

Occupational infection with herpes simplex virus type 1 after a needlestick injury

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TO THE EDITOR: A 27-year-old hospital medical officer received a penetrating needlestick injury to her left hand, drawing blood, after using a 22-gauge needle to deroof a vesicle for diagnosis in a two-year-old patient with orolabial herpes simplex virus type 1 (HSV-1). The medical officer had no significant medical history, took no regular medication, and had no previous history of oral or genital herpes.

On Day 4, a vesicle appeared at the site of inoculation, with surrounding erythema. The medical officer first presented on Day 6, by which time the vesicle was crusting over, with several satellite lesions (see Figure). She described mild pain in her left axilla, but no fevers or sweats. A 10-day course of oral famciclovir (250 mg, three times daily) was prescribed and she was restricted from work until the lesions had completely healed (Day 16). During 12 months of follow-up there has been no clinical recurrence.

Specimens from the two-year-old child were positive for HSV-1 by direct immunofluorescence, and HSV-1 DNA was detected by polymerase chain reaction (PCR). Specimens from the medical officer on Day 6 were negative for HSV-1 by direct immunofluorescence, but positive by PCR. There was no evidence of HSV-2 or varicella zoster virus in either specimen.

To our knowledge this is the first reported transmission of HSV-1 after needlestick injury. Herpetic whitlow (HSV of the hands), a well-recognised occupational

Herpes simplex lesion of the palm six days after a needlestick injury



hazard for dentists and anaesthetists, is frequently misdiagnosed, resulting in unnecessary surgical procedures and delayed healing. In healthcare workers, pain and also work restrictions to limit cross-infection reduce productivity. Horizontal transmission can occur in the absence of clinical lesions, but latex gloves are an effective barrier.¹

There are few guidelines available for postexposure prophylaxis for HSV-1, and no controlled clinical trials in humans. The short incubation period and early establishment of latency in HSV infection remain obstacles for effective delivery of postexposure prophylaxis. HSV can establish latent infection of neurones in the absence of peripheral replication.² In an animal model, postexposure treatment with famciclovir or valaciclovir inhibited peripheral replication of HSV, reducing latent infection but not preventing it altogether.² In one case report, a patient who started taking famciclovir within one hour of a needlestick injury did not develop whitlow and remained seronegative for HSV.⁴

Famciclovir and valaciclovir have high oral bioavailability, minimal toxicity and proven efficacy in treating HSV. Available data suggest that treatment with these drugs after documented exposure to HSV reduces the severity of acute disease, limits the

number of neurones infected and may reduce the frequency of subsequent recurrences. If started early enough, postexposure prophylaxis may prevent latent infection altogether.

Acknowledgements: We thank Mr Peter Farkas, Clinical Photographer at Royal Darwin Hospital.

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Serotonin toxicity with therapeutic doses of dexamphetamine and venlafaxine

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TO THE EDITOR: We report two episodes of serotonin toxicity (or serotonin syndrome) caused by drug interaction in one individual chronically treated with dexamphetamine. The interacting drugs were venlafaxine, then later citalopram. We are not aware of any previous reports of serotonin toxicity caused by dexamphetamine in combination with either venlafaxine or any selective serotonin reuptake inhibitor (SSRI).

A 32-year-old man presented after two days of marked agitation, anxiety, shivering and tremor. He was being treated with dexamphetamine, 5 mg three times daily, for adult attention deficit hyperactivity disorder. He had started venlafaxine (75 mg daily) two weeks previously, and this had been increased to 150 mg daily after a week. On examination, he was alert and oriented, but diaphoretic, shivering and had fine motor tremor. His heart rate was 140 bpm, blood pressure was 142/93 mmHg and temperature 37.3°C. Pupils were 3 mm diameter and reactive, with no nystagmus or ocular clonus. There was generalised hypertonia, hyperreflexia, 1-2

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beats of inducible ankle clonus, frequent myoclonic jerking and tonic spasm of the right side of his orbicularis oris muscle. His abdomen was tense, but non-tender, with normal bowel sounds. An electrocardiogram showed sinus tachycardia with a baseline tremor, but no other abnormality.

Therapy with dexamphetamine and venlafaxine was ceased, and cyproheptadine (8 mg doses up to a total of 32 mg over three hours) was given. The patient had a stepwise reduction in heart rate, with complete resolution of his symptoms, and was discharged the next morning. Dexamphetamine therapy was restarted three days later and citalopram therapy was commenced one week after discharge. Two weeks after discharge, he reported similar symptoms, and ceased citalopram. Three days later he was still agitated, with nausea, diarrhoea and teeth clenching. There was no rigidity, tremor or diaphoresis, and his heart rate was 76 bpm. He was given two 8 mg doses of cyproheptadine and was asymptomatic two days later.

