Iloprost-induced rash

We report a 59-year-old woman with a background history of CREST syndrome (calcinosis, Raynaud phenomenon, oesophageal dysmotility, sclerodactyly and telangiectasia) and secondary pulmonary hypertension who presented with a bilateral lower limb vasculitic rash.

She was previously admitted to hospital with pain in her back and limbs, which did not respond to analgesia. A couple of weeks earlier she had been initiated on nebulised iloprost (Ventavis; Bayer New Zealand, Auckland, New Zealand) for progression of her pulmonary hypertension while on treatment with Sildenafl. She started on 20 μg three times a day, increasing every 3 days to a total of 20 μg every 4 h. Within a few days of reaching the maximum dose she developed a painful vasculitic rash over both lower limbs, which did not respond to analgesia and emollients (see fig 1). The dose of iloprost was reduced slowly over a couple of weeks to 15 μg three times a day. During this time, the rash improved considerably.

Unfortunately, she continued to deteriorate and was admitted to hospital profoundly hypoxic. Oxygen therapy and diuretics were increased with minimal effect. The decision was made to re-challenge with an increased dose of iloprost, hoping that dual therapy with appropriate dosing may ameliorate her pulmonary hypertension.

After only two doses at 20 μg, the rash recurred dramatically and became intolerable. On reducing the iloprost dose to 15 μg, the rash again improved. She was discharged home with assistance from palliative care and died a week later.

Iloprost is a stable analogue of prostacyclin which is synthesised in the vascular endothelium, and it shows a pharmacological profile similar to that of endogenous prostacyclin. Its vasodilating effects are used clinically to treat moderate to severe pulmonary hypertension.

Various side effects of iloprost have been reported, including flushing, dizziness, cough, headache, spasm of the jaw muscles, back pain, vomiting and diarrhoea.

Bleeding events were common in clinical trials, especially in patients also taking antiagulants. Iloprost is known to interfere with platelet aggregation; however, this effect is more common and more pronounced with intravenous use. Of note, our patient did not develop thrombocytopenia.

Cutaneous drug reactions are common, with an incidence of 2–5% in hospital patients. Almost any drug can cause rash; most common are antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs). Drug-induced small vessel vasculitis (or hypersensitivity vasculitis) is rarer. This is generally limited to the skin, but can occur as an element of a systemic illness. The rash is purpuric, palpable and occurs in dependent areas. Biopsies show a cellular infiltrate of small vessels often with leucocytoclasia. The most common causes are drugs and infection.

Adverse drug reactions can be difficult to diagnose, and scoring systems may help. In our patient the vasculitic rash appeared after initiation of iloprost and improved when the dose was reduced. More importantly, it deteriorated with a repeat drug challenge. This gives a high probability of a drug reaction. In a different clinical scenario, cessation of the drug may well result in complete resolution of the rash.

To our knowledge, this is the first reported case of iloprost-induced vasculitic rash. The precise mechanism and frequency are unknown. Clinicians should be aware of this potential adverse effect, and the drug should be reduced or stopped if possible.
Hepatotoxicity and antituberculosis therapy: time to revise UK guidance?

Hepatotoxicity associated with antituberculosis therapy is an important clinical problem. Guidelines recommend baseline liver function tests (LFTs) before commencing treatment. In patients with risk factors for hepatotoxicity (ie, chronic viral hepatitis or liver disease, pregnancy or significant alcohol history) or abnormal baseline LFTs, further monitoring is indicated whilst on treatment. In patients with risk factors for hepatotoxicity and the use of the recombinant DNA hepatitis B vaccine, the incidence of hepatitis B virus infection was 10% (5/51). When HIV-positive individuals were excluded, this fell to 2% (1/44). Furthermore, all three subjects who were asymptomatic at the time of their rise in ALT/AST were HIV co-infected.

In conclusion, most cases of hepatotoxicity continue to be identified by current guidelines, although HIV coinfection does appear to impact upon both the incidence of hepatotoxicity and the use of the recommended algorithm (where LFT monitoring on treatment is indicated according to symptoms). The 1998 British Thoracic Society guidance implies that testing for viral hepatitis should be undertaken at tuberculous diagnosis. Our results suggest that routine HIV testing would identify patients not only requiring treatment for HIV but also at risk of hepatotoxicity.

Although a small sample size, we believe our findings will be reproducible in other tuberculous populations, and that this strengthens the argument for HIV testing to be offered universally in this setting; an approach which avoids “risk assessment” for HIV, which in itself can generate anxiety and stigma.

REFERENCES

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R S Finn, L Beckert and R Troughton

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