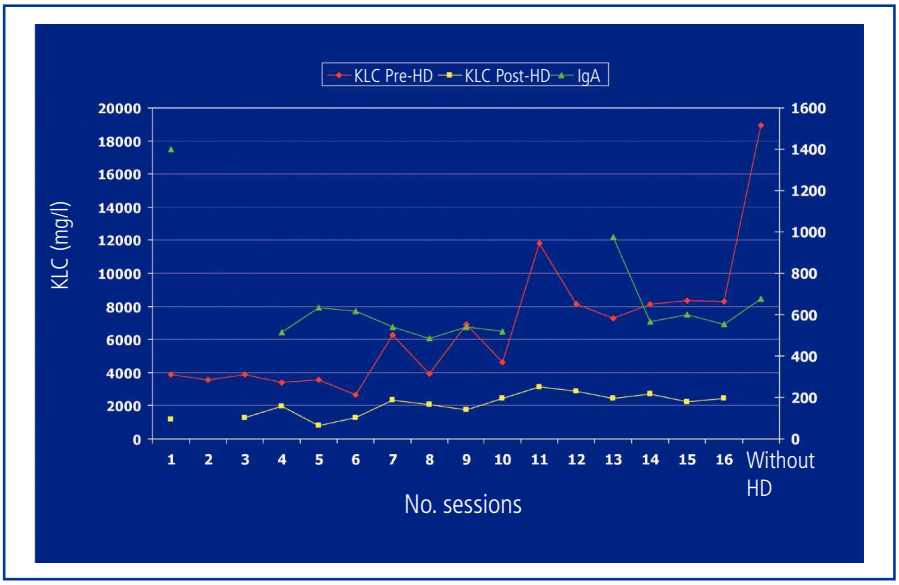


**Figure 2.** Monitoring of kappa light chains and immunoglobulin A.
KLC: kappa light chains, HD: haemodialysis, IgA: immunoglobulin A.
Discrepancy in the response to treatment.

diagnosis. The haematological argument for not advancing the abovementioned assessment is that a delay in the diagnosis of therapeutic ineffectiveness of 4-6 weeks does not really affect the final outcome, as far as the medullary response is concerned.[8] as nephrologists, we insist that the situation is different whenever there is a nephropathy due to light chains, since early diagnosis-treatment *is* vital in this case: we can cure medullary cell dyscrasia at a later stage, but we cannot do so for renal tubular cells, as demonstrated in the second biopsy carried out in our case.

Fortunately, more and more studies advocate the prognostic importance of FLC[9] and the inclusion of their monitoring in these protocols, which could even save a re-biopsy of the medulla.[7-11]

## CONCLUSION

Early chemotherapy and clearance of free light chains is fundamental in order for treatment to be effective in myeloma kidney. The monitoring of free light chains in blood helps to assess the therapeutic response. Good coordination between Nephrology and Haematology is essential for treatment to be effective in these patients.

### Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.


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# Dabigatran-induced upper intestinal bleeding in a patient with chronic kidney disease


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**To the Editor:**

Dabigatran has been shown to be more effective than heparin in total hip replacement thromboembolic prophylaxis and to have similar efficacy with less risk of bleeding in the treatment of deep venous thrombosis.[2] The RE-LY[3] study showed its greater efficacy in the prevention of ictus than warfarin in patients with atrial fibrillation. However, in the subgroup study, patients who were 75 years of age or older had a higher risk of extracranial bleeding, probably in relation to high concentrations of the drug.[4] With a peak plasma concentration 2 hours[5,6] after intake and a half-life of 12-17 hours,[5,6] it has a renal clearance of 80%.[5,6] It is recommended to reduce the dose for patients with an estimated glomerular filtration rate between 30 and 50ml/min/1.73m$^2$. If the GFR falls below 30ml/min/1.73m$^2$, the drug is contraindicated.[7]

We present the case of an 84-year-old female with high blood pressure, type 2 diabetes mellitus, atrial fibrillation, hypertensive heart disease with preserved systolic function, stage 3 chronic kidney disease with an estimated glomerular filtration rate of 30ml/min/1.73m$^2$ and normocytic normochromic anaemia, who presented with progressive general deterioration in recent months, without abnormalities in the characteristics of urine or the diuresis rate. She was being treated with several antihypertensive drugs (including angiotensin II receptor antagonists and beta-blockers), a statin and fibrate combination and dabigatran (75mg every 12 hours). Her general appearance was poor. The cardiac examination was normal, but auscultation revealed crackles in both lung bases. No abdominal abnormalities or increases in dependent oedema were found. The digital rectal examination was negative for melena and rectal bleeding. Blood pressure was 94/36mmHg. The electrocardiogram showed sinus rhythm of 54 beats per minute with V4-V6 straight ST segment not suggestive of acute myocardial ischaemia. The test results are displayed in Table 1. The x-ray showed cardiomegaly, bilateral posterior pleural effusion and vascular redistribution. There were no significant abnormalities in the abdominal x-ray. Due to the low blood haemoglobin concentration (5g/dl), she received an initial transfusion of three packed red blood cell units and antibiotic treatment with ceftriaxone and ciprofloxacin was started due to findings consistent with urinary tract infection and she was admitted to the Nephrology Department for studies. Due to the suspicion of upper intestinal bleeding, we decided to perform haemodialysis to clear dabigatran. Hours later, she produced melenic stools. A gastroscopy was performed, showing friable erythematous mucosa and a small clot in the angular notch. We performed another haemodialysis session twelve hours later. Clotting times gradually normalised over the following days and the patient did not display more bleeding.

