neuroleptic malignant syndrome (1, 2). Other investigators have reported typical neuroleptic malignant syndrome features from treatment with atypical antipsychotics (4). Although our patient presented with neck stiffness, no rigidity was found, and no fever was initially noted. Additionally, he did not manifest a number of symptoms associated with neuroleptic malignant syndrome, such as altered mental status, tremor, diaphoresis, mutism, incontinence, and sialorrhea.

Many patients who develop neuroleptic malignant syndrome with high creatinine phosphokinase levels develop renal failure, which is often a main cause of death. In the present case, despite extreme elevations of creatinine phosphokinase levels, renal function was preserved, although cardiac and pulmonary complications emerged. Nearly all reports of neuroleptic malignant syndrome within the past 5 years involved a creatinine phosphokinase level ≤10,000 U/l. Why do creatinine phosphokinase levels vary so markedly? Some investigators have suggested that the creatinine phosphokinase level is a prognostic indicator (3). If this is the case, our patient’s total recovery is striking.

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An Early Report on the Role of Nitrates in Erectile Dysfunction

TO THE EDITOR: In 1977, many years before the development of the drug sildenafil, a case report was published in The American Journal of Psychiatry suggesting that nitrates had an effect on erectile dysfunction (1). Another case report was published in 1985 in the Annals of Internal Medicine (2). The first studies of the effect of sildenafil on erectile dysfunction were published in 1996 and 1998 (3, 4), and the drug was approved by the Food and Drug Administration (FDA) in 1998.

The 1977 report presented the case of a 56-year-old man who suffered from recurrent depression as well as chest and leg pain. Treatment with glyceryl trinitrate induced an erection in the patient within several minutes after taking the drug as well as restitution of morning erections that had not occurred for more than 2 years. Pentaerythritol tetranitrate, a long acting vasodilator, was then prescribed, which also had beneficial effects on erection. The author suggested that the beneficial sexual effects of nitrates in the patient were the result of an inhibition of metabolism by the tricyclic antidepressant imipramine through a functional depletion of hepatic glutathione. This potential drug-drug interaction has not been studied since the 1977 report. The author noted that “further research may reveal nitrates or other vasodilators effective in diagnosing and treating atherosclerotic impotence” (1).

The 1985 report described the case of a man who suffered from angina pectoris and had rubbed a used patch of nitrates on his penis and noted an erection. The description of the case report reads as follows: “Within 5 minutes, he had a semi-rigid erection and became sexually aroused. Sexual intercourse with his wife followed. Several minutes later, she wondered why she had the worst headache she ever had had in her life. The patient then told her of his experiment, and its apparent success. His wife was not impressed and strongly discouraged any more investigation in this area.” The authors of the case report did not suggest that nitrates might be useful in erectile dysfunction. Instead, they concluded that they “doubt that further research in this area will be done” (2).

Almost 20 years separate the case report in The American Journal of Psychiatry from the publication of the sildenafil trials. Could this delay have been shorter, i.e., was there a lack of serendipity in the discovery of phosphodiesterase type-5 inhibitors in erectile dysfunction? The two early case reports (1, 2) also leave open the question of whether men suffering from cardiovascular disorders who were being treated with nitric oxide donors, such as nitrates, might have had improved erectile function during the decades before the development of phosphodiesterase type-5 inhibitors and that this beneficial effect remained unrecognized by practitioners.

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