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Dabigatran is a direct thrombin inhibitor licensed for treatment of venous thromboembolism and in stroke prevention for patients with non-valvular atrial fibrillation. It can be rapidly reversed when clinically indicated with idarucizumab, a humanised monoclonal antibody fragment.¹

A 64-year-old male taking dabigatran 110 mg daily for management of atrial fibrillation presented with abdominal pain and acute kidney injury. On presentation he was found to have a markedly elevated dabigatran concentration of 2230 ng/mL and deranged coagulation profile with a thrombin time of >200 seconds (RR 10–12 seconds) and INR of 11.2. Idarucizumab 5 g was administered and continuous renal replacement therapy commenced for persistent bleeding from a central line. However repeat dabigatran concentration performed 6 hours following idarucizumab administration had increased to 3722 ng/mL. A further dose of idarucizumab 5 g was administered 14 hours following the initial dose. Dabigatran concentration performed 4 hours following the second dose was 1787 ng/mL.

This case highlights a markedly elevated dabigatran concentration with significant coagulopathy in the context of kidney impairment and possibly concomitant amiodarone use. Despite idarucizumab the dabigatran concentration was markedly elevated, indicating idarucizumab resistance. Although uncommon, idarucizumab resistance must be excluded by repeat dabigatran concentration testing, particularly when the initial dabigatran concentration is elevated and/or kidney impairment.

Reference

1. Pollack CV Jr, Reilly PA, van Ryn J. Idarucizumab for dabigatran reversal—full cohort analysis. *N Engl J Med* 2017; 377: 431–41.

HYPEREOSINOPHILIA IN A PATIENT WITH REFRACTORY ECZEMA AND ALK-NEGATIVE ANAPLASTIC LARGE CELL LYMPHOMA

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A 41-year-old man with refractory eczema on immunosuppressants developed swinging fever and dyspnoea, with left pleural effusion and left axillary and groin lymphadenopathy (2–3 cm) found in physical examination. Clinically there was no eczema flare-up.

Laboratory tests showed hypereosinophilia ($79.1 \times 10^9/L$) and elevated LDH (520 U/L) and ALP (187 U/L). Some dysplastic eosinophils showing hyposegmented nuclei and hypogranular cytoplasm were noted on blood smears. Workup for parasites, allergy and autoimmune markers was unremarkable.

Thoracentesis yielded exudative effusate with numerous lymphocytes (WBC $>1000/mm^3$) but no malignant cell was evident. FNAC of lymph nodes found eosinophilic infiltrate only. Bone marrow examination revealed marked eosinophilia with similar dysplastic features and megakaryocytic hyperplasia, raising suspicion of myeloproliferative neoplasms. Karyotyping, molecular tests for JAK2 mutation and BCR-ABL1 fusion, and FISH for FIP1L1-PDGFR, PDGFRB and FGFR1 rearrangements were unremarkable.

Excisional biopsy of left groin lymph node was then pursued and demonstrated sheets of pleomorphic neoplastic cells with focal 'hallmark cells'. Anaplastic large cell lymphoma (ALK⁻ CD30⁺CD3⁺CD8⁺) was diagnosed. PET/CT scan revealed a stage-IV disease with extensive supra- and infra-diaphragmatic hypermetabolic lymph nodes and multiple bone involvements. The patient opted for brentuximab vedotin plus combination chemotherapy.

This case underscores the importance of exhaustive investigations and clinicopathological corroboration in the workup of hypereosinophilia.

NEUTRALISATION OF RIVAROXABAN INTERFERENCE ON APCR, FVIII AND FIX ASSAYS BY DOAC-STOP AND ANDEXANET ALFA

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Rivaroxaban is a widely utilised direct oral anticoagulant (DOAC), indicated for thrombosis treatment and prevention. Rivaroxaban binds to Factor Xa, affecting many haemostasis assays, including activated protein C resistance (APCR) and APTT based factor assays, including factor VIII (FVIII) and IX (FIX). Andexanet alfa is a clinical 'antidote' for anti-Xa agents, including rivaroxaban, neutralising activity *in vivo* and *in vitro*. DOAC-Stop is a commercial product that neutralises *in vitro* activity of DOACs.

We investigated whether rivaroxaban would induce false positive APCR and/or falsely reduced FVIII and FIX activity, and whether this could be neutralised by andexanet alfa or DOAC-Stop.

Four lyophilised plasma samples were prepared: normal plasma, and normal plasma spiked with rivaroxaban (200 ng/mL); rivaroxaban + DOAC-Stop; rivaroxaban + andexanet alfa. These were distributed to laboratories performing APCR and/or FVIII and FIX testing in RCPAQAP surveys. Data was analysed using robust statistics (mean, SD and CV).

In rivaroxaban 200 ng/mL samples, most APCR assays appeared largely unaffected, while FVIII and FIX assays showed a substantive reduction. Where assays were affected, DOAC-Stop neutralised rivaroxaban effects. Andexanet alfa did not completely neutralise the rivaroxaban effect, for APCR or FVIII and FIX, and unexpectedly lead to higher rates of false APCR than rivaroxaban alone.

THE CHANGING FACE OF TESTING FOR ACTIVATED PROTEIN C RESISTANCE (APCR) – A 10-YEAR RETROSPECTIVE

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Activated protein C resistance (APCR) is a hypercoagulable condition that increases the risk of venous thrombosis. The Royal College of Pathologists of Australasia Quality Assurance