Seizures Associated with Povidone-Iodine-Impregnated Antral Pack in a Child: a Case Report and Review of the Literature

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ABSTRACT

This is a case of an 11-year-old patient diagnosed of suppurative osteomyelitis of the right maxilla. He had incision and drainage with sequestrectomy under general anaesthesia, and povidone-iodine-impregnated antral pack. About 60 hours after surgery, the patient started having generalized, tonic-clonic seizures, with six episodes on the first night-- each lasting about one minute with post-ictal vomiting. An initial assessment of meningitis (to rule out cerebral abscess) was made. The seizure episodes which lasted for three days gradually reduced, and completely subsided 24 hours after the removal of the antral pack. However, when the patient had a CT scan with iodine-based contrast as requested by the paediatric neurologist (to rule out cerebral abscess), the episodes went up significantly again for another 24 hours, after which they reduced and finally subsided 48 hours after contrast administration. Povidone-Iodine (PVI) slowly liberates free iodine to exhibit its broad range of microbicidal activity. However, depending on the amount of iodine absorbed, there is a possibility of iodine toxicity, with different systemic manifestations including seizures, especially in children. The seizure is believed to be a result of disruption in the blood-brain barrier by free iodine from PVI and the iodine-based contrast medium. Therefore, caution should be taken in using PVI as an antiseptic agent in antral packs or on any mucosa surface, especially in children.

INTRODUCTION

Povidone-Iodine (polyvinylpyrrolidone iodine) is an iodophor solution, a combination of 9- 12.0% elemental iodine and polyvinylpyrrolidone.[1] Being a potent antiseptic agent effective against strains known to be resistant to other agents, [2,3], it its use for different purposes, including preoperative preparation of the skin and mucous membranes, and as an antiseptic for the treatment of contaminated wounds and disinfection of surgical equipment[2] is not surprising. However, caution is advised in its use because some adverse systemic effects of iodine have been reported with povidone-iodine (PVI) use. These include anaphylaxis, dermatosis, diarrhoea, renal failure, metabolic acidosis, abnormal thyroid function, hypernatremia, neutropenia, and mental status changes (rarely), seizures and death.[2,4,5,6] Systemic toxicity is usually attributable to the absorption of iodine into the systemic circulation.[2,7] We present a case of a patient who had sequestrectomy on account of maxillary osteomyelitis, with episodes of seizures following the use of a PVI-impregnated antral pack.

CASE REPORT

An 11-year-old male patient presented to the oral and maxillofacial surgery clinic with a

chief complaint of recurrent left-sided facial swelling and pus discharge from the left eye and cheek of one-week duration. There was a prior history of toothache on the same side of more than 1 year duration, for which the patient has used different kinds of unnamed over-the-counter drugs. He had a similar condition on the right side about six years prior to this presentation for which he underwent surgery under general anaesthesia. The departmental protocol for antral packing then was the use of tincture of benzoin compound (TBC) as the antiseptic. No known medical condition was reported.

Examination revealed a young patient in no obvious distress, pale, not dehydrated, acyanosed, anicteric, but with palpable tender cervical lymph nodes. There was obvious facial asymmetry, evidenced by a diffused left-sided facial swelling with pus discharge from the lateral canthus of the left eye and cutaneous discharging sinus around the left zygomatic arch, just about 2cm anterior to the tragus of the ear. Temporomandibular joints were palpable, not tender but with limited movement. Intra-oral examination revealed limited mouth opening with very poor oral hygiene and fetor oris. There were anterior, left and right maxillary wall defects with free oro-antral communications, and pus discharge from the left side. There were also retained roots of canine, first and second primary molars on the left maxillary arch.

A craniofacial CT scan showed erosion and sclerosis of the left maxillary, nasal, and zygomatic bones, suggestive of osteomyelitis. Further investigations showed haematocrit of 13.9%, and the microbial culture result revealed staphylococcus aureus, sensitive to ceftriaxone and augmentin. A diagnosis of chronic suppurative osteomyelitis of the maxilla in an anaemic patient was made. The patient was optimized with four units of blood and had incision and drainage with sequestrectomy under general anaesthesia via an upper vestibular incision. The retained roots were extracted and the maxillary defects were closed and packed with a povidone-iodine-impregnated single roll of gauze. Intravenous antibiotics were administered based on the sensitivity results. However, about 60 hours after surgery, the patient started having generalized, tonic-clonic seizures with about six episodes on the first night, each lasting about one minute with post-ictal vomiting. Subsequent breakthrough seizures were controlled with IM diazepam. The patient was reviewed by the paediatric neurologist and an assessment of meningitis (to rule out cerebral abscess) was made. He was commenced on IV chloramphenicol 100mg/kg/day in addition to already prescribed antibiotics, and a fresh CT scan was requested.

The seizure episodes lasted till the antral pack was removed five days post-operatively. Afterwards, the episodes of seizure subsided significantly at about 24 hours after antral pack removal. Nonetheless, the patient still went for the CT scan as requested by the paediatric neurologist (about 48 hours after antral pack removal), which required the administration of a contrast, and an iodine-based contrast was used. The brain CT scan showed no demonstrable intracranial abscess or features suggestive of inflammation. However, the episodes of seizure went up again after the CT scan for another 24 hours, after which it gradually subsided, till none was recorded 48 hours after contrast administration. The patient's condition improved significantly; he recommenced feeding orally, and was subsequently discharged.