Our case is an example of the potential disadvantages of administering dabigatran to patients with chronic kidney disease, since they have a higher risk of acute renal failure[8] and a critical increase in levels of the drug in serum. The patient received a dose adjusted to the glomerular filtration rate and displayed excessive anticoagulation due to exacerbation of her condition. Moreover, although it is often said that it does not require monitoring, there is no parameter that adequately assesses the anticoagulant activity of this new drug. Although the use of activated partial thromboplastin time or thrombin time have been established, these may underestimate the anticoagulant activity and are only useful for their negative predictive power. Prothrombin time is not useful either because it may be normal despite high serum dabigatran concentrations. The parameter that displays the best relationship with the level of dabigatran in serum is ecarin clotting time, which is not very useful because it requires a number of days for results to be obtained and it is not easy to perform. Despite the use of recombinant activated factor VIIa for patients with bleeding due to dabigatran, the only useful strategy for overdose management is clearing the drug via haemodialysis, taking advantage of its low molecular weight (471Da) and its low plasma protein binding rate (35%).[9] It should be taken into account that there is a rebound phenomenon for dabigatran concentration in plasma after the procedure, given its high distribution volume.[9] It is important to be aware that there are patients whose clinical condition is liable to change in a short period of time and that they will require regular check-ups. In these patients, such as those affected by chronic kidney disease, who are prone to erratic changes in drug concentrations, we should rationally consider the benefit/risk balance of using dabigatran.

### Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.


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**Table 1.** Data of test on admission

| | |
|---|---|
| **Venous blood** | |
| Glucose | 79mg/dl |
| Urea | 367mg/dl |
| Creatinine | 4.49mg/dl |
| Na | 138mEq/l |
| K | 4.2mEq/l |
| Cl | 97mEq/l |
| GOT | 40mEq/l |
| GPT | 20U/l |
| Total bilirubin | 1.17mg/dl |
| CRP | 25.1mg/l |
| pH | 7.42 |
| pCO2 | 32.8mmHg |
| Bicarbonate | 21.2mmol/l |
| Leukocytes | 6720/ul |
| Neutrophils | 86% |
| Eosinophils | 0.3% |
| Haemoglobin | 5g/dl |
| Haematocrit | 16% |
| Platelets | 184,000/ul |
| Quick | 17% |
| INR | 4.55 |
| Prothrombin time | 21.2s |
| Thrombin time | >120s |
| **Urine sediment** | |
| Leukocytes | 100-200/C |
| Bacteria | Abundant on direct vision |

GOT: glutamate-oxaloacetate transaminase, GPT: glutamate pyruvate transaminase, INR: International normalized ratio; CRP: C reactive protein.


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## Painful gynaecomastia secondary to cyclosporine A and tacrolimus in a patient with focal segmental glomerulosclerosis


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**To the Editor:**

Mammary gland hypertrophy is frequently observed as a side effect of medications such as calcium channel blockers, angiotensin II receptor antagonists, omeprazole or some immunosuppressants such as cyclosporine A.[1-3] In women with a kidney transplant on treatment with calcineurin inhibitors, mammary gland growth of varying intensity has been described, usually after more than one year. The patient may not always return after the drug is withdrawn and sometimes corrective mammoplasty is required to reduce the large volumes. However, we have not found this adverse effect reported in patients with glomerulonephritis on treatment with cyclosporin A.

### CASE STUDY

Our patient is a 48-year-old male who had been referred 9 months previously due to proteinuria. He had high blood pressure for 2 years and had been on treatment with amlodipine, atenolol and irbesartan for several years. The general test displayed: proteinuria of 1200mg/day, 448 red blood cells/µl in sediment, creatinine of 1.05mg/dl and negative immunology. The renal biopsy showed: 5-10 glomeruli without remarkable cellularity, without exudation, 2-4 glomeruli with complete sclerosis, discrete chronic interstitial lymphocyte-monocyte infiltrates, without vascular involvement and without tubular atrophy. In the immunofluorescence: IgM immunoglobulin deposits of focal and segmental distribution in 10 glomeruli, with + and + + intensity in the mesangial region. It was treated as focal segmental glomerulosclerosis with 2.5-5mg/day of ramipril being administered, and proteinuria decreased to <400mg/day. Three years ago, the patient had an increase in proteinuria of 1.6g/day, albuminuria of 895mg/day and 250 red blood cells/µl with normoalbuminaemia and oedemas. We treated him with prednisone and cyclophosphamide, with a decrease in proteinuria being observed after 7 months of treatment to 1.1g/day, but with proximal muscle weakness, which was interpreted as a myopathy due to steroids. Prednisone was discontinued and replaced by 1g/day mycophenolate mofetil and we withdrew amlodipine due to its potential influence on oedema, with 12.5mg of hydrochlorothiazide being administered due to poor blood pressure control. After 2 months we