

Topical Betadine Exposure Precipitating Sterile Cerebritis and Systemic Iodine Toxicity

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Key Clinical Message

Cerebritis may present with encephalopathy, seizures, localizing neurologic deficits, or death. Betadine is an antimicrobial solution with high iodine content, and iodine has well-known toxicity. Here we report a case of sterile cerebritis secondary to repeated betadine exposure from caring for an extensive open wound of the scalp.

Background

Cerebritis is a potentially fatal inflammatory condition typically with presenting symptoms of encephalopathy, seizures, or localizing neurologic deficits. Common culprits of cerebritis include autoimmune conditions as well as infectious causes.

Betadine (or povidone-iodine) is a commonly used antiseptic, made up of a combination of iodine and a water-soluble polymer.¹ Once applied, the iodine molecule dissociates and penetrates microbial cell membranes, interacts with proteins, nucleotides, and fatty acids within the cell, and ultimately results in rapid cell death.¹ This mechanism of action promotes a wide antimicrobial spectrum as well as efficacy in disrupting biofilms.^{1,2}

Betadine may cause irritant dermatitis when applied to the skin. This develops as iodine exerts similar destructive effects to those mentioned previously. The effect of betadine on neural tissue is less understood. In a study evaluating varying concentrations of betadine on rabbit brains, Li et. al. describe histologic evidence of neural tissue damage in the absence of clinical indications of such damage, and tissue damage worsened with increasing concentrations.³ This evidence is further supported by Wang et. al. who noted that lower concentrations of betadine (eg. 0.5%) was beneficial for tissue healing but higher concentrations (eg. 5% or more) had the opposite effect.⁴ To our knowledge there are no reports of iodine toxicity resulting in sterile cerebritis secondary to recurrent topical betadine application. Here we report an interesting presentation of sterile cerebritis precipitated by chronic topical betadine application during the care of an open scalp wound.

Objective

Here we report an interesting presentation of sterile cerebritis precipitated by chronic topical betadine application during the care of an open scalp wound.

Case Report

A 73-year-old woman with a pertinent past medical history of diabetes and squamous cell carcinoma (SCC) of the scalp presented with her family to her primary care provider for her annual Medicare visit (2/2023). During the visit, her family reported increased confusion and falls over the course of two weeks as well as increased foul smelling, purulent drainage emanating from a surgical site wound on her scalp. Review of systems was negative for fever, chills, headaches, dizziness, hypoglycemia, or other infectious symptoms. She reported taking her medications as prescribed. In addition, her PHQ score was 18 (previous was one in December 2021).

Physical exam revealed normal vital signs and an intact cranial surgical mesh with an adjacent area of hypertrophied, hardened skin and purulent drainage. Bloodwork from the visit revealed a mild leukocytosis of 11.9k/cu mm (4.5 – 11k/cu mm), elevated ESR and CRP of 75 and 11.7 (<30 and <0.5 respectively), and an elevated hemoglobin A1c of 10.3% (6.2% six months prior). With these results, a prompt evaluation in the nearest emergency department (ED) was recommended to assess for a central nervous system (CNS) infection.

The SCC of her scalp had previously eroded through her cranium to the dura, resulting in craniectomy with placement of a titanium fenestrated mesh. To close the defect, she underwent two flap procedures (most recently 4/2022); however, both attempts were unsuccessful. Not wanting to undergo additional procedures, the defect had been treated for at least six months using Betadine 10% solution which was discontinued two weeks prior to her presentation to her primary care clinic.

In the ED, her vitals were: 97.9F, heart rate 69, respiratory rate 20, blood pressure 110/45, and O2 saturation 100% on room air. She was alert and oriented with an intact surgical mesh on her head. The surgical site had clean, dry dressing wrapped around it. The surgical site was surrounded by brown/gray material that appeared to be a mix of matted hair and dried discharge without any obvious purulence, foul smell, or tenderness (Figure 1 A & B).