DISCUSSION

Povidone-Iodine (Polyvinylpyrrolidone iodine (PVI) is an iodophor solution that slowly liberates free iodine to exhibit a broad range of microbicidal activity against bacteria, fungi, protozoa, and viruses.[1] It has strong pharmacological activity against S.

aureus, N.gonorrhoea, syphilis, P. aeruginosa, hepatitis B virus, HIV, and T. vaginalis.[1] PVI has been used safely and effectively for various purposes for many years, including continuous irrigation to treat mediastinitis after median sternotomy.[2,8.] Its mechanism of action involves free iodine release and penetration of the cell wall of microorganisms and a quick lethal effect through the lipid iodination and oxidation of the cytoplasmic membrane of compounds. This disrupts protein and nucleic acid synthesis.[1] Though PVI is mostly generally considered safe for clinical use, a literature search showed that there is a possibility of iodine toxicity, which is often dependent on the amount of iodine absorbed.[4,9]

The absorbable quantity of iodine is a function of the concentration of the solution, the route of administration, and the duration of contact.[4,9] Iodine is more easily absorbed through the mucosa compared to skin. In our case, the concentration was 10%, and it is believed that the antral mucosa as well as the raw surfaces following the sequestrectomy most likely provided a faster absorption route for the free iodine. Also, the first two days of antral packing seemed to have provided enough duration of contact, as the first episodes of the seizures were recorded about 60 hours after surgery.

Meningitis as an initial differential diagnosis by the pediatric neurologist was very important as it is usually the first diagnosis to be considered in patients with fever, headache, altered mental status and neck stiffness.[10] Being a medical emergency, delays in instituting effective antimicrobial treatment of acute bacterial meningitis may worsen morbidity or mortality.[10] Similarly, cerebral abscess is a potentially fatal injury that must be treated promptly to avoid further complications.[11] Though the clinical presentation is usually non-specific, raised intracranial pressure, seizures, and focal neurological deficits (as was evident in this case) are the most common forms of presentation.[11] Therefore, early diagnosis with the aid of radiologic investigation using contrast enhanced CT scan or MRI, and with adequate subsequent treatment, is vital to the patient's full recovery.

The reduction in the seizure episodes at about 24 hours after the removal of the pack gave the first hint on the link between the PVI and the symptom in this case. While the surge in the seizure episodes after taking the requested CT scan (with the administration of iodine–based contrast agent) suggested that a similar substance was responsible, iodine-based contrast media for radiology imaging induces neurologic adverse effects, including seizures.[4,12] This supported our suspicion that the surge in the episodes of seizures was likely due to the increase in the serum levels of iodine and the known neurotoxicity induced by the injected iodine-based contrast medium.

Serum iodine levels was requested, but could not be done due to the patient's financial incapacity. However, the fact that the episodes of seizure completely subsided 48 hours after contrast administration, gave us reason to believe that the initial episodes were most likely precipitated by the high concentration of iodine in the bloodstream. The seizure may be explained by the ability of free iodine from PVI and the iodine-based contrast media to disrupt the blood–brain barrier through either the osmotic and hydrophilic qualities of the agent or the presence of ionic changes and lipid solubility.[2] Other studies have corroborated the adverse effects of using PVI in children.[5,9] We therefore recommend caution in using PVI as an antral pack or any other mucosal surface, especially in children. Alternatively, further dilution of the solution should be done to reduce the concentration of absorbable iodine through the mucosa, or, better still, a totally different antiseptic should be used.

REFERENCES

1. Bigliardi PL, Alsagoff SAL, El-Kafrawi HY, Pyon JK, Wa CTC, Villa MA: Povidone iodine in wound healing: A review of current concepts and practices. Int J Surg. 2017; 44:260-268.
2. Azzam ZA, Farhat D, Braun E, Krivoy N. Seizures: An Unusual Complication of Intrapleural Povidone–Iodine Irrigation. J Pharm Technol. 2003**;** 19:94**-**96**.**
3. Kunisada T, Yamada K, Oda S, Hara O. Investigation on the efficacy of povidone-iodine against antiseptic-resistant species. Dermatology. 1997; 195:14-18.
4. Zec N, Donovan JW, Aufiero TX.Seizures in a patient treated with continuous povidone-iodine mediastinal irrigation. N Engl J Med. 1992; *326*(26): 1784.
5. Kaur G, Swami AC, Sharma A, Kaur A. Povidone-iodine toxicity in a child posted for laparoscopic removal of hepatic and renal hydatid cysts. Indian J Anaesth. 2015 Feb;59(2):135-6.
6. Lakhal K, Faidherbe J, Choukhi R, Boissier E, Capdevila X. Povidone iodine: Features of critical systemic absorption. Ann Fr Anesth Reanim. 2011;30:e1–3
7. LeVeen HH, LeVeen RF, LeVeen EG. The mythology of povidone iodine and the development of self-sterilizing plastics. Surg Gynecol Obstet. 1993; 176:183-90.
8. Campistol JM, Abad C, Nogué S, Bertrán A. Acute renal failure in a patient treated by continuous povidone-iodine mediastinal irrigation. JCardiovascSurg **(**Torino**).**1988; *29*(4): 410–412.
9. Glick PL, Guglielmo BJ, Tranbaugh RF, Turley K. Iodine toxicity in a patient treated by continuous povidone-iodine mediastinal irrigation. Ann Thorac Surg. 1985; *39*(5): 478–480.
10. van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect. 2016;22(Suppl 3):S37-62.
11. Marcucci M, Papiri G, Tagliati C, et al. Diffusion-weighted imaging in the early diagnosis of intraventricular rupture of a brain abscess. Radiol Case Rep. 202;17 (9):3059-3063.
12. Luzzani F, Morisetti A, Bussi S, Tirone P, de Haen C. Neurotolerability of nonionic X-ray contrast media. The role of chemotoxicity. Invest Radiol. 1996; 31:338-344.