

Neonatal Hypothyroidism following Prolonged Exposure to Povidone-iodine in a Preterm Infant with Giant Omphalocele: A Case Report and Call for Awareness

Aimen E Ben Ayad¹, Mustafa Abdullatif²

Received on: 04 January 2025; Accepted on: 05 February 2025; Published on: 25 March 2025

ABSTRACT

Omphalocele is a congenital midline defect into the base of the umbilical cord, which frequently contains herniated abdominal viscera. Giant omphaloceles (GOs) are defined as larger than 5 cm. Management of omphaloceles is usually focused on closing the abdominal wall defect after supportive care to stabilize the patient. Some clinicians prefer a nonoperative “paint and wait” strategy without graft closure; the sac is maintained with topical medications such as silver sulfadiazine or combinations of polyvinylpyrrolidone and iodine (the most frequently used commercial preparation being povidone-iodine®) mixed with topical antibiotic powder sprays. Povidone-iodine can cause thyroid dysfunction, especially in preterm infants. The authors present one such case in the article; the goal is to sensitize the medical care-providers to these adverse effects. A female infant born at 26⁺² weeks’ gestation/birth weight of 830 gm showed a GO with intact membranes. A transparent silicone adhesion wound-contact dressing was used to cover the abdominal herniation, and on the 2nd postnatal day, the surgeon began applying povidone-iodine over the omphalocele followed by nonadherent dressings. Serum thyroid stimulating hormone (TSH), free T4, and iodine levels were followed over time. The iodine levels were monitored but the levels at 35 weeks’ corrected gestational age suddenly rose to 33,917 µg/L (normal 40–100 µg/L). The infant was still receiving daily povidone-iodine dressings at this time. These dressings were stopped immediately, and the serum iodine levels dropped to 97 µg/L in 2 months. The authors seek to remind that infants, especially preterm, who are exposed to repeated topical exposure to iodine-containing antiseptic solutions over a large surface area are at risk of developing transient hypothyroidism. There is a need to remain cognizant of these complications and be aware of the need for close monitoring of thyroid function in high-risk infants.

Keywords: Case report, Giant omphalocele, Iatrogenic hypothyroidism, Levothyroxine, Neonatal hypothyroidism, Neonatal screening, Omphalocele, Povidone-iodine, Preterm infants, Thyroid dysfunction, Topical iodine.

Newborn (2025): 10.5005/jp-journals-11002-0120

INTRODUCTION

Omphalocele is a congenital midline defect into the base of the umbilical cord. Most show a small periumbilical herniation. Giant omphaloceles (GOs) are typically larger than 5 cm in diameter and the peritoneal sac could contain herniated abdominal viscera, such as parts of the gastrointestinal system, uterus, ovaries, or spleen.^{1–3} The rates of occurrence in the Middle East can reach 2 in 10,000 newborns.^{4,5} The incidence is higher in infants born to mothers younger than 20 or older than 35, and is more common in males and in multiple births.⁶

Many infants with GOs show respiratory insufficiency, pulmonary hypoplasia, and chronic lung disease.⁷ Up to 35% have congenital heart defects and 15% may have diaphragmatic hernia.⁸ Some patients show clinically significant gastroesophageal reflux disease.⁷ Omphaloceles have also been associated with many complex genetic conditions such as the Beckwith–Wiedemann syndrome; trisomy 13, 18, and 21; pentalogy of Cantrell; Shprintzen–Goldberg syndrome; CHARGE syndrome; Marshall–Smith syndrome; Carpenter syndrome; and the Meckel–Gruber syndrome.^{6,9–19} Overall, infants with GOs may have mortality as high as 15–25%.²⁰

The management of GOs is challenging; some surgeons prefer to close the abdominal wall defect after supportive care to stabilize the patient. Others prefer a nonoperative “paint and wait” strategy; the sac is maintained with topical medications such as silver sulfadiazine or combinations of polyvinylpyrrolidone and iodine (the most frequently used commercial preparation being povidone-iodine®)

