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1. Rini BI, Garcia JA, Cooney MM *et al.* Toxicity of sunitinib plus bevacizumab in renal cell carcinoma. *J Clin Oncol* 2010; 28: e284–e285
2. Izzedine H, Brocheriou I, Deray G *et al.* Thrombotic microangiopathy and anti-VEGF agents. *Nephrol Dial Transplant* 2007; 22: 1481–1482
3. Frangie C, Lefaucheur C, Medioni J *et al.* Renal thrombotic microangiopathy caused by anti VEGF-antibody treatment for metastatic renal-cell carcinoma. *Lancet Oncol* 2007; 8: 177–178
4. Roncone D, Satoskar A, Nadasdy T *et al.* Proteinuria in a patient receiving anti-VEGF therapy for metastatic renal cell carcinoma. *Nat Clin Pract Nephrol* 2007; 3: 287–293
5. Kapiteijn E, Brand A, Kroep J *et al.* Sunitinib induced hypertension, thrombotic microangiopathy and reversible posterior leukoencephalopathy syndrome. *Ann Oncol* 2007; 10: 1745–1747
6. Eremina V, Jefferson JA, Kowalewska J *et al.* VEGF inhibition and renal thrombotic microangiopathy. *N Engl J Med* 2008; 358: 1129–1136
7. Stokes MB, Erazo MC, D'Agati VD. Glomerular disease related to anti-VEGF therapy. *Kidney Int* 2008; 74: 1487–1491
8. Choi MK, Hong JY, Jang JH *et al.* TTP-HUS associated with sunitinib. *Cancer Res Treat* 2008; 40: 211–213
9. Levey SA, Bajwa RS, Picken MM *et al.* Thrombotic microangiopathy associated with sunitinib, a VEGF inhibitor, in a patient with factor V Leiden mutation. *NDT Plus* 2008; 3: 154–156
10. Bollée G, Patey N, Cazajous G *et al.* Thrombotic microangiopathy secondary to VEGF pathway inhibition by sunitinib. *Nephrol Dial Transplant* 2009; 24: 682–685

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Haemorrhagic shock induced by subcutaneous insulin injection

Sir—A number of chronic kidney disease patients with diabetes receive intensive insulin therapy nowadays, and many of them are also treated for several comorbidities. The combination of insulin therapy and other comorbidities could result in an unexpected complication.

Case

A 61-year-old female with type 2 diabetes and rheumatoid arthritis was admitted to our hospital on February 2009 for the curettage of a knee prosthesis infection. Intensive insulin therapy with 32-gauge tip × 6 mm needles was initiated 3 years previously. She was administered warfarin 1.5 mg for atrial fibrillation, and prothrombin time-international normalized ratio was prolonged to 2.0. Other laboratory tests revealed decreased kidney function (serum creatinine, 124 µmol/L; estimated glomerular filtration rate, 26.3 mL/min/1.73 m²) and normal platelet count (220 × 10⁹/L).



Fig. 1. Abdominal computed tomography shows massive subcutaneous haematoma caused by insulin injection.

One day during her hospital stay, she injected her regular insulin by herself under the surveillance of a nurse in the left lower quadrant of the abdominal wall. Thirty minutes later, a subcutaneous haematoma appeared around the injection site. The haematoma enlarged rapidly despite the strenuous manual pressure performed immediately, and she subsequently developed haemorrhagic shock. Computer tomography detected a massive subcutaneous haematoma (Figure 1). Massive transfusion of 12 units of red blood cells and 12 units of fresh frozen plasma, along with further compression of the abdominal wall, was performed, and her haemodynamics stabilized. Follow-up abdominal angiography, however, did not detect the bleeding artery.

Discussion

Subcutaneous haematoma caused by insulin injection is a very rare complication [1–3]. One report described that inappropriate maneuver of insulin injection triggered haemorrhagic shock [2]. Although our case had several risk factors, such as chronic kidney disease, diabetes, rheumatoid arthritis, post-operative state and usage of warfarin, insulin injection was used properly. The fact that haemorrhagic shock occurred in this case is a warning of possible complications of insulin injection in high-risk patients.

Although fine needles are remarkably thin, therefore considerably reducing the risk of haemorrhage [4], lethal subcutaneous haematoma could happen even in a careful clinical setting.

Conflict of interest statement. None declared.

