Dermatology Practical & Conceptual

Diagnostic Yield of Abdominal Wall Fat Pad Biopsy for Systemic Amyloidosis in a Low-Prevalence Referral Cohort

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ABSTRACT

Introduction: Systemic amyloidosis is a rare disorder characterized by extracellular amyloid deposition in tissues, leading to variable organ dysfunction. Abdominal wall fat pad biopsy is widely used as a minimally invasive diagnostic approach, yet its sensitivity varies according to population and technique.

Objectives: To assess the diagnostic yield and adequacy of abdominal wall fat pad biopsy for systemic amyloidosis in a low-prevalence referral cohort.

Methods: A retrospective study was conducted at a tertiary university hospital including all consecutive abdominal wall fat pad biopsies performed between January 2021 and June 2025. Clinical data, histopathological findings, and biopsy techniques were reviewed. Adequacy was defined by the presence of well-preserved subcutaneous fat with vascular and stromal structures. Congo red–positive deposits showing apple-green birefringence confirmed amyloidosis.

Results: A total of 106 biopsies from 103 patients (mean age 71.1 ± 12.2 years; 56.3% male) were analyzed. Clinical indications included MGUS (65.0%), multiple myeloma (27.2%), and suspected infiltrative cardiomyopathy or nephrotic proteinuria (8%). Overall, 7/106 biopsies (6.6%) were positive for amyloid. Sensitivity among patients with known systemic amyloidosis was 66.6% (6/9), and specificity was 100%. Only two of 94 patients (2.1%) without prior diagnosis were newly identified. Three punch biopsies (2.8%) were inadequate due to insufficient fat.

Conclusions: Abdominal wall fat pad biopsy is safe and minimally invasive but demonstrates limited diagnostic yield in unselected low-risk populations. It should not be used as a screening tool in patients with monoclonal gammopathies without organ involvement. Adequate tissue sampling and careful patient selection are essential to optimize diagnostic performance.

Introduction

Systemic amyloidosis is a rare and heterogeneous disorder characterized by extracellular deposition of amyloid fibrils in organs and tissues, leading to significant morbidity and mortality [1]. Diagnosis often requires histological confirmation. Abdominal wall fat pad biopsy is widely used as a minimally invasive diagnostic tool, particularly in suspected immunoglobulin light-chain (AL) amyloidosis. Reported sensitivity varies widely depending on biopsy technique, population, and disease prevalence. This study evaluated the diagnostic performance of fat pad biopsy in a low-prevalence referral cohort dominated by patients with monoclonal gammopathies of uncertain significance.

Objectives

To determine the diagnostic yield and adequacy of abdominal wall fat pad biopsy for systemic amyloidosis in a low-prevalence tertiary referral population.

Patients and Methods

We conducted a retrospective observational cohort study at a tertiary university hospital, reviewing all consecutive abdominal wall fat pad biopsies performed between January 2021 and June 2025.

Clinical data were extracted from medical records, including demographic characteristics, clinical indications, and prior diagnoses of systemic amyloidosis. Patients undergoing biopsy for suspicion of systemic amyloidosis in the context of monoclonal gammopathies or unexplained organ involvement were included. Demographic data is provided in Table 1.

Biopsies were obtained from the periumbilical region using one of two techniques: i) a fusiform scalpel incision measuring 3 × 1 cm; ii) an 8-mm deep punch biopsy. Each specimen contained dermis and subcutaneous fat, was fixed in formalin, and stained with hematoxylin–eosin and Congo red. Slides were examined under polarized light by both a dermatopathologist and a general pathologist.

The primary outcome was diagnostic yield, defined as the proportion of biopsies demonstrating amyloid deposition. Secondary outcomes included sample adequacy and the sensitivity of the biopsy in patients with a previously established diagnosis of systemic amyloidosis. Biopsy adequacy was determined qualitatively based on the presence of well-preserved hypodermal adipose tissue with identifiable stromal and vascular structures. Specimens were classified as positive when Congo red staining demonstrated amyloid deposition in vascular walls, connective tissue, or adipose tissue with characteristic apple-green birefringence under polarized light, negative when no amyloid deposits were detected, or inadequate when the specimen contained insufficient or absent subcutaneous fat, precluding reliable evaluation.

Table 1. Demographic and clinical characteristics of the cohort (N=103 patients, 106 biopsies).

