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Case Report

Iodoform Intoxication ; A Case Report of Prolonged Consciousness Disturbance in a Patient with a High Plasma Iodine Level

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Abstract This report describes a case in which a consciousness disturbance was associated with a high plasma iodine level and which improved after the removal of iodoform gauze that had been applied to infected wounds. A 71-year-old male with poorly controlled diabetes underwent a laminectomy for an epidural abscess. On the 6th and 8th postoperative days, he underwent debridement for fasciitis in the both arms and iodoform gauze was applied to the wounds (both arms and lumbar region) at the end of the first debridement and then changed every day. His consciousness then gradually deteriorated after the debridement. His plasma iodine level was measured and was shown to be remarkably high (6,280 μ g/dl) 19 days after the laminectomy (13 days after the beginning of iodoform application). His consciousness recovered gradually with a concomitant decrease in the plasma iodine level. Three months after the removal of the iodoform he became almost alert. Caution should be exercised in using iodoform gauze because of the possibility that it could affect consciousness.

Key words: iodoform intoxication, plasma iodine level

Introduction

Iodoform is commonly used in gauze to disinfect the local infected area. However, it can potentially cause a consciousness disturbance in some patients. To promote the awareness of the complications of iodoform, this report describes a case where iodoform was thought to have caused a coma and consciousness improved with a reduction in the plasma iodine level, despite the maximal iodine level being more than 6 times higher than that reported previously.

Case report

A 71-year-old male with a history of hypertension and poorly controlled diabetes, who was taking amlodipine and glimepiride, underwent an L2 to L4 laminectomy for an

epidural abscess. The procedure was conducted under general anesthesia which was maintained with sevoflurane and fentanyl. A bacterial examination of the abscess revealed methicillin sensitive Staphylococcus aureus (MSSA), and therefore a few combinations of antibiotics including meropenem and vancomycin were administered. Around the onset of the epidural abscess, he showed pain and swelling in both arms. Bacterial examination of the punctured specimen from the right arm revealed MSSA. A diagnosis of fasciitis was made, and he underwent debridement in both arms under general anesthesia with fentanyl and sevoflurane on the 6th postoperative day. In order to eliminate the infection, the wounds were kept open and iodoform gauze was applied to them. The dressing with iodoform gauze was changed every day. The incision from the laminectomy had not totally healed and it thus produced discharge, therefore a strip of iodoform gauze was packed into the opened wound and the dressing was changed every day. Two days after the debridement, a further debridement was performed for the extended infection in both arms. Following the second debridement, 0.2 to 0.3 $\mu g/kg/h$ fentanyl was administered intravenously for postoperative pain, and intravenous ketamine 1 mg/kg was administered while changing the dressing. Although his coming out from anesthesia after the second debridement was uneventful, his consciousness deteriorated gradually during the postoperative course and he became restless and almost unresponsive 2 days after the second debridement. Although fentanyl was discontinued, his consciousness deteriorated gradually. Laboratory data including electrolytes, blood chemistry, thyroid function tests, and head CT scan were almost within the normal limits.

Thirteen days after the application of the iodoform gauze, his plasma iodine level was found to be elevated to 6,280 μ g/dl (normal range: 4-9 μ g/dl), and the iodoform gauze was discontinued after 19 days of application. Thereafter, the level of consciousness improved very slowly with the concomitant decrease in the plasma iodine level (Figure). On the 14th day after discontinuation of iodoform gauze dressing, he opened his eyes and began to speak on verbal command. Because sucrose with povidone-iodine was applied to the wound for 2 weeks approximately 40 days after the discontinuation of iodoform gauze, his plasma iodine level increased again from 19.9 to 54.8 μ g/dl, but his consciousness did not deteriorate any further. Although he remained confused





until 3 months after the discontinuation of iodoform gauze, he eventually became fully alert.

Discussion

There are some case reports in which plasma iodine levels were investigated after iodoform intoxication was first reported in 1903¹⁾. However, there have been no case reports in which the plasma iodine level exceeded 1,000 μ g/dl in patients with iodoform intoxication. In the present case, the iodine level was about 6 times higher than the highest level reported in the literature²⁾. The patient's level of consciousness, however, recovered almost completely, even though it took about 3 months to do so.

Because the plasma iodoform level is not normally measured in the clinical setting, a diagnosis of iodoform intoxication must be made indirectly by measuring the concentration of plasma iodine, which is released from iodoform dissolved in the tissue. Plasma iodine levels in patients with iodoform intoxication are reported to be in the range of 31.6 to 977 μ g/dl in the literature^{2)~8)}. In this case, the application of iodoform gauze, clinical features including unconsciousness and high plasma iodine level thus resulted in a definitive diagnosis of iodoform intoxication.

