Comment on: Think to prevent before than to treat renal impairment in multiple myeloma: do not forget tubular damage mimicking Fanconi syndrome

Piero Stratta†, Andrea Airoldi, Michele Battista, Gabriele Guglielmetti, Elisabetta Radin, Cristina Izzo, Guido Merlotti & Marco Quaglia
Amedeo Avogadro University of Eastern Piedmont, Department of Translational Medicine, Novara, Italy

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In a recent paper, renal impairment is correctly described as a common complication of symptomatic myeloma (20 – 40%) needing dialysis. Significant improvement has been attributed to novel therapeutic chemotherapy regimens coupled with extrarenal free light chain removal obtained by plasma exchange or dialysis [1].

As nephrologists, we would like to stress the importance of recognizing early symptoms of renal impairment other than by measuring renal function as glomerular filtration rate (GFR) [2]. An increase in serum creatinine and/or a decrease in GFR are not the only markers of renal impairment in patients with multiple myeloma. Although a serum creatinine > 2 mg/dl is one of the hypercalcemia, renal impairment, anemia, bone disease (CRAB) diagnostic criteria for symptomatic myeloma requiring therapy, it has been stated that "a variety of other types of end-organ dysfunctions can occur and lead to a need for therapy. Such a dysfunction is sufficient to support classifications of myeloma if proven to be myeloma-related" [3]. Tubular dysfunctions, and mainly proximal tubular dysfunctions with the picture of complete or incomplete Fanconi syndrome, constitute such "other end-organ dysfunctions" [1-3].

As far as the kidney is concerned, it is important to have early indicators of tubular dysfunction. This includes hypophosphatemia, hypouricemia, hypokalemia and metabolic acidosis coupled with urine loss of phosphate, urate, potassium, bicarbonate, low-molecular-weight proteins and glycosuria (in the presence of normal blood glucose levels). Therefore, even if free light chains detected in the urine (Bence Jones proteinuria) is not a sign of renal damage by itself, its transcellular "traffic" may cause tubular damage, eventually leading to tubular crystal-storing histiocytosis and Fanconi syndrome. Subsequently, tubular casts precipitating in the distal tubule may cause acute renal failure of the classical 'myeloma kidney' [4,5].

Therefore, a delay in diagnosis could allow irreversible kidney damage to occur and might shorten patient survival.

Declaration of interest

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Bibliography

1. Kastritis E, Terpos E, Dimopoulos MA. Current treatments for renal failure due to multiple myeloma. Expert Opin Pharmacother 2013;14:1477-95
2. Dimopoulos MA, Terpos E, Chanan-Khan A, et al. Renal impairment in patients with multiple myeloma: a consensus statement on behalf of the International Myeloma Working Group. J Clin Oncol 2010;28:4976-84
3. Markowitz GS, Flis RS, Kambham N, D'Agati VD. Fanconi syndrome with light chains in the urine. Am J Kidney Dis 2000;4:777-81
4. Stratta P, Airoldi A, Izzo C, et al. Free light-chains and renal disorders: when small is worse. Lancet 2010;376:1221; author reply 1221-2
5. Stratta P, Gravellone L, Cena T, et al. Renal outcome and monoclonal immunoglobulin deposition disease in 289 old patients with blood cell dyscrasias: a single center experience. Crit Rev Oncol Hematol 2011;79:31-42

Affiliation

Piero Stratta[†1] MD, Andrea Airoldi[2] MD, Michele Battista[2] MD, Gabriele Guglielmetti[2] MD, Elisabetta Radin[2] MD, Cristina Izzo[2] MD, Guido Merlotti[2] MD & Marco Quaglia[2] MD
[†]Author for correspondence
[1]Professor of Nephrology, Nephrology School Director of the Division of Nephrology and Transplantation, Department of Translational Medicine, Amedeo Avogadro University of Eastern Piedmont, Via Solaroli 17, 28100 Novara, Italy
E-mail: piero.stratta@med.unipmn.it
[2]Avogadro Medical School, Department of Translational Medicine, Nephrology and Transplantation Maggiore Carita di Novara, Corso Mazzini 18, 28100 Novara, Italy

Authors' reply

We agree with Stratta *et al.* that patients with an otherwise-indolent plasma-cell dyscrasia may present with renal dysfunction, which may not be reflected in the levels of serum creatinine and epidermal growth factor receptor.

We only briefly report Fanconi's syndrome in our review [1]; however, the term "monoclonal gammopathy of renal significance" (MGRS) has been introduced to include renal pathology which is not related to overt myeloma [2]. A position paper on the management of MGRS also includes an opinion on the management of Fanconi's syndrome in patients with monoclonal gammopathy [3]. Physicians should consider the possibility of this syndrome in patients presenting with unexplained osteoporosis, hypophosphatemia, hypouricemia, hypokalemia and metabolic acidosis together with a monoclonal gammopathy. Urine studies for phosphate, urate, potassium, bicarbonate, low-molecular-weight proteins and glycosuria (in the presence of normal blood glucose levels) should be considered. Early recognition may lead to effective intervention although there is limited experience regarding the treatment of this syndrome.

Declaration of interest

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Bibliography

1. Kastritis E, Terpos E, Dimopoulos MA. Current treatments for renal failure due to multiple myeloma. Expert Opin Pharmacother 2013;14:1477-95
2. Leung N, Bridoux F, Hutchison CA, et al. Monoclonal gammopathy of renal significance: when MGUS is no longer undetermined or insignificant. Blood 2012;120:4292-5
3. Fermand JP, Bridoux F, Kyle RA, et al. How I treat monoclonal gammopathy of renal significance (MGRS). Blood 2013; [Epub ahead of print]

Affiliation

Efstathios Kastritis[†] MD, Evangelos Terpos & Meletios A Dimopoulos
[†]Author for correspondence
National and Kapodistrian University of Athens, School of Medicine, Department of Clinical Therapeutics, Athens 10679, Greece
E-mail: ekastritis@gmail.com