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Letter to the Editor

Beyond the textbooks: Vacuolar cast as an emerging marker in urinary sediment

Más allá de los libros de texto: cilindros vacuolados como marcador emergente en el sedimento urinario

To the Editor,

We present the case of a 73-year-old woman who was diagnosed with diabetic nephropathy in May 2024 and who attended the nephrology service for follow-up consultation. Laboratory analyses prior to the visit revealed a hemoglobin concentration of 13.9 g/dl (reference: 12–16 g/dl), a glucose concentration of 178 mg/dl (70–110 mg/dl), a urea concentration of 113 mg/dl (21–43 mg/dl), a uric acid concentration of 5.7 mg/dl (2.5–6.2 mg/dl), a total cholesterol concentration of 203 mg/dl (<200 mg/dl) and a triglyceride concentration of 334 mg/dl (<150 mg/dl). In the urine study, the dipstick indicated glycosuria (2000 mg/dl) and proteinuria (1000 mg/dl), and microscopic examination revealed the presence of hyaline, leukocytic, and waxy casts; notably, unusual casts composed of a slightly granular or waxy matrix were detected, within which multiple vesicles of variable morphology, size and number were observed. Additionally, the casts were nonbirefringent and fluid-filled, with an appearance similar to that of lipid inclusions (Fig. 1).

These casts have been referred to previously as denatured vacuolar (or vacuolated) casts.[1] These unusual casts structures are not described in microscopy textbooks of urinary sediments,[2,3] and little literature exists on this subject.[1,4] Among existing studies, Rosenbloom et al.[4] published a multinational observational study in February 2024 in which 46 cases were collected involving vacuolated casts, which were identified via urinary microscopy. The authors reported that the presence of these casts was consistently associated with nephrotic-range proteinuria (82% of cases) and advanced chronic kidney disease (62% in stages 3B-5). In histopathological analyses, all of the biopsied patients exhibited glomerular lesions, and the most frequent diagnoses were diabetic nephropathy (48%), arteriolonephrosclerosis (30%), podocytopathies (15%) and proliferative glomerulonephritis (15%). Compared with a control cohort lacking vacuolated casts, these patients demonstrated significantly higher proteinuria and a more advanced degree of glomerular sclerosis. Taken together, the results of this study suggest that vacuolated casts constitute a distinct urinary marker of advanced proteinuric glomerulopathies and could have prognostic value for the progression to end-stage renal disease.

The correct identification of these casts in the urinary sediment is highly clinically important, since different types of cast provide specific diagnostic information and are associated with different pathological entities. However, their differentiation from lipid or hematic casts can be complex.

Lipid casts are characterized by the presence of multiple, rounded lipid droplets of different sizes, which generate the typical Maltese cross sign under polarized light. In contrast, vacuolated casts contain vesicles exhibiting a more heterogeneous morphology (rounded, oval or elongated); moreover, unlike lipid casts, vacuolated casts lack birefringence. Conversely, hematic casts demonstrate abundant contiguous red blood cells, which are generally of a rounded morphology and uniform size, which facilitates their differentiation from vacuoles, which can be considerably larger or smaller than red blood cells.

Figure 1. Unusual casts composed of a slightly granular or waxy matrix, containing multiple vesicles of variable morphology, size, and number, resembling lipid inclusions (phase-contrast microscopy, ×400).

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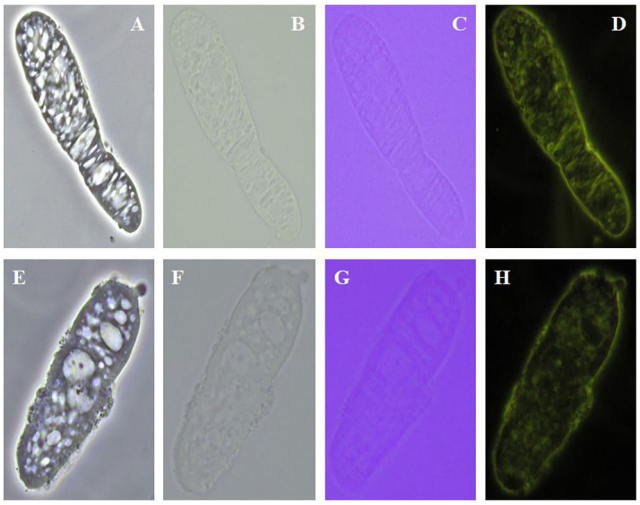

Figure 2. Vacuolated casts observed under ×400 magnification using different microscopy techniques: phase-contrast (A and E), bright field (B and F), polarized light (C and G), and dark field (D and H).

Despite these differences, the risk of erroneous interpretation persists; therefore, it is essential to complement urinalyses with different microscopy techniques, such as phase contrast, bright field, polarized light and dark field microscopy (Fig. 2). The combination of these methodologies allows a more accurate identification and reduces the possibility of incorrect diagnostic conclusions with potential clinical implications.

The origin of the vacuolated casts is still unknown, although various hypotheses have been proposed. One of the most accepted proposes the notion that these casts arise from vacuolated renal tubular epithelial cells that release aqueous vesicles that remain trapped in the matrix of the cylinder after they degenerate and lose their membranes. Another possibility is that these casts constitute a modified variant of lipid casts after loss of their fat components, which would explain their vesicular morphology without the presence of birefringence under polarized light. It has also been suggested that these structures could originate from injured podocytes, whose vacuolated cellular remains are incorporated into the structure. These casts may even originate from foam cells of macrophage origin, as described in proteinuric glomerulopathies. Although studies involving lipid stains suggest that the vacuoles are mostly aqueous in nature, the existence of heterogeneous forms with different compositions cannot be ruled out.[4]

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