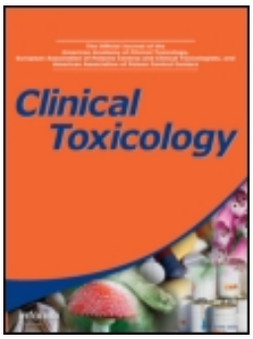

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CASE REPORT

Severe iatrogenic bismuth poisoning with bismuth iodoform paraffin paste treated with DMPS chelation

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Background. Bismuth iodoform paraffin paste (BIPP) is used for the packing of wound and surgical cavities. Features of both bismuth and iodoform toxicities have been associated with the use of BIPP, but there are no previous reports of 2,3-dimercaptopropane-1-sulphonate (DMPS) chelation therapy for bismuth poisoning secondary to its use. *Case Report.* A 67-year-old man presented with a pelvic tumor requiring extensive surgical resection. BIPP packing was required post-operatively for surgical wound breakdown. A few days after insertion, the patient developed neurological features of bismuth toxicity (blood and urine bismuth concentrations were 340 μg/L and 2800 μg/L, respectively), which was treated with removal of the BIPP packing and DMPS chelation [27 days of intravenous DMPS (5 mg/kg 4 times daily for 5 days, 5 mg/kg three times daily for 5 days followed by 5 mg/kg twice a day for 17 days) followed by 24 days of oral DMPS (200 mg three times a day for 10 days, followed 200 mg twice daily for 14 days)]. This resulted in improvement in his symptoms and a decline in his pre-chelation bismuth concentration of 480 μg/L to 5 μg/L following chelation. There were no adverse effects during chelation. *Conclusions*. DMPS chelation appears to be a potentially effective chelating agent in bismuth toxicity.

Keywords Bismuth; Toxicity; DMPS; Encephalopathy; Chelation

Introduction

Bismuth iodoform paraffin paste (BIPP) is widely used for packing wounds and cavities in ear, nose, and throat (ENT) and maxillofacial surgery as it acts as a hemostatic agent, reduces wound colonization, and promotes granulation tissue formation and wound repair (1).

Bismuth toxicity (encephalopathy, confusion, fits, hepatorenal impairment, and methemoglobinemia) has been associated with the use of BIPP; however, there have been no previous reports of severe bismuth poisoning related to BIPP packing treated with chelation therapy (2,3).

We report a case of a patient who developed severe bismuth toxicity following the use of BIPP to pack a sacral wound after resection of a large tumor who was successfully treated with removal of the BIPP packing and 2,3-dimercaptopropane-1-sulfonate (DMPS) chelation therapy.

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Case report

A 67-year-old man presented with a sacral chondroma. The tumor was surgically resected and found to be extensively infiltrating locally in the pelvis, necessitating a radical excision and sacral reconstruction with metal implants. Two weeks post-operatively the sacral wound started to ooze and the wound broke down, exposing the metalwork. Following failure to respond to conservative medical treatment with intravenous broad spectrum antibiotics, he was taken back to theatre, 63 days after the initial operation. Following surgical debridement, the wound was irrigated with saline and packed with gauze soaked in BIPP (OxBipp™; Oxford Pharmaceuticals Ltd., Middlesex, UK).

On the fifth day following packing of the wound with BIPP he became acutely confused and was disorientated, delusional, and verbally aggressive to the medical and nursing staff. In addition he had abdominal discomfort, nausea, and tremor, although no cerebellar signs were present. An apical hospital-acquired pneumonia was diagnosed. However, his confusion failed to resolve over the next five days, despite appropriate therapy for his sepsis (he was apyrexial, and his white blood cell count had fallen to 8.9×10^9 and CRP to <3 mg/L). Bismuth toxicity was suspected and Guy's and St Thomas' Poisons Unit was contacted for further advice. By now the patient's condition had deteriorated and he had developed

myoclonic jerks with intermittent episodes of drowsiness and worsening confusion. Blood and urine bismuth concentrations were determined and were 340 μg/L and 2800 μg/L, respectively [Reference urine bismuth concentration < 20 μg/L (4)].

The BIPP packing was removed and replaced with an alginate dressing. Due to the high bismuth concentration and significant neuropsychiatric symptoms, intravenous chelation therapy with DMPS was commenced: 5 mg/kg four times daily for 5 days, 5 mg/kg three times daily for 5 days followed by 5 mg/kg twice a day for 17 days. This was subsequently followed by oral DMPS 200 mg three times a day for 10 days, then 200 mg twice daily for further 14 days. A total of 51 days of chelation therapy was given. His abdominal symptoms settled within 5 days of initiation of DMPS, and the confusion and tremor improved gradually over the next month. The patient's general condition improved; wound healing was satisfactory and repeated blood and urine bismuth levels declined (Figure 1). During the chelation therapy, his renal function remained within normal limits and he did not develop proteinuria; his copper, zinc, manganese, and magnesium concentrations were monitored and remained normal.

