CASE REPORT

Retroperitoneal haematoma associated with enoxaparin use in an elderly woman with chronic kidney disease

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SUMMARY

An 81-year-old woman with chronic kidney disease was on enoxaparin (1 mg/kg subcutaneously two times a day) for 4 months to manage pulmonary embolism. While admitted for diagnostic evaluation of frequent falls, transient ischaemic attacks and pain management, she developed vomiting, diarrhoea, melena and hypotension. Her estimated glomerular filtration rate decreased from an admission value of 34 mL/min/1.73 m² to 13 mL/min/1.73 m². CT scan showed retroperitoneal haematoma. She was placed in intensive care and stabilised with aggressive fluid replacement, blood transfusion, and discontinuation of enoxaparin and concomitant aspirin. We attribute this major bleeding to enoxaparin use in an elderly woman with chronic kidney disease and concomitant aspirin intake. We will review reported cases of enoxaparin-associated retroperitoneal haematoma. We suggest that enoxaparin be used with caution in elderly patients with chronic kidney disease, and stress that treatment monitoring and reversal may not be readily available.

BACKGROUND

Enoxaparin, a low-molecular-weight heparin (LMWH), needs to be used with caution among elderly patients with chronic kidney disease. This is because, first, enoxaparin is primarily excreted through the kidneys. Consequently, in severe renal insufficiency, enoxaparin's peak anticoagulation (anti-factor Xa) level is higher and the risk of bleeding greater.¹ Second, the elderly have kidney functions that could rapidly fluctuate with acute conditions. Enoxaparin prescribed for elderly patients with moderate renal insufficiency could quickly turn into an overdose in conditions compromising renal function (for example, in acute dehydration). Hence, the dosage of enoxaparin in the elderly needs to be adjusted to changing health conditions.

We will describe an enoxaparin-associated retroperitoneal haematoma in an elderly woman with chronic kidney disease. We will review reported cases and summarise recommendations for enoxaparin use in chronic kidney disease. We aim to increase awareness of the possibility of serious bleeding associated with enoxaparin use in the elderly.

CASE PRESENTATION

An 81-year-old woman was admitted to an acute care hospital for diagnostics on frequent falls, pain

management for spinal disease and physical rehabilitation. She had other comorbidities including chronic kidney disease, hypertension and type 2 diabetes mellitus, as well as a history of diverticulitis, anaemia and transient ischaemic attacks. She also had a pulmonary embolism 4 months prior to admission, for which she had been treated and maintained on enoxaparin (1 mg/kg subcutaneously two times a day). Her other medications included aspirin (81 mg), ferrous sulphate, neutral protamine Hagedorn (NPH) insulin and metformin, oxycodone and acetaminophen and hydromorphone, gabapentin, mirtazapine, levothyroxine, zopiclone and lorazepam, valsartan, and pantoprazole and domperidone.

On admission, her laboratory results were consistent with chronic kidney disease and anaemia. She had a creatinine of 129 µmol/L (normal 50–105 µmol/L) and an estimated glomerular filtration rate (eGFR) of 34 mL/min/1.73 m² (normal >59 mL/min/1.73 m²). Based on these parameters, she was classified as having chronic kidney disease with moderately to severely decreased glomerular filtration rate (category G3b).² Her haemoglobin was below normal at 114 g/L (normal 120–160 g/L).

The patient's hospitalisation was uneventful until the fourth hospital day, when she developed vomiting, diarrhoea, melena and hypotension. An abdominopelvic CT scan showed a large retroperitoneal haematoma extending along the left iliopsoas muscle and into the pelvis (figure 1). The acute blood loss was consistent with other laboratory results: her haemoglobin dropped to 60 g/L;

Figure 1 Abdominopelvic CT scan (cross-sectional plane): large left retroperitoneal haematoma (delineated by arrows) along the left iliopsoas muscle. The haematoma extended into the pelvis.

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creatinine increased to 304 µmol/L; and eGFR dropped to 13 mL/min/1.73 m². The assay for anti-factor Xa was not available.

DIFFERENTIAL DIAGNOSIS

We attributed the retroperitoneal haematoma to the use of enoxaparin in an elderly patient with chronic kidney disease and concomitant use of aspirin. Other surgical causes of the haematoma, such as ischaemic colitis, were ruled out by the CT. A remote possibility could be a fall that the patient had suffered while ambulating to the washroom. However, the severity of the fall was minor and assessed to be non-remarkable to the development of retroperitoneal haematoma.

TREATMENT

We immediately discontinued the enoxaparin and aspirin. The patient was placed in intensive care, and had aggressive volume replacement and transfusion of 4 units of packed red blood cells. We did not administer protamine because it was not available. The haematoma did not require surgery.

OUTCOME AND FOLLOW-UP

Supportive care was provided until the patient's renal function recovered. She was subsequently discharged to a continuing-care facility.

DISCUSSION

A PubMed search and subsequent cited-reference search yielded 36 reported cases of retroperitoneal haematoma associated with enoxaparin use (see online supplementary appendix 1). The cases had a mean age of 71 years±10 (range 29–86 years), with 53% having some degree of renal insufficiency. In 61% of cases, enoxaparin was given with concomitant aspirin or other non-steroidal inflammatory drugs, antiplatelet drugs, or other anticoagulants. Monitoring for anti-factor Xa was reported in only one case. Protamine was used to reverse enoxaparin in only five cases. Seven cases (19%) underwent surgery and two had embolisations. The haematoma was fatal in 33% of the cases.

Enoxaparin dose reduction is recommended in chronic kidney disease.^{1–3} The American College of Chest Physicians (ACCP)⁴ recommends that enoxaparin be avoided in severe renal insufficiency (creatinine clearance <30 mL/min). However, if enoxaparin is to be used, the ACCP recommends a dose reduction of the therapeutic dose to 50% the usual dose (ie, 1 mg/kg once daily instead of two times a day).⁵ The American Society of Hematology (2014) also cautions on the use of LMWH in severe renal insufficiency.⁶ Neither of these organisations have recommendations for enoxaparin use in patients with creatinine clearance above 30 mL/min.

Coagulation monitoring is not required for most patients on LMWH but is suggested in patients who have renal insufficiency.⁵ An enoxaparin monograph also recommended monitoring for bleeding among elderly patients.³ Activated partial thromboplastin time (APTT) should not be used to measure enoxaparin's anticoagulation effect.⁷ Rather, when monitoring

is required, anti-factor Xa level is the recommended test.^{5–7} However, anti-factor Xa assay may not be available.

When bleeding does occur, reversing LMWH is a challenge. Protamine may or may not be beneficial.⁵ Protamine (1 mg per 1 mg enoxaparin in previous 8 h) may only provide 60–80% reversal of LMWH.⁶ This is in contrast to protamine's 100% reversal of heparin. Additionally, recombinant activated factor VII, when available, may be beneficial.⁷

With an increasing elderly population, coupled with a 25–30% prevalence of kidney disease in the elderly,^{8–9} the use of enoxaparin needs to be judicious.

Learning points

- ▶ Retroperitoneal haematoma has been associated with enoxaparin use in elderly patients with chronic kidney disease and concomitant medications.
- ▶ Enoxaparin's anticoagulation effects may not be readily monitored and reversed.
- ▶ The use of enoxaparin in the elderly needs to be judicious, considering that they have an increased prevalence of renal disease and are prone to rapidly fluctuating renal function.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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