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ORIGINAL ARTICLE

Presentation and Outcomes of Localized Immunoglobulin Light Chain Amyloidosis: The Mayo Clinic Experience

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Abstract

Objective: To describe treatment types, outcomes, and relapse patterns in patients with localized immunoglobulin light chain amyloidosis (AL_L).

Patients and Methods: We included all patients with AL_L seen at Mayo Clinic in Rochester, Minnesota, from January 1, 1968, through June 30, 2014. The diagnosis of AL_L was predicated on the presence of a Congo red–positive biopsy specimen and negative serum and urine immunofixation. Treatment response categories were response, stability, and progression. Localized and systemic progressions were defined as progression of disease at the site of origin or appearance of clonal plasma cells in a bone marrow biopsy sample, respectively.

Results: Of 5551 patients with AL, 413 (7%) had AL_L. The most common site involved was urothelial tissue (n=85, 21%), followed by the larynx (n=57, 14%). Coexisting autoimmune diseases were reported in 7% of patients (n=28). The most common first-line treatment was excision of the amyloid deposits (61%), followed by observation or supportive care (28%). When considering symptomatic patients only (n=284), 205 (72%) improved, 23 (8%) had stable disease, and 55 (19%) could not be evaluated for response. Ten-year survival was 78% and was not different from that of the general population. There were no systemic progressions, but 17% of patients (n=72) had localized progression.

Conclusion: Localized AL is associated with a relatively distinct pattern of organ involvement. The initial laboratory evaluation to exclude systemic disease could be limited to serum and urine immunofixation in most patients. Recurrence after first-line therapy is common, but long-term outcomes are excellent.

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Localized immunoglobulin light chain amyloidosis (AL_L) is characterized by the localized deposition of light chain amyloid fibrils. The pathogenesis of the disease is not clear, but it is thought to be produced by a localized, self-limited plasma cell clone.[1] Typically, patients with AL_L have no circulating monoclonal immunoglobulins in the serum or urine and no evidence of bone marrow involvement by clonal plasma cells. AL_L is an uncommon disease and constitutes approximately 12% of all AL cases.[2] Despite its rarity, it can cause substantial morbidity and can represent a diagnostic challenge because sites typically associated with AL_L can also be affected in patients with systemic AL. Furthermore, the optimal type of therapy and appropriate follow-up for these patients is not well established. In this study, we present one of the largest series of patients with AL_L diagnosed at Mayo Clinic in Rochester, Minnesota, over a 46-year period with an emphasis on treatment types, outcomes, and recurrence patterns.

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METHODS

Patients and Inclusion Criteria

From January 1, 1968, through June 30, 2014, clinical laboratory and treatment data were extracted from a prospectively maintained database. Patients before 1968 were excluded because immunofixation and immunoelectrophoresis were not available before that time. The Mayo Foundation Institutional Review Board approved the study, and all the patients consented to have their medical records reviewed according to institutional review board practices. The diagnosis of AL_L was predicated on the presence of a biopsy specimen that stained positive by Congo red and exhibited green birefringence under polarized light as well as negative electrophoresis and immunofixation of the serum and urine. If a circulating monoclonal protein was present, the light chain isotype had to be different from that of the amyloid deposits. If the serum or urine had the same light chain restriction as the tissue, systemic AL was comprehensively ruled out (including bone marrow and fat pad biopsies and comprehensive clinical staging). If amyloid was present in the fat or the bone marrow, patients were not considered to have AL_L. Complete hematologic staging was defined as negative serum and urine immunofixation, a fat aspirate negative for amyloid deposits, and a bone marrow biopsy negative for amyloid deposits and clonal plasma cells.

We identified 807 patients with suspected AL_L. After review of their medical records, 35 patients with seminal vesicle amyloidosis were excluded because amyloid deposits in this anatomical location are almost always semenogelin rather than AL.[3] We excluded 302 patients with synovial tissue/carpal tunnel amyloidosis because amyloid deposits in this anatomical location are frequently of the transthyretin type.[4,5] Finally, of the remaining 470 patients, 57 were excluded because they did not have serum/urine immunofixation testing performed, leaving 413 patients for this study.

Patient Follow-up and Definition of Response and Progression

Median follow-up for overall survival (OS) and progression for the entire cohort were 64 months (range, 1-594 months) and 46 months (range, 1-594 months), respectively. Complete follow-up was available for 122 patients (30%).

Three treatment response categories—response, stability, and progression—were considered and were defined using clinical, radiographic, and endoscopic examination findings when applicable. All patients who required an endoscopy at diagnosis (eg, urothelial, tracheobronchial, pharynx, larynx, gastrointestinal) had a follow-up endoscopy for response assessment. If no endoscopy was available, these patients were noted as "not evaluated" for response analyses. Some patients were lost to follow-up and could not be evaluated for response. Localized recurrence was defined as recurrence of disease at the site of origin as documented by the presence of progressive amyloid deposits established by clinical, radiographic, or endoscopic examination. Progression to systemic AL was defined by detection of a clonal plasma cell population in a bone marrow biopsy with involvement of other organs by amyloid.

Statistical Analyses

Progression-free survival (PFS), OS, and time to progression (TTP) were estimated by the Kaplan-Meier method. Patients were censored at the last known date of follow-up for OS, PFS, and TTP analyses. For OS analyses, we used an age sample of the general population as controls. Expected survival was calculated based on decennial life tables for the US population; each patient was matched to the control population on age, sex, and diagnosis date. The log-rank test was used to compare OS and PFS between groups. The Pearson χ^2 test and the Kruskal-Wallis test were used to ascertain differences between nominal and continuous variables, respectively. Because we performed multiple comparisons across multiple organ groups we chose a more stringent cutoff value for statistical significance ($P<.01$). All the statistical analyses were performed using JMP software (SAS Institute Inc).

RESULTS

Patient Characteristics and Presentation of AL_L

Of 5551 patients with AL seen at Mayo Clinic in Rochester, Minnesota, during the study