Unexpected outcome (positive or negative) including adverse drug reactions

Peripheral oedema as a side-effect of fluticasone

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A 14-year-old girl had experienced gross peripheral oedema for nearly 2 years. She was under review by several paediatric specialists for a variety of problems. Her local paediatric team were unable to find the cause of her oedema, despite extensive investigations. Eventually, her mother discovered the cause was inhaled fluticasone, prescribed at normal dosage for asthma. As far as the authors are aware, this is the first reported case of peripheral oedema associated with the use of fluticasone. Peripheral oedema is a rare side-effect of fluticasone in the form of either seretide or flixotide. Physicians should be aware of this possibility in cases of resistant peripheral oedema with no other identified cause.

BACKGROUND

Fluticasone is an inhaled corticosteroid commonly used to treat asthma, chronic obstructive pulmonary disease and rhinitis. Fluticasone propionate is the active ingredient in flixotide and, together with salmeterol, in seretide. Both are made by Allen and Hanburys, who also make flixonase, a nasal-spray preparation of the drug.

Side-effects are generally uncommon. Occasionally, patients develop oral thrush and can also experience an allergic reaction, joint swelling or indigestion. Rarely, anxiety or sleep disorders may occur, or those using the medication, usually only in high doses, can exhibit systemic signs of steroid use, such as Cushing's syndrome, adrenal suppression or reduced growth velocity.¹

There are rare reports (<1 in 10 000) of facial angio-oedema.² However, as far as we are aware, this is the first reported case of peripheral oedema associated with the use of fluticasone.

CASE PRESENTATION

A 14-year-old girl with a complex Cantu-like syndrome (microcephaly, dwarfism, keratosis follicularis) had gross, pitting, peripheral oedema for nearly 2 years.

She was under review by several different paediatric specialists for a number of problems. Her past medical history included resolved hypertrophic cardiomyopathy, asthma, a previous Sinding-Larsen syndrome, hypertrichosis (also now resolved), hirsuties with facial acne and a previous episode of airway obstruction with vocal-cord paresis.

During pregnancy, the patient's mother, 34 years old at the time, had developed polyhydramnios. A diagnosis of Beckwith-Wiedemann syndrome was made antenatally.³ At term, an emergency lower-segment caesarean section was performed due to fetal distress. The baby required resuscitation with bag and mask ventilation at delivery but responded well, with Apgar scores assessed as 5 at 1 min and 8 at 5 min. She was admitted to the special care baby unit directly from the delivery suite where it was noted that she had low-set ears and was macrosomic. The earlier

diagnosis of Beckwith-Wiedemann syndrome was questioned because she did not have the characteristic appearance. She has since gone on to develop a number of other clinical signs through childhood and adolescence that would also suggest an alternative syndrome. She had been reviewed by several geneticists at three specialist centres; however, a unifying diagnosis has not been established.

At around 12 or 13 years of age she began to develop pains in her right hip and knee. A diagnosis of juvenile arthritis was considered but ruled out. She had started gaining weight through eating more, and her body mass index rose to 22. Eventually, she was diagnosed with Sinding-Larsen syndrome. This resolved with conservative management.

Hypertrophic cardiomyopathy had been diagnosed using echocardiography during childhood. This had never been clinically manifest, and she continued to be cardiovascularly normal on frequent tertiary review.

She had mild asthma – not severe enough, however, to require hospital admission – and acne.

The only medications taken by the patient were seretide, occasional salbutamol, frusemide and minocycline.

At about the age of 13, she started to develop pitting oedema in both legs.

INVESTIGATIONS

Her previous diagnoses were re-examined. It was considered whether this could be a sign of cardiovascular decompensation, part of a rheumatological problem, or even another constituent of her unusual syndrome. Possible new diagnoses were also considered.

Echocardiogram and joint x-rays were unremarkable. Blood tests, including antinuclear antibodies, rheumatoid factor and extractable nuclear antibodies, were all normal. Liver and renal function were investigated with blood and urine screens – all results were within normal limits. Abdominal ultrasound with Doppler revealed no mass or suggestion of vascular compression as a cause.

TREATMENT

The development of such obvious peripheral oedema was extremely distressing for this adolescent girl. While investigations failed to enlighten the team as to the cause of her oedema, measures were taken to try and alleviate her symptoms. She tried taking furosemide 5 mg on alternate days. She was advised by staff at the lymphoedema clinic to try compression stockings. She also tried keeping her legs elevated for periods of time through the day. None of these interventions was helpful.

OUTCOME AND FOLLOW-UP

Throughout this time she had been undergoing treatment for mild to moderate asthma. She had experienced wheeze, mainly with colds, from the age of 3 years. She had been treated on and off with fluticasone, budesonide and prn salbutamol.

Her mother, who has no formal medical training, in an attempt to find a cause for her daughter's oedema, had checked the side-effect profile on the literature accompanying seretide. This mentioned swelling (in the context of facial angioedema). She therefore stopped and restarted fluticasone on three occasions (in the form of either seretide or flixotide). Each time she stopped treatment the oedema improved over the course of 1–2 weeks, but her daughter became wheezy. Within 3 days of restarting the medication her daughter's legs became swollen again.

The demonstration was convincing, and fluticasone was removed as a treatment. Her peripheral oedema has improved, and her asthma is now well controlled on salbutamol, regular budesonide and montelukast for exacerbations.

DISCUSSION

This was a diagnosis made by a parent with no medical training. The patient's mother was able to take a simple approach to solving the dilemma without being distracted by an extensive knowledge of all the possible causes of oedema.

It is interesting that the oedema/swelling she had read about did not, in fact, relate to peripheral oedema, but rather to angioedema. However, this did not dispel her concerns regarding her daughter's medication.

This case was reported to, and discussed with, Allen and Hanburys. They confirmed that this was the first reported case of peripheral oedema associated with fluticasone. It may be that our patient has a genetic abnormality associated with alterations in steroid metabolism, and the responsible geneticist at Great Ormond Street Hospital has also been contacted in light of this. We can find no other reports in the literature regarding peripheral oedema associated with fluticasone. The mechanism for how it may occur is not known.

Learning points

- ▶ Peripheral oedema is a very rare side-effect of fluticasone therapy.
- ▶ Physicians should be aware of this as a possibility, especially in cases of resistant peripheral oedema with no other identified cause.
- ▶ Sometimes the most simple explanation is the correct one.

Competing interests None.

Patient consent Obtained.

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