiogram, echocardiogram, 24-h urine creatinine and chest X-ray were normal. A computerized tomography (CT) scan was arranged and demonstrated a massive gross adenopathy bilaterally involving all nodal groups with no infiltration of the surrounding structures (Fig. 1b). Hepatic enlargement was noted. The CT scan also revealed some enlarged lymph nodes in the median retroperitoneal space, both at renal and sub-renal level.

A hepatic, cervical, inguinal and axillary lymph nodes fine needle ago biopsy (FNAB) was performed; all samples stained pink with haematoxylin and eosin and all showed distinctive apple-green birefringence under polarized light under Congo red staining (Fig. 2). Immunohistochemistry on lymph nodes samples showed lambda light chains. A diagnosis of primary systemic (AL type) amyloidosis with hepatic, cervical, retroperitoneal, axillary and inguinal lymph node localizations was made. The patient was initially treated with Melphalan and prednisone, then with Thalidomide and desametazone but the cervical mass continued growing. Bilateral selective neck dissection (levels 1–5) was performed with the aim of improving efficacy of the medical treatment and in order to avoid major respiratory complications (Fig. 1c). The surgical procedure was uneventful. Definitive histopathology confirmed the initial diagnosis of amyloidosis. The patient was dismissed on day 4 post-op, with no complications. At six months from surgery the patient underwent autologous bone marrow obtaining a partial response. Eight months later the disease progressed (abdominal localizations) and the patient started treatment with Thalidomide and steroids again. Such therapy, continued for about 12 months was able to stabilize the disease. On September 2008, because of progressive enlargement of abdominal lymph nodes, thalidomide was stopped and the patient started lenalidomide (15 mg/d for 21 days/month) with progressive volumetric reduction of abdominal lymphoadenopaties. On January 2009 such therapy was interrupted for renal toxicity. At the time of writing, four years after surgical approach, the patient is still alive in partial remission. No cervical recurrences were recorded.

3. Discussion

Amyloidosis is defined as a deposition of amyloid, an extracellular fibrillar protein with unique ultrastructural, X-ray diffraction, and biochemical properties, in one or more sites of the body [1]. More than 25 distinct biochemical forms of amyloid have been identified, but characteristically they are all composed of linear, rigid, nonbranching protein fibrils that can replace and destroy normal tissues [2].

Amyloidosis can be either a localized or a systemic disease. Systemic amyloidosis can be subclassified as (i) primary, when it is associated with a plasma cell dyscrasia; (ii) secondary, when it represents the result of a chronic indolent inflammatory condition; and (iii) hereditary or familial [3]. This classification is frequently

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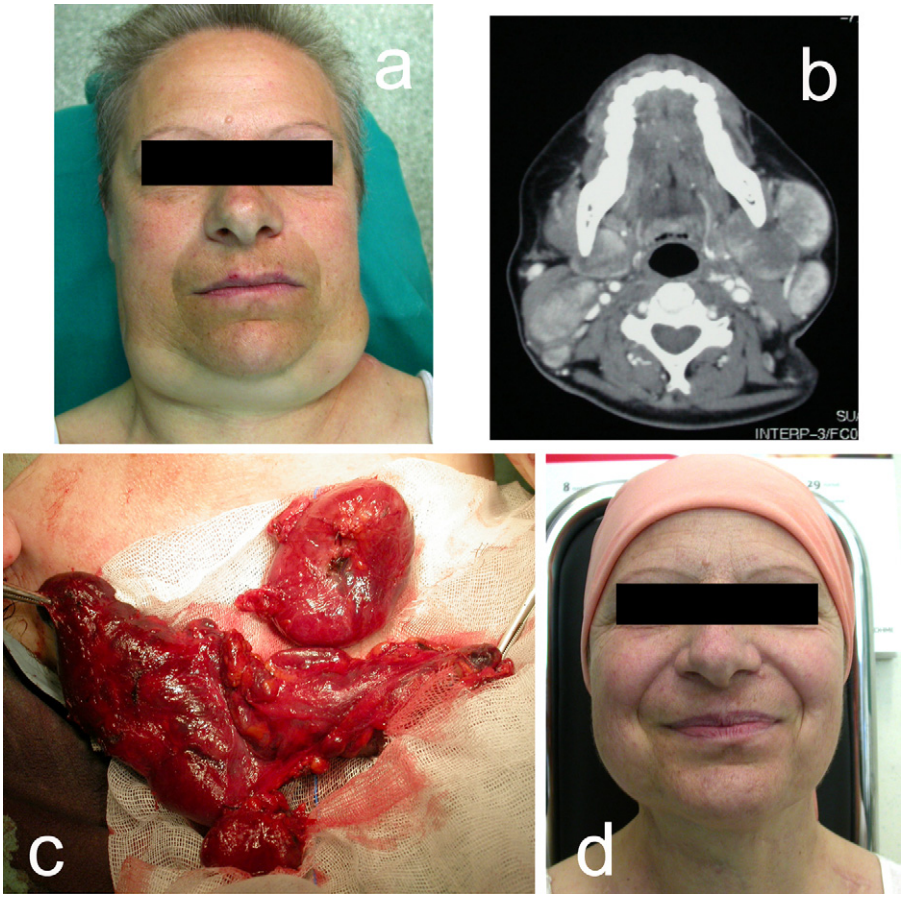