Characteristic	Value
Mean age, years (± SD)	71.1 ± 12.2
Sex, N (%)	Male: 58 (56.3) Female: 45 (43.7)
Clinical indication, N (%)	MGUS: 67 (65.0) Multiple myeloma: 28 (27.2) Infiltrative cardiomyopathy: 7 (6.8) Nephrotic-range proteinuria: 1 (1.0)
Known systemic amyloidosis at biopsy, N (%)	Total: 9 (8.2) – AL amyloidosis: 7 – Wild-type ATTR: 2
Biopsy technique, N (%)	Fusiform scalpel incision: 25 (23.6) 8-mm punch biopsy: 81 (76.4)

MGUS: monoclonal gammopathy of undetermined significance; **ATTR:** transthyretin amyloidosis.

Results

A total of 106 biopsies from 103 patients were analyzed (Table 2). Mean age was 71.1 ± 12.2 years, and 56.3% were male. Clinical indications included MGUS (65.0%), multiple myeloma (27.2%), suspected infiltrative cardiomyopathy or nephrotic proteinuria (8%).

Nine patients (8.2%) had known systemic amyloidosis at the time of biopsy. Among them, 6/9 biopsies (66.6%) were positive for amyloid (Figures 1 and 2). Specificity was 100%.

Table 2. Histopathological results of abdominal fat pad biopsies (N=106).

Results	N (%)
Adequate sample	103 (97.2)
Inadequate sample (all punch biopsies)	3 (2.8)
Positive for amyloid deposits	7 (6.6)
– Patients with known amyloidosis	6/9 (66.6% sensitivity)
– Patients without prior diagnosis	2/94 (2.1% new diagnostic yield)
Specificity	103/103 (100)

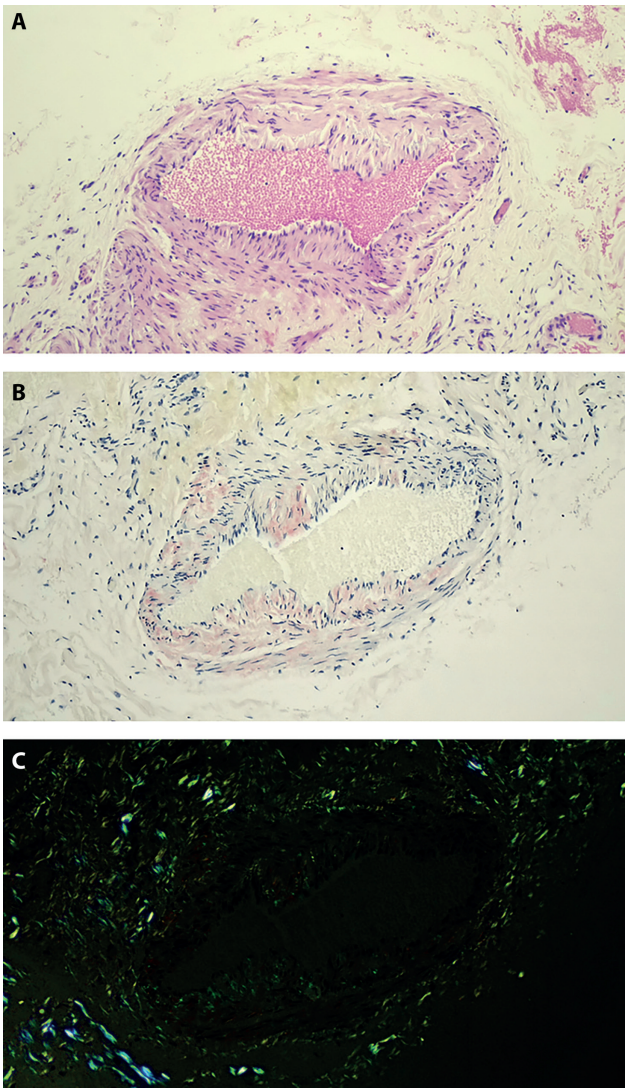

Figure 1. Magnification 200x. Amyloid deposits in the vascular wall of a dermal vessel. (A) Hematoxylin and eosin (H&E) stain showing eosinophilic amorphous material within the vessel wall. (B) Congo red stain highlighting amyloid deposition. (C) Congo red stain under polarized light demonstrating the characteristic apple-green birefringence.

In the broader cohort, amyloid was newly diagnosed in only two of 94 patients (2.1%). Thus, overall positivity rate was 6.6% (7/106 biopsies).

Three biopsies (2.8%), all via punch technique, were inadequate due to insufficient fat (Figure 3).