^{1,2}Department of Pediatrics, Tawam Hospital, Al Ain, Abu Dhabi, United Arab Emirates

Corresponding Author: Aimen E Ben Ayad, Department of Pediatrics, Tawam Hospital, Al Ain, Abu Dhabi, United Arab Emirates, Phone: + 971 503356837, e-mail: aimenbenayad@gmail.com

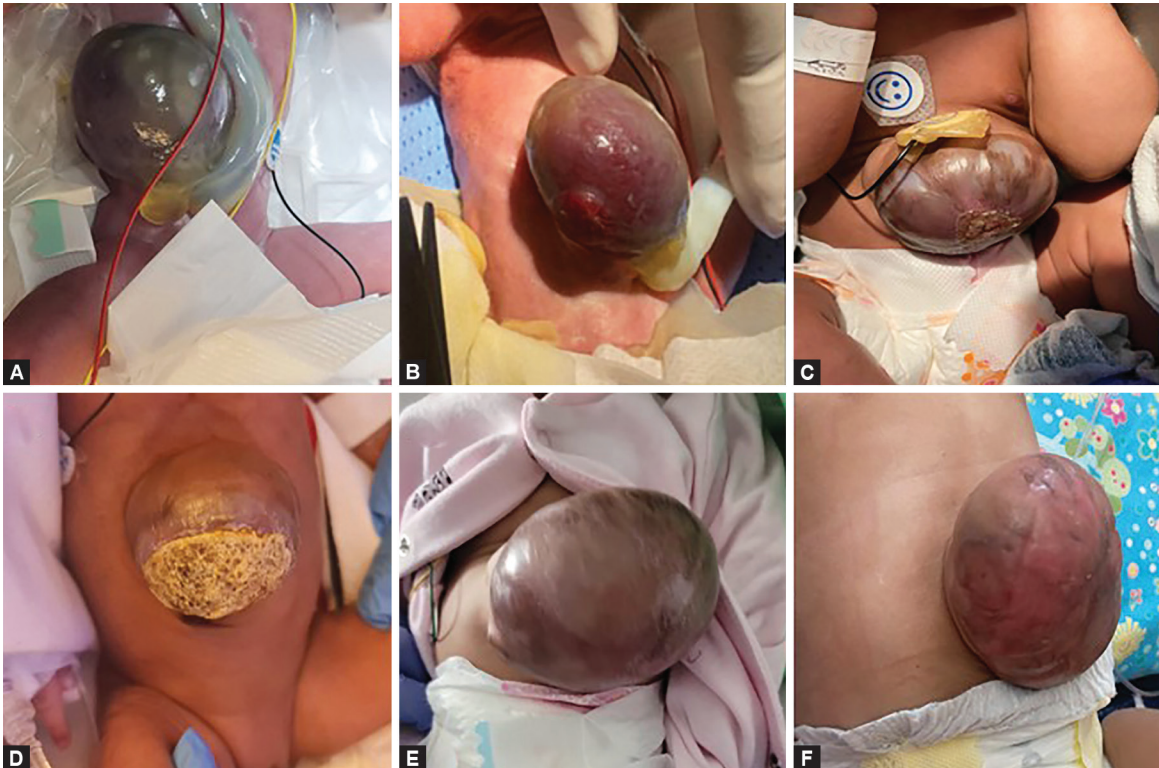
How to cite this article: Ayad AEB, Abdullatif M. Neonatal Hypothyroidism following Prolonged Exposure to Povidone-iodine in a Preterm Infant with Giant Omphalocele: A Case Report and Call for Awareness. *Newborn* 2025;4(1):53–57.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

mixed with topical antibiotic powder sprays (polymyxin B sulfate, bacitracin zinc, and/or neomycin).^{21–26} Studies have shown that the combining topical povidone-iodine with powdered antibiotics may accelerate epithelialization of omphaloceles.^{10,20} Regular dressings to wrap the infant’s torso with an elastic bandage can promote epithelialization and wound contracture to obliterate the abdominal wall defect, and also the closure of the ventral hernia with delayed surgery.^{27,28} Both silver sulfadiazine and povidone-iodine have unique advantages and disadvantages; silver sulfadiazine is less expensive over time and facilitates early granulation with good