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1. Monsein LH, Davis M. Radionuclide imaging of a rectus sheath hematoma caused by insulin injections. *Clin Nucl Med* 1990; 15: 539–541
2. Yoshida T, Harayama T, Kusunoki C *et al.* A case of type 2 diabetes mellitus with a giant subcutaneous hematoma caused by rough insulin injection. *J Japan Diab Soc* 2008; 51: 929–932
3. Kahara T, Kawara S, Shimizu A *et al.* Subcutaneous hematoma due to frequent insulin injections in a single site. *Intern Med* 2004; 43: 148–149
4. Arendt-Nielsen L, Egekvist H, Bjerring P. Pain following controlled cutaneous insertion of needles with different diameters. *Somatosens Mot Res* 2006; 23: 37–43

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Renal thrombotic microangiopathy induced by β -interferon

Sir,

We read with interest the recent case report ‘Minimal change disease with interferon- β therapy for relapsing remitting multiple sclerosis’ [1]. In this paper, the authors include renal thrombotic microangiopathy (TMA) among rare side effects of interferon (IFN) therapy, more frequently described with IFN- α [2]. We report here our experience about this topic.

A 36-year-old white female with a 3-year history of multiple sclerosis and normal blood pressure and renal function was admitted for acute renal failure and pulmonary oedema. Three months previously, she started subcutaneous IFN- β -1a treatment of 22 μ g thrice weekly. On admission, physical examination showed high blood pressure and severe pleuropericarditis without neurological or dermatological findings. Laboratory tests revealed microangiopathic haemolytic anaemia. Other immunological and microbiological laboratory tests were unremarkable. A renal biopsy disclosed signs of TMA; among 43 glomeruli, light microscopy revealed focal ischaemic signs and mild mesangial cell proliferation; vessel narrowing with thrombi and thickening of arteriolar walls and intimal onion skin-like swelling; light interstitial lymphomonocytic infiltration and focal tubular atrophy. Immunofluorescence showed mesangial IgM, C1q and fibrinogen staining. A diagnosis of haemolytic–uraemic syndrome was made. She was treated with transfusions, haemodialysis, plasma exchange and methylprednisolone i.v. followed by oral prednisone. Her cardiac function improved, and haematological signs progressively disappeared, but renal function did not recover. IFN- β treatment was discontinued. She is now receiving peritoneal dialysis treatment. IFN- α is known to cause a variety of renal lesions, including TMA [3,4], but to our knowledge, our observation is the first report of TMA induced by INF- β .

Editorial note: This letter had been sent to Aravindan A. *et al.*, but we did not receive a response.

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1. Aravindan A, Yong J, Killingsworth M *et al.* Minimal change disease with interferon-beta therapy for relapsing remitting multiple sclerosis. *NDT Plus* 2010; 3: 132–134
2. Magee CC. Renal thrombotic microangiopathy induced by interferon-alpha. *Nephrol Dial Transplant* 2001; 16: 2111–2112
3. Vacher-Coponat H, Opris A, Daniel L *et al.* Thrombotic microangiopathy in a patient with chronic myelocytic leukaemia treated with α -interferon. *Nephrol Dial Transplant* 1999; 14: 2469–2471
4. Badid C, McGregor B, Faivre JM *et al.* Renal thrombotic microangiopathy induced by interferon- α . *Nephrol Dial Transplant* 2001; 16: 846–848

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Membranous glomerulonephritis with superimposed ANCA-associated vasculitis: another case report

Dear Sir,

We report here another case of primitive membranous nephritis with superimposed anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, in addition to 10 cases recently reported by Nasr *et al.* [1]. This association has since been reported in relation with systemic lupus erythematosus, hepatitis B or C virus infection and treatment with penicillamine, hydralazine and propylthiouracil [2–5].

A 67-year-old Caucasian male was presented at the emergency department with anorexia, nausea and vomiting. Routine laboratory tests revealed severe renal failure and a consultation with a nephrologist was requested. Blood pressure was 170/100 mm Hg, and urine output over 24 h was 2.2 L. Medical history was remarkable for hypertension (in treatment with β -blockers) and possible upper respiratory infection about 4 weeks before admission (treated with amoxicillin 2 g/day orally). Urinalysis revealed haematuria (+++) and non-selective proteinuria (4.8 g/24 h), in front of seric albumin levels of 2.6 g/dL. Skin examination revealed no significant lesions.

LAC, ANA, anti-DNA, ENA, HBsAg, anti-HCV, cryoglobulins, complement levels, ANCAs and serum protein electrophoresis were normal. Perinuclear ANCA was positive at 1:40.

A renal biopsy was performed, and sampling for LM included 11 glomeruli, three of which were globally sclerotic. Light microscopy revealed the presence of extracapillary proliferation which compressed the glomerular tuft and vasculitis with fibrinoid necrosis of the arterial wall. Cellu-