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Letters to the Editor

Toxic epidermal necrolysis after paroxetine treatment

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Serotonine reuptake inhibitors, fluoxetine, fluvoxamine and paroxetine, are second generation antidepressant drugs. Their indications are mainly depressive syndromes in which their efficacy is comparable with those of tricyclic antidepressants. Other indications are bulimia in which fluoxetine favours weight loss, addictive disorders such as alcoholism, obsessive-compulsive and impulsive disorders. Fluvoxamine has been available for prescription in France since 1986, followed by fluoxetine in 1988 and more recently by paroxetine in 1993. Serotonine reuptake inhibitors are supposed to be safe and well tolerated yet some studies have reported suicide attempts during such treatments in response to increased anxiety. We report herein to our knowledge the first patient who developed a severe toxic epidermal necrolysis (TEN) after starting paroxetine.

A twenty-three year old girl without familial history of skin disease was hospitalized for a depression with psychotic features. Daily doses of cyamepromazine 40 mg, trihexyphenidyle 3 mg and paroxetine 30 mg were prescribed. Two weeks later (day 14), she developed a widespread febrile bullous eruption with mucous membrane involvement. Two days later (day 16) she was referred to our institution. On admission she presented with an epidermal detachment of the trunk, face and the proximal limbs involving 35% of body surface area (BSA). Nikolsky's sign was positive over large areas. Painful oral, ocular and genital erosions were present, and temperature was 40°C. Histological examination of the skin showed a total necrosis of the epidermis consistent with the diagnosis of TEN. Direct immunofluorescence was negative. Extensive investigations for virus and *Mycoplasma pneumoniae* eliminated exceptional infection-induced TEN. Rapidly, she developed an alteration of pulmonary function. The bronchoscopy confirmed a limited destruction of the tracheal and bronchial epithelium. On day 34, she was discharged. One month later she presented depigmented skin areas and a persisting photophobia.

Discussion

According to the method used by the French drug surveillance system, the culpability of cyamepromazine, trihexyphenidyle and paroxetine was probable. Trihexyphenidyle and cyamepromazine have been available for prescription since the 1950s and the 1970s, respectively, *versus* 1993 for paroxetine. In data bases including Medline, these three drugs have never been implicated as TEN inducers (Srebrnik *et al*, 1991). Because of more recent use, paroxetine was considered as more suspect. Thus, to our knowledge, we report the first case of TEN observed after paroxetine treatment.

Second generation antidepressant drugs, especially serotonine reuptake inhibitors, are supposed to be safe (Freeman *et al*, 1991). Nevertheless one case of TEN and one case of Stevens-Johnson syndrome have already been reported after fluoxetine treatment (Bodokh *et al*, 1991; Wagner *et al*, 1992). Since 1986, one case of Stevens-Johnson syndrome was reported to the French drug surveillance system with fluvoxamine probably responsible, but the possibility of herpes and mycoplasma infections were not investigated. We reported one case of TEN after fluvoxamine treatment (Wolkenstein *et al*, 1993). Thus serotonine reuptake inhibitors appeared to be possible inducers of life threatening adverse cutaneous drug reactions. These drugs are becoming best-selling antidepressants. For example, fluoxetine is one of the most prescribed antidepressant drugs in France representing about 20% of antidepressants prescribed in 1991 and 1992 (Menard *et al*, 1992). Serious side effects may be rare but potentially very severe.

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