After obtaining initial bloodwork (Table 1) and blood cultures, she underwent imaging, a lumbar puncture (Table 2), wound cleaning (Figure 1 C & D), and was started on intravenous antibiotics and supportive cares (vancomycin, cefepime, and metronidazole at CNS penetration dosing).

Magnetic resonance imaging (MRI) of her brain revealed left frontal cerebritis with associated bifrontal leptomenigitis and pachymeningitis without any intra- or extra-axial abscess. After discussing the case with Neuroradiology and comparing current imaging (Figure 2) to images obtained one year prior (Figure 2), there were no significant changes noted in the primary area of concern.

Discussion

Betadine is a topical antimicrobial agent with a large iodine content frequently used for wound care. Excessive iodine intake has well-characterized toxicities within the body. Specifically, elevated serum levels of iodine may lead to thyroid dysfunction resulting in both psychological and metabolic effects. In this patient, iodine likely permeated tissues during wound care therein entering the meninges. Furthermore, iodine absorption is enhanced on denuded skin or other tissues without a protective barrier.⁵ Every milliliter of betadine 10% contains 10 mg of iodine. Once iodine is absorbed, it reaches equilibrium rapidly with the extracellular space and distributes evenly except in certain areas, one of which is the thyroid where it is used to make thyroxine (T4) and triiodothyronine (T3). Excessive iodine may result in a transient reduction in thyroid hormone synthesis (Wolff-Chaikoff effect) by inhibiting thyroid peroxidase (TPO) activity.⁶ Iodine also prevents the release of preformed thyroid hormones (called the Plummer effect) by inhibiting proteolysis of thyroglobulin.⁶ Upon checking her thyroid status, she was found to have a low normal TSH at 0.44 (0.3 – 4.2) and a low normal FT4 at 1.1 (0.9 – 1.7).

A reduction in thyroid hormone influences other organs, such as the pancreas and the brain. In the pancreas, it may lead to decreased insulin secretion, via decreased stimulatory signal on pancreatic beta cells, thus leading to hyperglycemia and worsening of diabetes.⁷ In the brain, reduced thyroid hormones may result in pseudo-depression due to alterations in metabolic activity of neurons.⁸ Thinking back at our patient's initial

presentation to her PCP, we suspect that the systemic absorption of iodine from betadine was exacerbating her chronic medical conditions leading to her worsening mood and diabetes despite taking her medications as prescribed. Given that the half-life of iodine is about 66 days, we theorize that her actual plasma iodine level was much higher.

Given the lack of significant differences seen on imaging as well as her benign physical exam and lab results, we suspected that the patient had a chronic sterile cerebritis due to the Betadine used in wound cares and an acute soft tissue infection of the scalp. We theorized that the irritation seen on imaging resulted from Betadine exposure via seepage thru the cranial mesh fenestration. To confirm this theory, a serum iodine level was obtained which returned elevated at 404 (normal: 40 – 92). Unfortunately, we were unable to obtain an iodine level from the CSF as no such test exists.

During her hospital course, her creatinine improved with intravenous fluids and was determined to be secondary to dehydration from poorly controlled diabetes. She declined any additional procedures to close the defect. Despite being on broad spectrum antibiotics, she began to experience new episodes of confusion. Repeat imaging revealed new enhancement of the scalp overlying the craniectomy defect as well as extra-axial abscess formation, concerning for a worsening scalp infection with involvement of the mesh. The patient was ultimately discharged home on hospice with empiric oral antibiotics for the scalp soft tissue infection and new wound care instructions (using Vashe moistened sterile gauze rather than betadine to avoid worsening of condition).

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Figure Legends :

Figure 1 :

Initial images of patients scalp wounds upon arrival (A and B) and after initial wound cares (C and D).

Figure 2 :

Neuroradiologic magnetic resonance imaging during acute cerebritis (Left) and similar imaging obtained one year prior (Right).

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