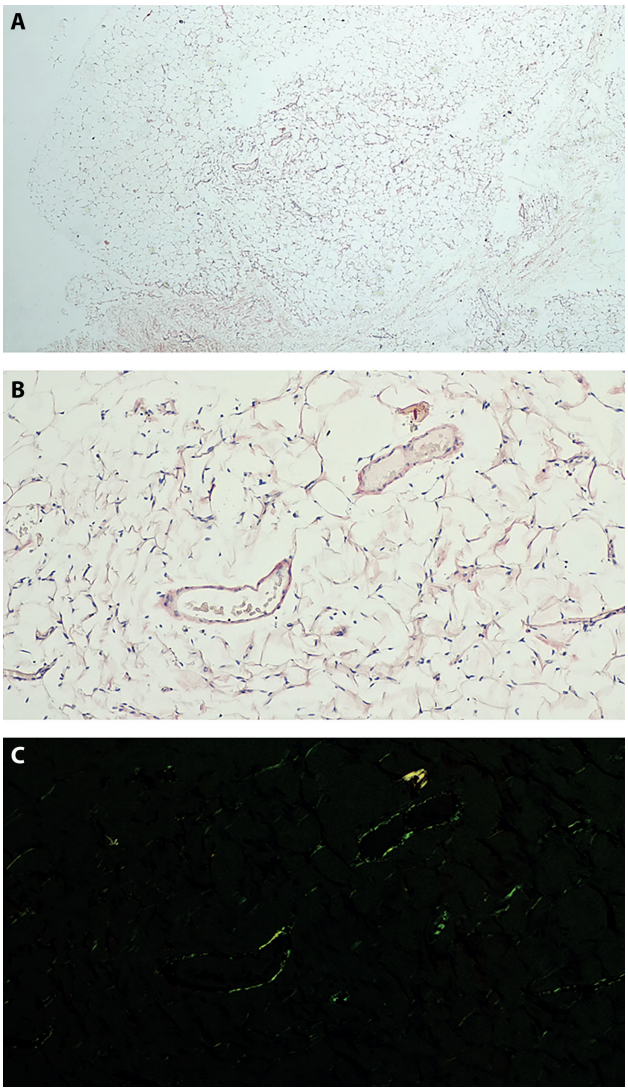

Figure 2. Magnifications 40x and 200x. Congo red stain showing amyloid deposits in the vascular wall and subcutaneous fat. (A) Congo red stain at low magnification (40x) demonstrating deposits along the vessel wall and within the surrounding fat tissue. (B) Congo red stain at higher magnification (200x) highlighting the extent of amyloid deposition. (C) Congo red stain under polarized light (200x) revealing the characteristic apple-green birefringence of amyloid.

Discussion

Systemic amyloidosis is a rare disorder [1], and the diagnostic utility of abdominal wall biopsy is highly dependent on the characteristics of the population under study. Prior studies demonstrating high sensitivity typically examined cohorts with known or strongly suspected amyloidosis, where the pretest probability of amyloid deposition was high [2-4]. In those settings, fine-needle aspirates of abdominal fat pad achieve sensitivities of approximately 70–80% and specificities above 90%, particularly for AL amyloidosis, while excisional biopsies may reach sensitivities around 79% for AL but only 12% for ATTR, underscoring the influence of amyloid type and tissue sampling technique [2-4]. Our data,