Fig. 1. Clinical features of systemic amyloidosis with massive cervical involvement: (a) on physical pre-operative examination, gross adenopathy extending bilaterally from mastoids to clavicles, mainly affecting the submandibular lymph nodes; (b) CT scan with medium contrast, showing inhomogeneous enhancement of the masses; (c) intra-operative view; (d) 2-year-post-operative view.

matched with the code that indicates the amyloid's composition (AL, AA, etc.), so that this biochemical–clinical combination better defines the disease *per se* [1]. Generally, systemic amyloidosis can be considered a fatal disease, with no uniformly accepted treatment [4]. Localized amyloidosis, also called amyloidoma [5], is a benign and indolent process, responsible only for local symptoms varying on the base of the localization of the lesion.

From a clinical point of view, amyloidosis has an extremely variable modality of presentation, with weakness and weight loss as the most common symptoms registered [6]. The liver is frequently affected by primary systemic amyloidosis [2]. Symptoms of hepatic involvement may include weight loss, chronic nausea, dyspepsia, and right upper quadrant fullness. Our patient showed weight loss, asthenia of 8 months duration, and hepatomegaly, but initially it was connected to her chronic hepatic disease.

Amyloidosis affecting the head and neck region is uncommon; the most affected areas are, in a decreasing order of frequency, the larynx, trachea and subglottis, tongue, oropharynx, maxillary antrum and nasal septum [4]. Other areas of deposition of amyloid may include the orbits, palate, temporomandibular joint, salivary and lachrymal glands, thyroid gland, and cranial nerves [7].

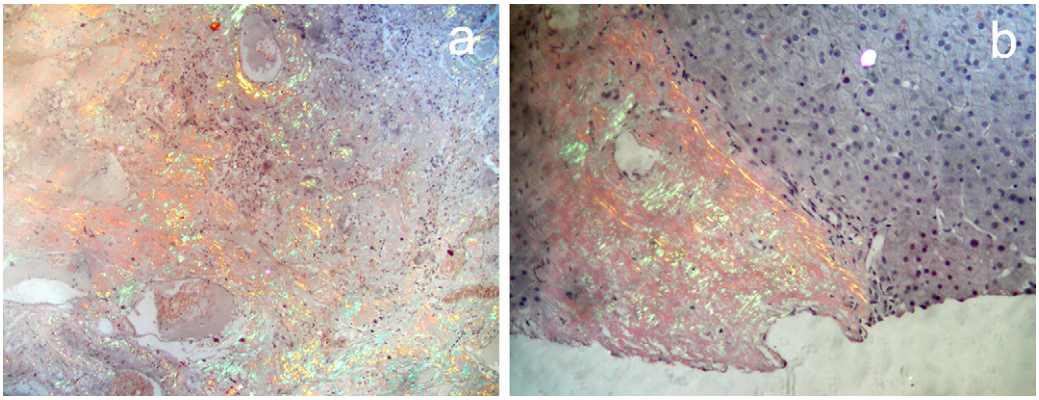

Fig. 2. Amyloid demonstrating apple-green birefringence by polarized light with Congo red, in both cervical lymph node (a) and hepatic (b) samples. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.).