Povidone-iodine is water-soluble and

delivers free iodine. Unlike iodoform intoxication, iodine intoxication following usage of povidone-iodine usually presents with diarrhea, confusion, agitation, liver dysfunction, renal failure and metabolic acidosis and the result is fatal. Some authors reported that patients with iodine intoxication presented with severe metabolic acidosis and that their plasma iodine levels reached 5,600 to 48,000 $\mu g/dl^{9)\sim 11}$. The present case, with a plasma iodine level of 6,280 μ g/dl, did not show signs of metabolic acidosis or renal failure. Therefore, the high plasma iodine level in iodoform intoxication seems to have much less effect on acid-base balance or renal function than in iodine intoxication.

While the level of the consciousness in this patient did not decline during his recovery period, the plasma iodine level increased again to 54.8 μ g/dl due to the application of povidone-iodine to the wound. Some authors reported that consciousness deteriorated with a plasma iodine level of 31.6 to 40.2 μ g/dl in patients with iodoform intoxication³⁾⁴⁾. It seems unlikely that the plasma iodine is a major factor in the disruption of consciousness; there may be some other factors involved in iodoform intoxication.

The human body contains 15–20 mg of iodine, 70–80% of which is located in the thyroid gland. Iodine excretion is directly related to renal function¹², with plasma iodine level maintained in the range of 4–9 μ g/dl. Although no specific renal lesion has been identified in patients with high plasma iodine level, acute tubular necrosis and pronounced vacuolar degeneration of the proximal convoluted tubules were found¹⁰⁾¹³. Kanakiriya et al. speculated that oxidant-dependent pathways of tissue injury, in which myeloperoxidase released by activated leukocytes utilizes iodide, may be driven by large concentrations of iodine¹⁴⁾.

The most common symptoms in iodoform intoxication reported in the literature are headache, disorientation, confusion, delirium, drowsiness and semi-coma, and the recovery time after discontinuation of iodoform is 2 weeks to 1 month. This case ended with a coma and required 3 months of recovery time, which implies that the iodoform intoxication was severe. Although the dosage of postoperative fentanyl and ketamine was less than that of the usual clinical use with no effect on the hemodynamic status, they masked the effect of iodoform; it took several days to suspect iodoform intoxication. On the other hand, the wound surface area in the both arms and in the lumbar region, which had been contact with iodoform gauze, was so extensive that the amount of iodoform absorbed must have been large. These factors must have contributed to the increased plasma iodine level.

Since iodoform (CHI₃) has similar structure to chloroform (CHCl₃), it is likely that iodoform has an anesthetic effect if it is in the brain. Roy et al.¹⁵ measured the total iodine concentration and iodoform and its metabolite (diiodomethane) concentrations in plasma (n=6), in patients with encephalopathy after the application of iodoform gauze. They showed high concentrations of total iodine and low but detectable concentrations of iodoform and diiodomethane. They also found high concentrations of iodine and detectable iodoform and diiodomethane in the cerebrospinal fluid (n=2), and suggested that since these compounds are lipophylic, they can therefore penetrate into the brain.

Kanakiriya et al.14) reported a case of

iodine toxicity successfully treated with hemodialysis and continuous venovenous hemodiafiltration. Since iodine is excreted primarily by the kidneys, it is reasonable to use hemodialysis or continuous venovenous hemodiafiltration to decrease the iodine concentration in patients with renal insufficiency. Those may be useful in the case of iodoform toxicity, as well. The current patient, however, had poorly controlled diabetes, which caused severe infection, and he presented with no renal failure. Due to concern about additional infection, catheterizing him for hemodialysis or continuous hemodiafiltration was avoided.

In conclusion, a patient experienced iodoform intoxication causing his consciousness to deteriorate with a high plasma iodine level, however, he recovered almost completely about 3 months thereafter. Although iodoform gauze is useful and costeffective, caution should be exercised when it is applied while coming into contact with a wound demonstrating a large surface area.

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(和文抄録)

ヨードホルム中毒;血清ヨード濃度が高値で 長期間に渡る意識障害を呈した症例報告

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我々は感染創に対するヨードホルムガーゼの使用中に意識障害が出現した症例を経験した.意識 障害時の血清ヨード濃度は、過去に報告された最高値の6倍を超える高値であった。直ちに使用を 中止したところ、徐々に意識回復を認め3ケ月後に完全回復したので文献的考察を加えて報告す る.【症例】コントロール不良の糖尿病を合併した71歳の男性.硬膜外膿瘍に対して椎弓切除術及 び両側上肢の筋膜炎に対してデブリードメントが施行された。術後にヨードホルムガーゼを創部に 使用し、定期的に交換していたところ意識障害(Japan Coma Scale で 100~200)が出現した。ヨー ドホルム使用開始後13日目に血清ヨード濃度を測定すると、6,280μg/dlと著しい高値を呈した。 ヨードホルム使用中止後は血清ヨード濃度の低下に伴い意識も徐々に回復し、中止後37日で血清 ヨード濃度は19.9μg/dlまで低下し、3ケ月後に意識清明となった。ヨードホルム中毒においては 血清ヨード濃度が高値を示す報告が散見されるが、これほどの異常高値を呈しながら意識回復した 報告は本症例のみであった。ヨードホルムガーゼは、意識障害が出現することを念頭に置いて注意 深く使用すべきである。