Ciprofloxacin-induced oral facial dyskinesia in a patient with normal liver and renal function

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CASE REPORT

A 49-year-old Chinese woman with good past health presented to a general practitioner with fever, chills, dysuria, and loin pain. Urinary tract infection was diagnosed and she was treated with oral ciprofloxacin. She was hospitalized because of persistent chills and fever. Physical examination showed hyperpyrexia of 38.6°C, together with suprapubic and bilateral loin tenderness. White cell count was 11.2×10^9/litre. Ultrasonogram of kidneys showed no structural abnormality. She was treated as having acute pyelonephritis with ciprofloxacin 200 mg intravenously twice daily. Her symptoms improved. Urine and blood culture yielded negative results.

She developed involuntary facial grimacing 2 days after starting ciprofloxacin treatment. Neurological examination did not reveal other abnormal findings. Her only other medication was paracetamol 500 mg orally four times a day. She had no prior history of similar involuntary movements. The oral facial dyskinesia occurred intermittently every 4–6 hours, with each attack lasting about an hour. She maintained a clear sensorium during the involuntary movements. Computed tomography and magnetic resonance imaging of the brain, as well as lumbar puncture, yielded normal results. Electroencephalogram showed normal wave form. The levels of liver transaminases were raised transiently after starting ciprofloxacin treatment, with aspartate aminotransferase 82 U/litre (normal 12–28 U/litre) and alanine aminotransferase 176 U/litre (normal 5–31 U/litre). Serum albumin, bilirubin, prothrombin time and creatinine levels were normal. The involuntary movements improved slightly with clonazepam therapy, but did not subside completely. In view of the possibility of ciprofloxacin-induced neurotoxicity, ciprofloxacin was stopped and substituted with netromycin. Her oral facial dyskinesia stopped and did not recur. The patient had an uneventful recovery.

INTRODUCTION

Ciprofloxacin is a fluoroquinolone antibiotic commonly used in clinical practice. Apart from its antibacterial action, it also inhibits gamma-aminobutyric acid (GABA) binding to GABA receptors in the brain. Consequently, quinolones are recognized as potentially neurotoxic, with hallucination, delirium and seizure being the more common neurological manifestations.

Oral facial dyskinesia (OFD) is an extremely rare neurological side-effect of ciprofloxacin. It has been reported in one patient with cirrhosis (Pastor et al, 1996). We present a patient who developed OFD after being treated for acute pyelonephritis with ciprofloxacin. The occurrence of OFD in the setting of normal liver and renal function has never been documented previously.

DISCUSSION

Quinolones have been used to treat bacterial infections for more than two decades (Lindsay et al, 1992). Ciprofloxacin is a fluoroquinolone derivative with proven efficacy against a broad spectrum of both Gram-negative and Gram-positive organisms.

Side-effects of ciprofloxacin can be gastrointestinal or neurological. The latter can manifest as headache, dizziness, hallucination and seizure. Since the drug is mainly excreted by the kidneys, patients with impaired renal function are more prone to the side-effects, and drug dosage should be adjusted according to the renal function.

OFD is an uncommon neurotoxic manifestation, and has been reported in one patient with underlying hepatitis C cirrhosis after taking ciprofloxacin 500 mg orally twice daily for 5 days (Pastor et al, 1996). In addition, two cases of suspected ciprofloxacin-induced OFD have been reported to the Committee on Safety of Medicine (personal communication). The patients were 85 and 87 years old; one patient had renal impairment, but the renal and liver function of the other patient were not well documented. OFD is a well-recognized complication of chronic phenothiazine therapy, but the chewing movements of the face, lips, and tongue can also occur in elderly subjects with dementia (Patten, 1995).

The brain imaging, electroencephalogram and lumbar puncture findings in our patient did not suggest meningoencephalitis. No other drug apart from ciprofloxacin could be implicated. It is interesting to note that raised liver transaminase levels are also a recognized complication after ciprofloxacin treatment, and this occurred in our patient and in the patient reported by Pastor et al (1996). However, in our patient this transient abnormality was not associated with liver decompensation. Ciprofloxacin withdrawal was followed by resolution of both the liver abnormality and the disappearance of OFD. Although the patient was not rechallenged with ciprofloxacin, the sequence of events strongly suggested that the OFD was caused by ciprofloxacin.

The postulated mechanisms of ciprofloxacin-induced neurotoxicity

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relate to the partial GABA inhibition resulting from its competitive binding to the $GABA_A$ receptors (Green and Halliwell, 1997). This induces a hyper-excitable state in the neurones. However, this usually manifests clinically as a reduction of seizure threshold (Stoelting, 1995). That some patients develop OFD may relate to individual predisposition, which in turn may be associated with over responsiveness of the extrapyramidal system to the selective GABA receptor blockade. In view of the involvement of GABA in the pathophysiology of OFD, drugs with GABAergic properties have been used in the treatment of OFD. Benzodiazepines (e.g. clonazepam) are useful since they facilitate the binding of GABA to its receptors. The resulting enhanced opening of chloride channels leads to hyperpolarization of cell membrane and reduced neuronal excitability.

CONCLUSIONS

OFD can be an uncommon presentation of ciprofloxacin-induced neurotoxicity, even in patients with normal liver and renal function. In view of the widespread use of quinolones, it is important that this side-effect be duly recognized. **HM**

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