Some of this patient's symptoms could be attributed to noradrenaline excess. However, the combination of neuromuscular and autonomic features is more consistent with serotonin toxicity. The fact the symptoms resolved after administration of cyproheptadine (a 5-HT₂-receptor antagonist) supports this hypothesis. There is no theoretical reason why the interaction of citalopram (a pure SSRI) and dexamphetamine should cause catecholamine excess, and again the more likely explanation is serotonin toxicity.

Dexamphetamine causes psychostimulation and increased peripheral sympathomimetic activity. Centrally it causes presynaptic release of serotonin,¹ and dopamine and catecholamine release.² Venlafaxine and its metabolite, *O*-desmethylvenlafaxine, inhibit both neuronal 5-HT reuptake and noradrenaline reuptake,³ whereas citalopram, an SSRI, has little effect on noradrenaline reuptake.⁴ The combination of serotonin reuptake blockade and either presynaptic release of serotonin or monoamine oxidase inhibition by dexamphetamine will cause increased serotonin levels in the central nervous system, and is the likely mechanism of toxicity in this patient. This is consistent with the mechanism for other reports of serotonin toxicity.⁵

Increased awareness and cautious monitoring is advised when using a combination of dexamphetamine and either venlafaxine or an SSRI. This is particularly important in people using amphetamines recreationally and in children taking dexamphetamine for attention deficit hyperactivity disorder.

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Venlafaxine and bilateral acute angle closure glaucoma

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TO THE EDITOR: We report a case of bilateral acute angle closure glaucoma associated with venlafaxine.

A 45-year-old woman with a history of bipolar affective disorder and borderline personality traits was admitted with increasing depression and suicidal ideation. She was taking sodium valproate (1500 mg/day) and slow-release lithium (450 mg/day). She had also taken dothiepin (50 mg nightly) for seven days, but this therapy was ceased on admission. Her only previous ophthalmological history was hypermetropia, and she had been taking low-potency neuroleptic medications and selective serotonin reuptake inhibitors in the past with no significant adverse effects.

She was treated with chlorpromazine (up to 150 mg daily), and venlafaxine therapy (extended release, 75 mg/day) was commenced.

After three days of taking venlafaxine, she developed left retro-orbital pain associated with nausea and vomiting, with subsequent swelling and drooping of the left upper lid and a dilated and fixed pupil. The eye was congested and visual acuity was reduced to counting fingers. She was diagnosed with acute angle closure glaucoma, treated with timolol, and transferred to a tertiary referral hospital. During this period, she sustained an injury to her right eye following an assault by a third party. A computed tomography scan revealed a right blow-out fracture with inferior rectus muscle entrapment.

On admission, intraocular pressures were 16 mmHg in the right and 50 mmHg in the left eye, and gonioscopy revealed closed

angles (grade 1–2). Ninety minutes after being given intravenous mannitol, topical apraclonidine hydrochloride, latanoprost and pilocarpine eye drops, the intraocular pressure dropped to 35 mmHg in the left eye. Initial laser iridotomy was unsuccessful because of a hazy cornea. Laser iridotomy was repeated several times after topical steroid therapy until it was successful. The right orbital floor fracture was repaired with a Medpor implant (Porex Surgical Products Group, Atlanta, Georgia).

Eight days after starting venlafaxine therapy, she developed similar symptoms in her right eye, despite prophylactic treatment with pilocarpine eye drops four times a day. Venlafaxine was discontinued, and three days later a successful right laser iridotomy was performed. Her visual acuity was 6/5 in her right and 6/18 in her left eye. After eight weeks she was receiving no ophthalmic treatment and her intraocular pressures were well controlled.

In a MEDLINE search, we found no published reports of venlafaxine associated with acute angle closure glaucoma. The manufacturers report it as a rare adverse event (fewer than 1/1000; data on file; Wyeth-Ayerst laboratories). There has been one previous report of increased intraocular pressures in two patients with known narrow-angle glaucoma who began taking venlafaxine.² Glaucoma has also been reported with paroxetine.³⁻⁴ Our patient had no associated family history of glaucoma, but her eyes were predisposed to angle closure glaucoma owing to hypermetropia.

Patients with acute angle closure glaucoma usually have a structural defect that produces a narrow drainage angle, and thus moderate dilation of the pupil may precipitate an attack. Drugs like tricyclic antidepressants cause mydriasis and may cause the narrow angles to close as a result of anticholinergic effects. Venlafaxine, however, is a serotonin and noradrenaline reuptake inhibitor without anticholinergic activity. This fact and the time course suggest that a combination drug interaction may have occurred in this patient, perhaps by the hepatic inhibition of chlorpromazine metabolism by venlafaxine, increasing anticholinergic activity, or by a direct effect of venlafaxine on the eye unrelated to mydriasis.

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