Patients with multiple myeloma with the shortest survival have the most kidney damage

August 31 2021

Dr. Gurmukh Singh. Credit: Michael Holahan

Nearly 20% of patients with multiple myeloma have a form in which they make extreme quantities of one component of the abnormal

antibody they are producing, and these so-called "free monoclonal light chains" pile up and damage the kidneys, investigators say.

These patients likely could benefit most from early identification and additional interventions like plasmapheresis and dialysis, which would help remove the damaging, circulating light chains, says Dr. Gurmukh Singh, vice chair of clinical affairs for the Department of Pathology at the Medical College of Georgia at Augusta University.

Multiple myeloma is a cancer in which our plasma cells, white blood cells which are supposed to make a variety of antibodies to protect us, instead become abnormal and start producing a single, Y-shaped protein, sometimes referred to as a monoclonal protein, or M-spike, that can do damage body-wide.

The proteins have two chains, called heavy and light chains, and the disease may be classified by the type of each of those chains it produces. In fact, normal antibodies typically have two of each, although in both sickness and health plasma cells make more light chains.

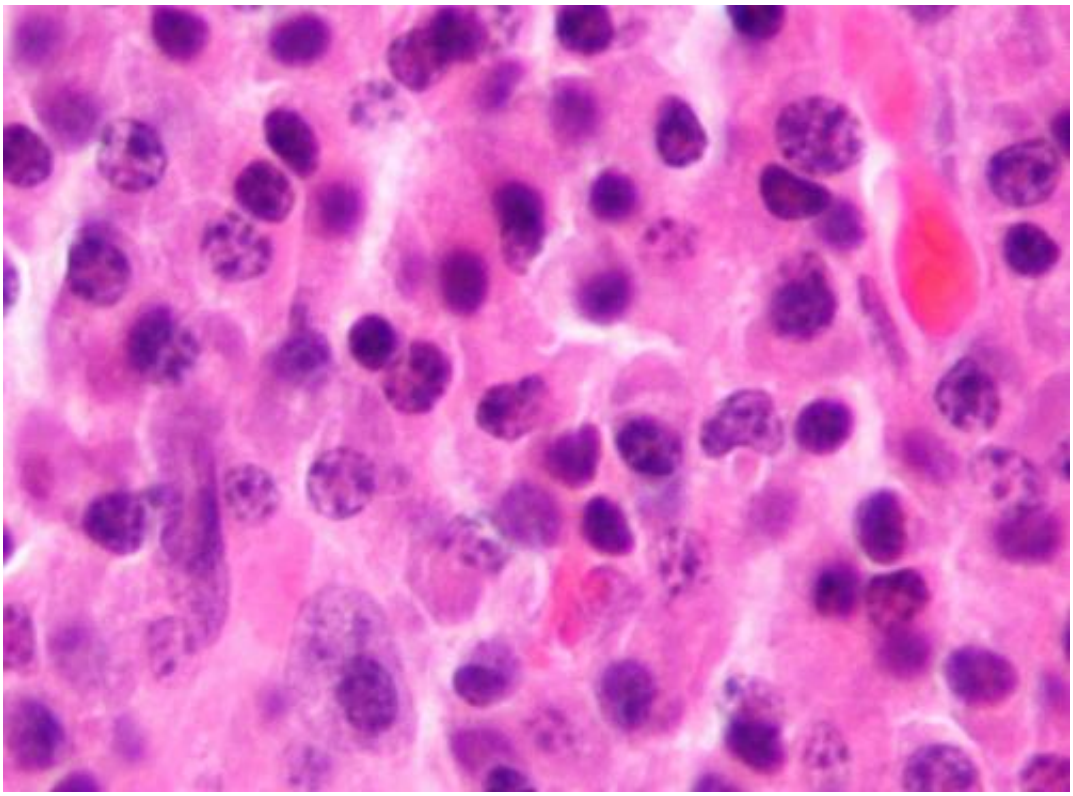
Some patients, like the ones Singh is studying, make even more light chains, and because those excessive light chains don't pair up with heavy chain proteins, that leaves a lot more free and circulating, which is how they can end up accumulating in the kidneys, Singh says of light chain predominant multiple myeloma.

For the study published in the journal *Lab Medicine*, they looked at nearly 400 patients from a 10-year period at a single, medical school affiliated health system to assess why these patients typically have a shorter survival.

They found they have higher rates of kidney dialysis and clear signs of kidney damage like higher blood pressure and higher concentrations of

protein in the urine.

Mortality rates in patients with this light chain predominant multiple myeloma were nearly three times higher than for conventional multiple myeloma, Singh and his colleagues say, with the survival graph for most patients looking like a gradual hill, and for these patients more like a cliff.



Micrograph of a plasmacytoma, the histologic correlate of multiple myeloma. H&E stain. Credit: Wikipedia/CC BY-SA 3.0

The shorter survival of these patients is clearly associated with their kidney damage caused by excessive light chains traveling in their blood and clogging up the kidney tubules, which carry urine away from the

kidney's filtering units and where needed items like salt and water get resorbed, says Singh, corresponding author and Walter L. Shepheard Chair in Clinical Pathology.

More of these patients also needed blood transfusions to help supplement the work of the bone marrow that also is under attack from the abnormal plasma cells. They also had more hypertension, which can both damage kidneys and result from kidney damage. While multiple myeloma tends to impact the kidneys in all patients, this subset with excessive light chains appears to have worse damage, Singh says.

An important bottom line is shorter survival, he says, and excessive free light chains and associated kidney damage have a clear role in that.

Kidney damage may be reduced and quality of life improved by early intervention strategies like plasmapheresis, where excessive light chains could be filtered out of the blood or dialysis that uses a specialized filter to also trap circulating light chains, Singh says, but clinical trials are needed to evaluate these and other strategies.

Tests can be done to identify these individuals by measuring free light chains, but right now there are no targeted treatments when they are identified, which is why clinical trials are needed, Singh notes.

In healthy individuals, these excess light chains are simply filtered out by the kidneys and eliminated in the urine, Singh says. However with this form of multiple myeloma, "Everything is multiplied, the kidneys get bombarded and the tubules get clogged," Singh says. You can see the protein deposits in a biopsy, he adds.

There are two different types of light chains, kappa and lambda, which are distinctive in their amino acid sequence. We normally make about twice as many kappa light chains as lambda, and while cancer can affect

both light chains and/or multiple heavy chains as well, kappa light chains go up more, Singh says.

He and his colleagues reported in 2019 that to more accurately diagnose and monitor multiple myeloma, concentrations of each light chain needed to be evaluated differently.

Multiple myeloma can also interfere with the immune response and form actual masses or tumors, according to the Leukemia & Lymphoma Society. Symptoms of multiple myeloma may include bone pain, particularly in the back and ribs; anemia that results in weakness and fatigue; and kidney trouble; or it may be essentially asymptomatic.

More information: *Lab Medicine*, academic.oup.com/labmed/advanc… bmed/lmab054/6350864

Provided by Medical College of Georgia at Augusta University

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