Six months following discharge he remained well and his sacral wound was healing well. Blood and urine bismuth concentrations were both below the limit of detection (< 0.21 μg/L), and he had no chronic neurological, renal, or psychiatric sequelae secondary to bismuth toxicity.

Discussion

BIPP consists of one part of bismuth subnitrate and two parts of iodoform in a liquid paraffin base. It is used for packing small wounds and cavities in maxillofacial and ENT surgery (1,5).

Our patient had significant neurological symptoms, but his renal and hepatic function remained normal despite the presence of significantly elevated blood and urine bismuth concentrations. The characteristic symptoms reported in bismuth-related neurotoxicity are myoclonia, unsteady gait, ataxia, dysarthria, disorientation, delirium, and coma (6). Due to the proximity of the BIPP packing to the sacral nerves and spinal cord in our patient, there was the potential for greater neuronal uptake of bismuth with subsequent retrograde axonal transport leading to more prominent neurological toxicity (7).

As well as bismuth, BIPP contains iodoform, which along with its metabolite di-iodomethane is highly lipophilic and known to cause neurotoxicity even in the absence of bismuth (8). The topical absorption of iodoform and its metabolites can cause acid–base/electrolyte disturbances, ioderma, hypo- or hyperthyroidism, abnormal liver function, and neutropenia (8,9). It is possible that some of the neurological features seen in our patient were related to iodoform in addition to bismuth. However, none of the other features of iodoform toxicity were present. Although we were unable to measure iodoform or iodine concentrations to confirm the potential role of iodoform in the patient's clinical symptoms, we do not feel that this would have affected management because previously reported cases advocate removal of the packing and supportive care for iodoform toxicity (5,8).

Previous reports of bismuth toxicity secondary to the use of BIPP have described supportive care, with the removal of the dressing and paste from the wound or the cavity (2,3). Due to the high concentrations of bismuth in this case together with the significant neurological features, we felt that chelation therapy was indicated in addition to removal of the BIPP. Dimercaprol (British Anti-Lewisite, BAL) was contraindicated in this case as the patient had a peanut allergy (10).

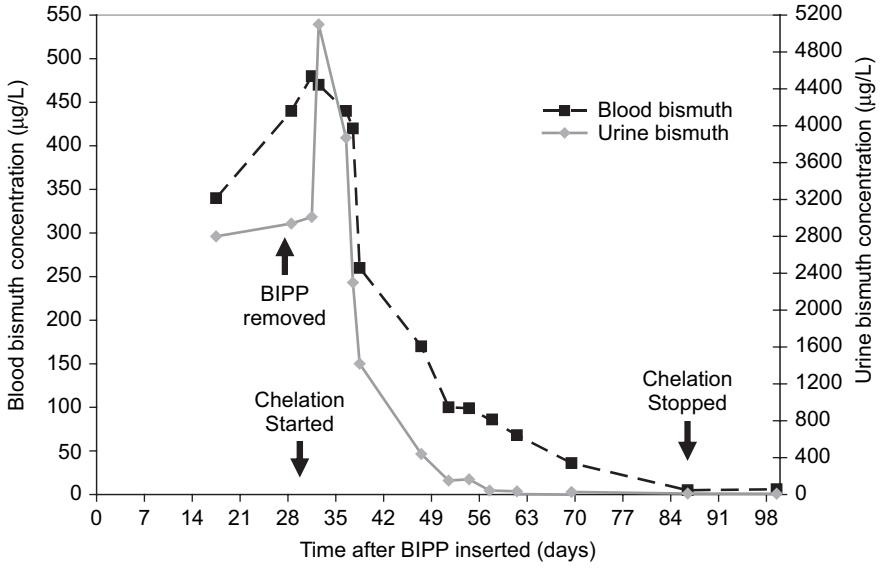

Fig. 1. Blood and urine bismuth concentrations following bismuth iodoform paraffin paste (BIPP) insertion, and the effect of DMPS [2,3-dimercaptopropane-1-sulphonate] chelation therapy.

In vivo studies suggested that DMPS is a more potent chelator of bismuth than DMSA (2,3-dimercapto-succinicacid) (11,12). DMPS increases urinary clearance of bismuth in rats fourfold compared with placebo (11). In human trials a 50-fold increase in urinary bismuth excretion has been reported with DMPS and DMSA (12). Previous reports have described successful use of DMPS in patients? acute bismuth poisoning (13,14). DMPS is generally well tolerated and has low toxicity, even with long-term use (15). Reported adverse reactions associated with DMPS use include allergic reactions, nausea, vertigo, and Stevens-Johnson syndrome (16).

The patient was, therefore, managed with DMPS chelation therapy in addition to removal of the BIPP packing. Rapid symptom and cognitive state improvements were seen along with a marked increase in urinary bismuth concentrations, suggesting increased removal of bismuth by DMPS chelation. It is not possible to determine from this single case to what extent the clinical improvement and fall in bismuth blood concentrations seen was due to removal of the BIPP packing and to what extent the DMPS chelation contributed. However, the significant increase in the urinary bismuth concentration seen at the time of initiation of the DMPS chelation therapy suggests that the DMPS played at least some role.

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