Letters to the editor

OVERVIEW

Please submit letters for the editor's consideration within 3 weeks of receipt of *Clinical Medicine*. Letters should ideally be limited to 350 words, and sent by email to: clinicalmedicine@rcplondon.ac.uk

Adverse reactions

Editor – I read with interest 'Lesson of the month 1: A rare adverse reaction between flucloxacillin and paracetamol', published in March's *Clinical Medicine*, and write with a similar case seen recently in our institution, to further highlight this issue. In addition, although the diagnostic test of choice (urinary organic acids) was unavailable locally we were able to confirm the diagnosis by liaising with another hospital laboratory within our region.

An 80-year-old patient with left leg cellulitis and a non-drainable calf abscess, requiring a 3-week course of intravenous flucloxacillin, developed marked hypokalaemia and was found to have a severe, high anion-gap metabolic acidosis (pH 7.16, bicarbonate 7.4 mmol/L, base excess -22.4 mmol/L, serum anion gap 30 mmol/L), without acute kidney injury. Pyroglutamic acidosis was suspected and flucloxacillin and paracetamol were discontinued, and N-acetylcysteine was administered. The acidosis resolved over the course of several days. Urinary organic acid testing was performed at another hospital in the region, showing grossly increased levels of pyroglutamic acid, which had resolved when a repeat specimen was sent 9 days later. ■

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Reference

1 Osborne W, Chavda A, Katritsis G, Friedland JS. Lesson of the month 1: A rare adverse reaction between flucloxacillin and paracetamol. *Clin Med* 2019:19;127–8.

Pulmonary embolism

Editor – The article on acute pulmonary embolism by L Howard covered most of the key areas of difficulty in managing patients presenting with a possible pulmonary embolism (PE),[1] however the questions in the self-assessment continuing medical education (CME) were not very clear and in some cases contradict national guidelines.

Doppler ultrasound of the leg veins was recommended in investigating PEs in the pregnant patient, and in the CME was recommended in the absence of calf pain. The Royal College of Obstetricians and Gynaecologists guidelines were updated in 2015 to only recommend this investigation in patients with symptoms and signs of deep vein thrombosis (DVT).[2] This is because of the high likelihood of false negative results as the patients have a higher incidence of isolated iliac vein DVT, or no DVT at all – in one case series, Chan *et al* found no cases of DVT in 67 women presenting with suspected PE.[3]

Another CME question highlights the difficulties with both the Wells score and cancer investigations. In Q10, one answer states a negative d-dimer would not avoid the need for a computed tomography pulmonary angiogram or ventilation–perfusion scan. This double negative means the Wells score has to be 'unlikely' for a suspected pulmonary embolism for this answer to be incorrect. The patient has a tachycardia of 108 beats per minute (1.5 on the Wells score) and there are three points available for whether a PE is considered the likely diagnosis or equally likely – which would take the score over four and therefore make a suspected PE 'likely'.

This is the most difficult part of the Wells score and the terminology of this phrase varies. Wells originally described it as 'the presence of an alternative diagnosis that was as likely, or more likely than pulmonary embolism to account for the patients signs and symptoms' and went on to say it was possible to enrol a patient (into the study) with an alternative diagnosis of pneumonia if the physician still thought a PE could not be ruled out.[4] In Q10 it is debateable whether a patient with chronic obstructive pulmonary disease (COPD) who describes 2 days of worsening dyspnoea and right sided chest pain, coughing up more clear sputum with some blood in the sputum can clearly be described as having an exacerbation of COPD without considering a PE – it would be helpful to know if they usually have a cough, their baseline saturations etc and patients with COPD are recognised to have as high a risk for venous thrombo-embolic (VTE) disease as the oral contraceptive pill and cancer (odds ratio between 2 and 9).[5] Therefore, if the clinician thought that PE could not be ruled out then a negative d-dimer would not avoid the need for further investigations.

The same question has the correct answer as 'if he is found to have a PE, he should have a computed tomography (CT) of the abdomen and pelvis'. While this may seem pedantic, the 2012 National Institute for Health and Care Excellence (NICE) guidelines (updated in 2015) only recommend that cancer screening be 'considered'.[6] The article was clearer on this distinction, but this remains an area under discussion. In 2012, the guideline group based this recommendation predominantly on the significant difference in VTE management of patients with cancer compared to those without cancer, both in terms of choice of anticoagulants and duration of anticoagulation, and the impact of this on VTE recurrence rates. They also concluded that patients might want to undergo further investigation knowing that the risk of cancer is 1 in 10 patients.

Subsequent studies suggest that the occult cancer rate may not be this high, (nearer 5% over a 30 month follow-up in one large prospective study).[7] The 2018 Cochrane review found insufficient evidence to support this strategy.[8] A UK cohort study reported that none of the CT abdomen/pelvis done as per the 2012 NICE recommendations for occult cancer screening in patient with unprovoked VTE revealed any occult cancer over a median follow-up period of 22 months.[9]

Clinicians should keep a low threshold for suspicion for cancer in patients presenting with unprovoked VTEs, and all patients should undergo a thorough medical history, examination, baseline laboratory blood tests and a chest X-ray if they did not undergo any chest imaging. There are further tools being developed to identify subsets of patients who would benefit from extensive screening, although they are not yet validated.[10] An example of this is the RIETE prediction score in which, one point is assigned for male sex, chronic lung disease, or raised platelet count; two points are assigned for age >70 years or anaemia; and points are deducted for a postoperative or a prior VTE.[11] ■

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References

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