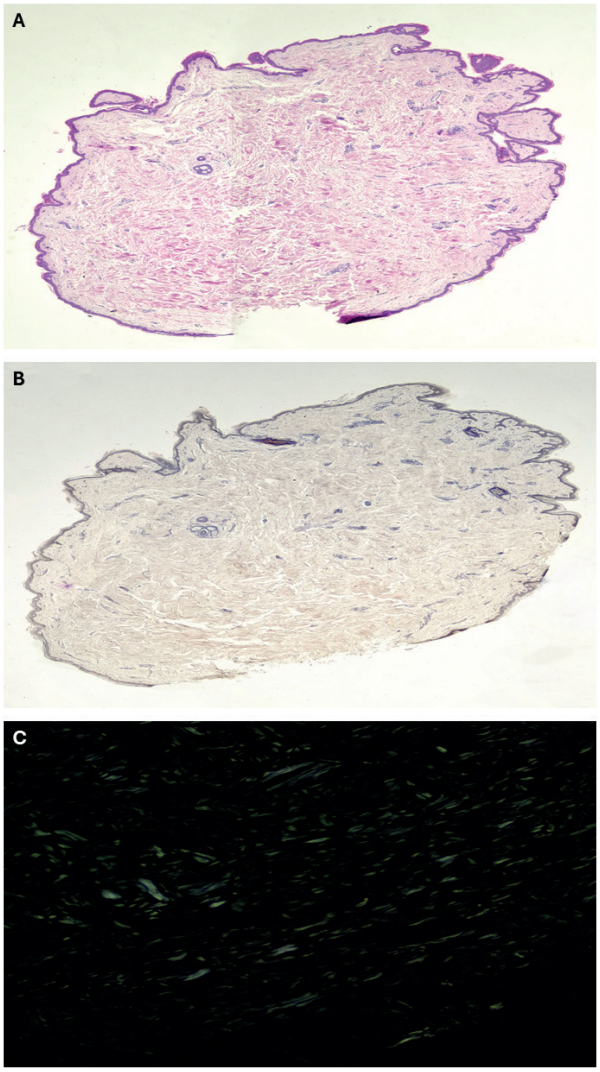

Figure 3. Magnifications 20x and 100x. Hematoxylin and eosin (H&E) and Congo red stains from an abdominal wall fat pad biopsy obtained with an 8-mm punch. After serial sectioning and reinclusion, no sufficient subcutaneous fat was identified; therefore, the biopsy was signed out as inconclusive due to minimal to absent fat representation. (A) H&E stain at low magnification (20x) showing dermis with absent subcutaneous tissue. (B) Congo red stain (20x) showing no amyloid deposition in the dermis. (C) Congo red stain under polarized light (100x) revealing absence of apple-green birefringence.

by contrast, reflect real-world use in a referral population with a predominance of MGUS and smoldering myeloma, groups in which the overall risk of systemic amyloidosis is substantially lower [1,5]. While the procedure remains safe and minimally invasive, its yield in unselected low-risk patients is modest, and a negative result is expected in most such cases.

Our experience reinforces the principle that abdominal fat biopsy should not be used as a general screening tool in patients with monoclonal gammopathies unless there are clinical or laboratory features suggesting organ involvement. The diagnostic efficiency in this context is low, and the utility of biopsy must be weighed against procedural burden and cost, particularly in older or frail patients. Recent studies suggest that the use of noninvasive diagnostic modalities such as serum free light chain analysis, cardiac scintigraphy, and advanced imaging may effectively triage patients before biopsy is considered and, in some cases, establish definitive diagnosis without tissue sampling [6,7]. For instance, cardiac scintigraphy combined with the absence of monoclonal protein can establish the diagnosis of transthyretin amyloidosis noninvasively, further reducing reliance on fat pad biopsy [7].

The adequacy of the specimen remains an important technical factor. Although our study was not designed to compare techniques, we note that all inadequate samples were obtained via punch biopsy (Figure 3). Lee et al. have shown that ultrasound-guided fat biopsy yields comparable or superior diagnostic sensitivity to bone marrow sampling in suspected amyloidosis, with relatively few nondiagnostic samples [8]. Regardless of the method used, ensuring sufficient volume and inclusion of subcutaneous fat is critical to accurate diagnosis [9].

Although both aspirate and excisional biopsy are acceptable approaches to abdominal fat sampling, excisional biopsies may offer greater tissue volume and diagnostic precision. However, aspirate-based techniques are generally considered less invasive and more commonly performed in hematology and internal medicine settings [2,5]. When tissue confirmation is required, combining fat pad and bone marrow sampling can potentially improve detection rates compared with either technique alone. Importantly, neither this study nor recent dermatopathology reports directly compare the sensitivity of abdominal wall skin biopsy with that of fat aspirate. Further prospective work comparing these techniques is needed.

Strengths

This study is its reflection of real-world practice in a tertiary dermatopathology referral center, encompassing over 100 biopsies across a broad spectrum of clinical indications. Dual review of samples by both a dermatopathologist and a general pathologist ensured consistency in histopathological interpretation. The study also provides practical insights into sample adequacy and the impact of biopsy technique, which are directly relevant for clinical practice.

Limitations

The retrospective nature of the study, its single-center design, and the absence of a direct comparison between punch, excisional, and aspirate-based techniques are the main limitations. The relatively small number of patients with confirmed systemic amyloidosis limits precision in estimating sensitivity. Furthermore, follow-up data were not uniformly

available for all patients, precluding assessment of negative predictive value. Finally, as a referral cohort with a predominance of MGUS, the findings may not generalize to populations with higher pretest probability of amyloidosis.

Conclusions

Abdominal wall fat pad biopsy is safe and minimally invasive, but its diagnostic yield is limited in unselected referral populations with low prevalence of systemic amyloidosis. In this context, it should not be used as a general screening tool for patients with monoclonal gammopathies. Optimal tissue sampling and careful patient selection are critical to enhancing diagnostic accuracy.

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