Persistently elevated inflammatory markers and marked proteinuria due to Castleman disease

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In May 2014, a 26-year-old Caucasian woman presented to our outpatient clinic with edema of the lower extremities, nephrotic-range proteinuria (15.0 g/24 h), and preserved kidney function. Her history revealed elevated levels of C-reactive protein (CRP) since 2009 and mild normocytic anemia. The patient was admitted to the hospital. On examination, she was afebrile, with pale skin and pitting edema of both shanks. Otherwise, the physical examination was unremarkable. Laboratory tests showed changes typical for chronic inflammation with normocytic anemia (hemoglobin, 8.6 g/dl with a mean corpuscular volume of 82.7 fL; hyperfibrinogenemia, 12.8 g/l; and elevated serum CRP levels, 44.2 mg/l) and polyclonal gammopathy. No laboratory signs of autoimmune reactivity were detected.

Abdominal computed tomography scans showed a periaortic mass of 38 × 33 × 45 mm in size (FIGURE 1A).

Due to marked proteinuria, a kidney biopsy was performed. The principal pathological feature was an early stage of renal AA amyloidosis (FIGURE 1BC).

To reduce an inflammatory reaction, a high-dose glucocorticoid therapy was instituted (3 daily doses of methylprednisolone, 1000 mg IV followed by 32 mg/d orally). Serum CRP levels normalized within 2 weeks, and in July 2014, the patient underwent surgery with the total excision of the abdominal mass located in the small bowel mesentery. A histopathological examination revealed a mass consistent with unicentric Castleman disease of the human herpesvirus 8 (HHV-8)-negative, mixed hyaline-vascular and plasma-cell type (FIGURE 1D).

Glucocorticoids were tapered and eventually discontinued. During 15 months of follow-up, CRP levels remained within the normal range and proteinuria stabilized at 2.5 g/24 h with preserved kidney function.

Castleman disease (angiofollicular lymph node hyperplasia) is a lymphoproliferative disorder which comprises anatomically unicentric or multicentric forms, with histological variants including hyaline-vascular, plasma-cell, or mixed type.

Castleman disease is rare. No data are available regarding its incidence in the population, while an estimated 10-year prevalence of its multicentric form in the United States is 2.4 per million population.

The median age at presentation is approximately 35 years for the unicentric type and between 50 and 65 years for the multicentric type.

Unicentric form is a localized disease characterized by enlarged, pathological lymph nodes within a single area. In contrast to its multicentric form, unicentric Castleman disease is potentially completely curable by surgery, leading to partial or complete disease remission, with regression of tissue amyloid deposits, normalization of serum CRP levels, and functional improvement of the affected organs.

Acquired amyloidosis is a rare complication of Castleman disease, and is usually of the AA type, resulting from persistent acute phase response. Kidney amyloidosis with nephrotic syndrome as a result of unicentric Castleman disease is extremely rare. The reported cases of Castleman disease complicated by AA amyloidosis include the plasma-cell type and, less frequently, mixed type.

As demonstrated in the current case, glucocorticoids followed by tumor resection lead to a prompt decrease of serum CRP levels and a stable decrease of proteinuria. Most probably, the
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Reduction of chronic inflammation inhibits the amyloid production. Furthermore, as shown previously, amyloid deposits can regress once the supply of amyloid precursors is reduced.

Laboratory signs of chronic inflammation present for several years without an apparent cause, even without clinical symptoms, should raise suspicion of Castleman disease. Unfortunately, its diagnosis is usually significantly delayed, which may lead to irreversible organ damage as a result of secondary AA amyloidosis.

REFERENCES


FIGURE 1  A – abdominal computed tomography scan; there is a tumor on the left side of abdominal aorta, superior to the aortic bifurcation (arrow); B – Kongo red positivity of focal deposits in renal glomeruli; C – immunopositivity of amyloid deposits in the kidney stained for AA amyloid; D – the tumorous lymph node of the mesentery; on the left side, lymph follicle with a small, “burnt out” germinal center and widened distinct mantle zone; on the right, sheets of plasma cells