Phenytoin-induced toxic epidermal necrolysis in a neurosurgical patient

Sir

A 50-year-old man was admitted for treatment of a posterior fossa cyst with hydrocephalus. It was planned to do a ventriculoperitoneal (VP) shunt for rapid relief of pressure symptoms, followed by endoscopic decompression of the cyst through the fourth ventricle in the same admission, but different sitting. Phenytoin was started after VP shunt was done. However, two days later, the patient started developing an erythematous rash, beginning in the perioral and periorbital areas, which spread to involve the whole trunk and limbs centrifugally over the next one day. Over 50% of the total surface area was involved. Next day, wrinkling and sloughing of the skin began and sloughing could be provoked by gentle stroking of the skin (Nikolsky's sign), even in areas apparently uninvolved. Large flaccid bullae developed and exfoliation continued in large sheets over the front and back of trunk, leaving behind denuded areas of red, glistening, but non-purulent skin [Figure 1A, B].

Since he was being treated with multiple drugs, including netilmicin, chloramphenicol, phenytoin, and NSAIDS, drug eruption was considered a strong possibility and all medications were stopped. In consultation with dermatologists, he was managed with topical antibiotics for the skin, eyes, and oral cavity, along with systemic steroids. Prophylactic intravenous antibiotics (vancomycin, levofloxacin, and piperacillin-tazobactam) were added when the patient developed fever after one week of illness. High dose cyclophosphamide/intravenous immunoglobulin were considered after one week of illness. High dose cyclophosphamide/intravenous immunoglobulin were considered in treatment but were not used in view of their side effects and improvement in patient's condition with the ongoing treatment. Multiple cultures from blood and raw areas of skin were either sterile or grew multiple contaminants. Other drugs were slowly restarted but phenytoin was replaced with sodium valproate. Care was taken to maintain the fluid and electrolyte balance. The entire illness persisted for 3 weeks. The patient progressively improved, was discharged, and was planned for endoscopic cyst decompression on a later date.

Toxic epidermal necrolysis (TEN) is the most serious of the cutaneous drug reactions. It is blistering disorder, with erosions of multiple mucous membranes and small skin blisters developing on dusky or purpuric macules. The onset is usually acute, as in our case and epidermal necrosis involves >30% of body surface area. It can be distinguished from Steven-Johnson syndrome (SJS), where the total surface of body surface area detachment is <10%, by definition. Pathologically, TEN produces a dermal-epidermal cleavage plane, causing the characteristic bullae.\(^1\)

A morbilliform rash is the most common reaction to phenytoin, occurring in as many as 5% of cases overall. However, a wide variety of cutaneous reactions can occur, including acniform lesions, exfoliative dermatitis, erythema multiforme, SJS, vasculitis, gingival hyperplasia, heel pad thickening, and lupus like reaction.\(^2-4\) In a hospital-based adverse drug reaction reporting program from an Indian tertiary care hospital, phenytoin was the individual drug most frequently reported as a cause of adverse drug reaction.\(^5\) As calculated by Naranjo's adverse drug reaction probability score, the causal relationship between phenytoin and TEN in our case is 'probable'. TEN can also occur as a complication of other drugs.\(^1,2\)

Steroids are the treatment of choice in severe cases, to limit the inflammatory process, along with prophylactic systemic and topical antibiotics. If severe drug reactions such as TEN occur, the suspected drugs, including antiepileptic drugs (AED), should be stopped immediately. A new AED can be started, if necessary, before the resolution of the rash, without increasing the risk of further reactions.\(^4\) However, in cases of phenytoin reactions, carbamazepine, and phenobarbitone should be avoided as they can cross react in such patients.

Our case reemphasizes that the neurosurgeons/neurologists/physicians should be aware of the potentially life threatening complications of phenytoin, which is so commonly used by them.

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Letters to Editor


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