CASE 4: DRUG INTERACTIONS

History

A 24-year-old woman presented to the hospital with lower abdominal pain and vomiting. She reported that the symptoms had developed suddenly, approximately 45-min earlier. She had felt well earlier in the day and denied any other symptoms. She had eaten some toast for breakfast and nothing since. She had not experienced any diarrhoea and had no contacts with similar symptoms. Her past medical history included gastro-oesophageal reflux disease and a recent diagnosis of pulmonary tuberculosis, for which she was being treated currently. Her regular medications included: isoniazid, rifampin, pyrazinamide, omeprazole and the combined oral contraceptive pill. She worked as a salesperson and did not smoke, drink alcohol or take recreational drugs.

Examination

The patient appeared pale and distressed. Her heart rate was 140 bpm and her blood pressure was 106/74 mmHg. Her abdomen was generally tender, with particularly pain over the right iliac fossa, with guarding present.

Results

Bloods: WCC 14.2, Hb 105, Plt 460, Na 135, K 3.8, Creat 60, CRP 122

Urine dip: positive for leucocytes, and positive for the beta subunit of human chorionic gonadotropin (hCG)

Questions

1. What diagnoses should be considered for this young woman presenting with sudden-onset right iliac fossa pain?
2. Are there any potential interactions from her medication history that should be considered?

ANSWERS

1. There is a broad differential diagnosis for right iliac fossa pain. Assuming the patient has no past history of appendicectomy, appendicitis is one of the likely diagnoses and an urgent ultrasound or CT scan of the patient's abdomen should be arranged to look for signs of this.

   Pyelonephritis is a common cause of abdominal pain and vomiting and occurs more frequently in female patients. This patient's blood tests show elevated inflammatory markers and her urine dip is positive for leucoyctes, which may indicate a urinary tract infection. The patient has not reported dysuria or fevers, however, and pain from pyelonephritis typically has a gradual onset, rather than a sudden onset as with this case. Renal colic is another possibility, although patients typically complain of pain radiating from the flank to the groin, which comes on in spasms. The presence of renal stones usually results in red blood cells being detected on the urine dipstick test also.

   The patient has a positive pregnancy test (hCG present on the urine dip) and thus the most important diagnosis to exclude is an ectopic pregnancy, where the fertilised egg has implanted outside the uterus, usually in the fallopian tube. As the ectopic pregnancy progresses, the fallopian tube can rupture requiring emergency surgery.

2. The patient is taking the oral contraceptive pill, which has a 9**%** annual pregnancy rate with typical use, and less than 1**%** annual pregnancy rate with correct use. The effectiveness of both the combined (contains an oestrogen and a progester- one) and the progesterone-only oral contraceptive pill, as well as the etonogestrel-releasing contraceptive implant, are considerably reduced by co-administration of drugs that induce hepatic enzyme activity.

   Such medications promote upregulation of the hepatic cytochrome P_{450} system, thus increasing the rate of metabolism of other drugs that are metabolised by cytochrome P_{450}, including most hormonal oral contraceptives.

   This case highlights the importance of reviewing potential drug interactions whenever a new medication is commenced, and considering methods to reduce the impact of this. In this situation, the patient needed treatment for pulmonary tuberculosis with the enzyme-inducing drug, rifampicin, and should thus have been advised to consider alternative methods of contraception, such as condom use or intra-uterine device insertion, to reduce the chance of pregnancy. You should ideally take the opportunity to review a patient's drug history at every new clinical encounter and consider potential interactions between their medications. As the use of electronic prescribing increases, prescribers are now often automatically alerted to potential drug interactions when they prescribe a medication, thus reducing the risk of harm to patients.

Key Points

1. The efficacy of many oral contraceptive agents is reduced by co-administration of drugs that induce hepatic enzyme activity.
2. As a prescriber, you should review potential drug interactions whenever a new medication is commenced, and consider methods to reduce the impact of this.

REFERENCE

Layne, Kerry, and Albert Ferro. *100 Cases in Clinical Pharmacology, Therapeutics and Prescribing*. Boca Raton, FL, CRC Press, Taylor & Francis Group, 2020.