A case of green urine due to a traditional Chinese medicine containing methylene blue

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Abstract
Abnormal discolouration of the urine is always alarming to the patient and intriguing to physicians. Green colouration in urine can be of endogenous or exogenous aetiology. We present a case of green urine caused by a side effect of a traditional Chinese medicine (TCM) containing methylene blue, an uncommon occurrence. This case also highlights the importance of thorough history taking from the patient, especially diet and medications. Simple analysis in the clinical biochemistry laboratory can play a role in avoiding other expensive and unnecessary investigations.

Case report
An 86-year-old female presented to the Accident & Emergency Department with a 2-day history of inability to pass urine, dysuria, suprapubic pain, and constipation. Her past medical history included diabetes mellitus, ischaemic heart disease, hypertension, hyperlipidaemia, chronic renal failure, and congestive cardiac failure. Physical examination was remarkable of an elderly lady in mild dehydration, afebrile, stable blood pressure of 110/70 mmHg and a palpable bladder.

The patient was on the following medication: tolbutaminde, isosorbide dinitrate, carvedilol, omeprazole, aspirin, ezetimibe, simvastatin, frusemide, and potassium chloride.

On further questioning, the patient’s daughter revealed the patient had been taking a traditional Chinese medicine (TCM) known as Wilisan pills for the past 2 months prior to admission. The content of a Wilisan pill was identified as follows: extract buchu 15 mg, extract uva ursi 15 mg, and methylene blue 15 mg. The following urine sample was received in the clinical biochemistry laboratory (Figure 1).

Figure 1. Green urine sample
Discussion

Normal freshly voided urine appears amber-yellow, is sterile and clear, and has an average slightly acidic pH of 6.0 and a characteristic odour.

Abnormal discolouration of urine can indicate an underlying pathogenic or benign condition. Most frequently, the abnormal discolouration of urine is caused by gross haematuria, where a pink to red-brown urine is encountered. Green urine encountered in our case is an uncommon occurrence.

Green colouration in urine can be of endogenous or exogenous aetiology. It must be noted that blue compounds may appear green or blue-green in the urine, due to presence of urochrome which is a major yellow pigment in the urine.

Endogenous causes include pathological conditions such as chronic obstructive jaundice where presence of biliverdin (oxidation product of bilirubin) in urine can give a green hue. Urinary tract infection caused by *Pseudomonas* can turn urine green due to pyocyanin and pyoverdin pigments produced by the bacterium.  

A rare inherited metabolic disorder known as the Blue Diaper Syndrome in which there is tryptophan malabsorption, can also give rise to blue-green urine. In this metabolic disorder, excessive production of indoles from bacterial metabolism of unabsorbed tryptophan leads to indicanuria where tryptophan indole metabolites cause a blue-green colouration in urine.

Exogenous causes of green urine are more likely causes and are mostly due to oral or intravenous administration of certain compounds. Some medications can give rise to green urine. Certain phenol-containing drugs have the disposition to cause green urine due to phenol metabolites excreted in urine.

Propofol, a commonly used phenol-containing intravenous anaesthesia drug has been reported to give green colouration in urine. Other phenol-containing drugs of the same green urine effect are cimetidine and promethazine. In addition, a number of other medications such as triamterene, indomethacin, methocarbamol, magnesium salicylate and the antibiotic rinsapin can produce green to blue-green urine as possible side-effects.

Water-soluble artificial dyes can cause green urine. Food dye FD&C blue no. 1 has been reported to give green urine when it was added to enteral feed during tube feeding. Other benign artificial dyes such as indigo carmine, methylene blue (methylthioninium chloride) and indigo blue can be filtered in the urine causing a green colouration.

Of these, methylene blue is a well-known culprit of causing green or blue-green urine. In medicine, methylene blue is used as a contrast dye and also for treating conditions such as cyanide poisoning and methaemoglobinemia. Multi-ingredient medications containing methylene blue either as pigment or treatment purposes can potentially colour urine green.

Methylene blue excretion in the urine is slow; with bulk of the dye is excreted as a stabilized form leucomethylene blue and the remainder as unchanged methylene blue.
In our case, methylene blue was found to be a component of a traditional Chinese medicine (TCM) pill which the patient was consuming.

Samples of the patient’s green urine and a few Wilisan (TCM) pills were sent to the clinical biochemistry laboratory for investigation. A spectrophotometric scan was performed on the patient’s green urine sample (Figure 2). An absorbance maximum at around $\lambda = 660$ nm was found.

Spectrophotometric scans were also performed on a normal control urine sample (Figure 3), and on a normal control urine sample spiked with dissolved Wilisan pill in water (Figure 4). The absorbance peak of 660 nm was absent in the normal urine sample but present in the other two spectra. Absorbance spectrum of the green urine resembled closely to that of the dissolved pill, strongly suggesting the presence of the contents of the pill in the urine.

Methylene blue absorbs light at a wavelength of 550–700 nm, with a preferential maximum absorbance at 660 nm and 609 nm (shoulder peak). Presence of these two peaks in the green urine sample and Wilisan pills confirm the presence of methylene blue in both.

**Figure 2. Absorbance spectrum of green urine sample**
Figure 3. Absorbance spectrum of a normal urine sample
Other significant investigation findings include a urine culture positive for *E. coli*. pH of urine measured was 7.8 at time of collection. Urine bilirubin was negative.

Lessons learnt from this case include excluding the endogenous and exogenous causes of green urine through a careful examination of the patient’s clinical history, diet and medications. The patient was managed by discontinuing the offending drug, in this case the TCM and treating the urinary tract infection with appropriate antibiotics.

On review at the outpatient clinic 2 months later, the green urine had cleared.

Abnormal discolouration of the urine is always alarming to the patient and intriguing to physicians. In this case, green urine was caused by a side effect of a TCM drug containing methylene blue. In patients suffering from chronic renal failure as in our case, excretion of methylene blue in urine could be compromised. Although methylene blue is a harmless dye, it is not known if chronic accumulation of the dye would be benign or potentially toxic in patients with compromised renal function.
This case brings to our awareness that not all abnormal discolourations in urine are pathologic. Moreover, careful history-taking and the physician’s awareness of potential side effects of medications as well as a quick, simple analysis in the clinical biochemistry laboratory had merit in avoiding unnecessary and expensive investigations.

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**References:**