Chemical burns to the perineum from podophyllin use

We recently managed a 37-year-old man who had made use of podophyllin, prescribed by his general practitioner, to eradicate perianal condylomata. After two applications and removal after the appropriate duration, the patient became frustrated with its apparent inefficacy, and applied a solution by spray over his scrotum and perineum.

He presented to the emergency department three days after application, and was referred to our service after a period of observation by the internal medicine service. The patient was clinically well, but in significant pain. A thorough examination was only possible under sedation, during which the remaining adherent solution was removed, and the areas involved assessed and covered with a dressing of Jelonet™ and Polyderm™. The extent of the scrotal and perianal cutaneous injuries is demonstrated in Figures 1 and 2. The clinical examination and bloodwork were otherwise unremarkable.

The area was dressed with Jelonet and polyderm daily until healed (12 days). There were no sequelae and the patient had no evident scarring at three weeks after injury. An alternative method would have been to apply Flammazine twice daily on 9 by 9 inch gauze, also secured in place with a Surgilast (TM) pair of net pants for a few days (changing the dressings as required after bowel motions), before reverting to Polysporin when he can tolerate wearing standard underwear.

Podophyllin resin is believed to have been discovered in 1835 by King, and was used for several indications before it was popularised by Kaplan in 1942 for its main indication, the eradication of venereal condyllomata.[1] The resin is extracted from the rhizome of the *Podophyllum peltatum* (American mandrake and Mayapple plant, origin in North America) and the *P. emodi* (higher resin content; found in the Himalayas).

Figure 1: Partial-thickness burns to the scrotum and perineum

Ligans are the active group of compounds in podophyllin, and act by destabilising the polymerisation of tubulins into helical microtubular structures, resulting in the mitotic arrest of human and/or viral cells during metaphase.[2] As with other chemotherapeutic modalities, the anti-mitotic effects of podophyllin are most evident in tissue with a rapid rate of proliferation. Podophyllin is available in a number of formulations. There is no standardisation of the lignan compound content, and therefore different batches, even marketed as the same product, may have significantly different toxicity and efficacy.

The clinical efficacy of podophyllin has been disputed in several studies.[3-7] Some authors maintain that fewer than one third of patients have any response after a single application, and that as many as 50% of these experience recurrences. Many patients, desperate for curative therapy, often require treatment with other agents, like trichloroacetic acid, or resort to surgical excision, usually with cautery. Poor clinical response to podophyllin has been noted in patients with multiple lesions, where the lesions have been present for ≥ 6 months, or when involving the urinary meatus or skin, rather than the prepuce, which responds more readily to topical treatment.

Some authorities advocate that podophyllin should only be applied by physicians to small areas, and should always be removed within 4-6 hours of application.[3-7] Patients who apply it themselves should be particularly vigilant. Applying petroleum jelly to the neighbouring uninvolved skin or mucosa is one method of reducing injury. Patients can expect an acute inflammatory reaction around the lesions. Necrosis of the lesions themselves is the desired end-point. Balanitis and phimosis have sometimes necessitated circumcision, and cases of severe anogenital fibrosis and fistulae have resulted from podophyllin therapy. Givens described a case of genital burns following the application of podophyllin, resulting in part to the patient's inability to contain the solution in the affected area, despite making use of the supplied dropper. As a result, the solution spread over his scrotum and upper thighs.[5]

Systemic toxicity, following the topical application of podophyllin, is well described.[4,6] Percutaneous absorption is most likely following

Figure 2: Partial-thickness perianal and perineal burns

application in the context of extensive, vascular lesions in areas of thin, undulating epidermis. Symptoms most commonly present between 12 and 48 hours of contact. The clinical features are tabulated in Table 1. Podophyllin is well known to be responsible for teratogenicity. Therefore, it is contraindicated in pregnancy.[4,6]

Table 1: Acute systemic consequences of podophyllin toxicity

System	Symptoms
Neurological	Lethargy, dizziness, hallucinations, seizures, psychosis and peripheral neuropathy
Gastrointestinal	Nausea, vomiting, diarrhea and ileus
Respiratory	Depression and arrest
Genitourinary	Retention
Hepatobiliary	Dysfunction
Reticuloendothelial	Pancytopaenia

We applied an initial dressing of Jelonet™ and polyderm™ daily for four days, after which polderm alone was applied three times daily until all areas were healed (12 days). There were no sequelae and the patient had no obvious scarring at three weeks after injury. An alternative method of management would have been to apply silver sufadiazine twice daily to gauze, also secured in place with a surgilast (TM) pair of pants for a few days (changing the dressings as required after bowel motions), before reverting to polysporin when he can tolerate standard underwear. More severe cases of chemical burns (and especially those requiring surgical intervention) may require fecal diversion with the Flexi-Seal™ device.

We have reported on a case of exuberant inflammation of the scrotum and perianal region, following the inappropriate use of podophyllin for perianal condylomata, requiring admission of the patient to the burn centre for wound care. In the light of its low efficacy, difficulties in self-application and the significant potential for systemic toxicity, as well as the unstandardised nature of podyphillin-containing products, we advocate that its use should be restricted (or reconsidered altogether) for the management of perianal condylomata.[7] At the very least, podophyllin should be restricted to use by the specialist, to small areas of intact skin, following a test application, and at weekly intervals. Regulatory guidelines are likely to support the use of a more standardised, more efficacious and less toxic podophyllotoxin variant, at concentrations up to 0.5%.

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