Medicinal mishap

Cabergoline-induced valvulopathy

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Case

A 36-year-old female, who had been taking low-dose cabergoline for incapacitating restless legs syndrome, presented with symptoms that she ascribed to increasing restless legs syndrome. For more than two months she had complained about increasing ankle swelling, abdominal discomfort and worsening leg discomfort.

She had been prescribed cabergoline five years earlier because other treatments had not helped her restless legs. Biperiden helped slightly but for a limited time, while levodopa/benserazide (up to 600 mg/150 mg per day) helped considerably until a rebound effect occurred. She had been prescribed 0.5 mg cabergoline daily and told about possible fibrotic reactions. The symptomatic response was excellent, but she had gradually required an increase in the dose to 2 mg daily in order to achieve relief. The woman did not return for neurological review and also changed her general practitioner.

On examination she had a regular pulse of 70 beats per minute. Her blood pressure was 140/85 mmHg and her jugular venous pressure was elevated with prominent V-waves. Heart sounds were dual with ejection and early diastolic murmurs. Her liver edge was pulsatile and there was severe pitting oedema to her mid calves. These clinical findings were suggestive of right heart failure.

ECG showed sinus rhythm and an incomplete right bundle branch block. There was some T wave inversion over the right precordial leads.

A chest X-ray showed borderline cardiomegaly with clear lung fields. There was no evidence of interstitial oedema or fibrosis or pleural effusions. Blood tests were normal.

Echocardiography showed severe (grade 4/4) tricuspid regurgitation, moderate aortic stenosis with moderate regurgitation, mild pulmonary stenosis, mild mitral stenosis and regurgitation.

Cabergoline was ceased. Frusemide and spironolactone produced a diuresis with a 5 kg reduction in weight. There was an excellent clinical response to this diuretic regimen and echocardiographic surveillance will be maintained. There may yet be a requirement for corrective surgery.

Comment

Ergot-derived dopamine agonists, such as pergolide and cabergoline, are used in the treatment of Parkinson's disease. Although the indications may not be approved, lower doses are used for restless legs syndrome and hyperprolactinaemia.

Pulmonary fibrosis is a recognised, if uncommon, complication of these drugs.[1] Two recently published studies[2,3] have found increased frequencies of significant cardiac valvulopathy in patients taking the ergot-derived dopamine receptor agonists pergolide and cabergoline. The excess risk was 33 cases per 10 000 patients per year with pergolide and 21 cases per 10 000 patients per year with cabergoline.[3] Pergolide has now been withdrawn from the market in the USA.

Pergolide and cabergoline are agonists of the 5-HT_{2B} receptor found on heart valves. This could cause valvular hyperplasia. Fenfluramine, ergotamine and methysergide have all been reported to cause cardiac valvulopathy, probably by similar mechanisms.

Conclusion

This case shows severe multi-valvular pathology probably as a result of cabergoline. Prescribers need to be aware of the risk of cardiac valvulopathy associated with the use of ergot-derived dopamine agonists. Patients should be warned about the potential adverse events, particularly if the drugs are prescribed for 'off-label' indications. They must be advised to report any unusual symptoms and to have regular clinical reviews to look for possible fibrotic complications. Baseline and periodic echocardiography may be needed.

References

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3. Schade R, Andersohn F, Suissa S, Haverkamp W, Garbe E. Dopamine agonists and the risk of cardiac-valve regurgitation. N Engl J Med 2007;356:29-38.

Conflict of interest: none declared