Figs 1A to F: A 26⁺² weeks' gestation/830 gm female infant was born with a GO. She was managed conservatively: serial photographs show gradual maturation of the lesion at (A) birth; (B) 2 weeks' postnatal age; (C) 1 month; (D) 3 months; (E) 6 months; and (F) 1 year after birth

broad-spectrum antibiotic coverage.²⁹ However, it might disrupt the granulation tissue in some situations.²⁷ Povidone-iodine can cause thyroid dysfunction, especially in preterm infants.³⁰ We present one such case in the article; the goal is to sensitize the medical care-providers to these adverse effects.

CASE DESCRIPTION

A 27-year-old primigravida mother with an *in-vitro* fertilization pregnancy was diagnosed to have an omphalocele on sonography at 23 weeks' gestation. Except for a unicornuate uterus, the pregnancy was otherwise uneventful. The fetus did not show any other congenital anomalies. She was transferred to our hospital for premature labor and vaginal bleeding. On arrival, a prenatal ultrasound scan showed an omphalocele (3.9 × 3.9 cm²). She was admitted and given one dose of betamethasone 7 hours before delivery per protocol for prematurity and one dose of magnesium sulfate for neuroprotection.

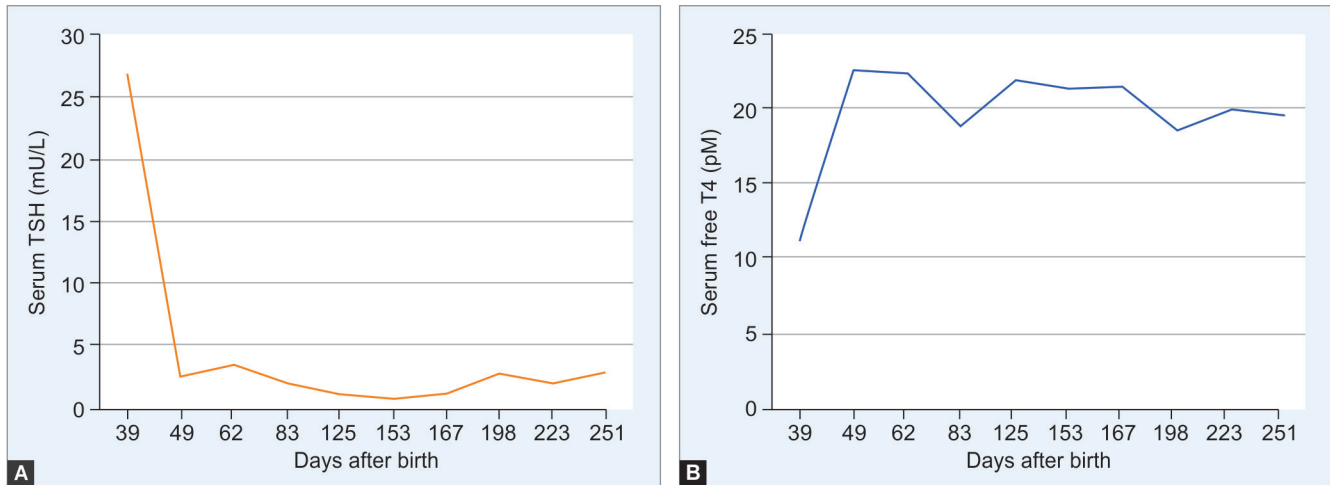
A female infant was born at 26⁺² weeks' gestation with a birth weight of 830 gm by an emergency cesarean section in view of premature labor, antepartum hemorrhage, and breech presentation. At birth, the baby was resuscitated per protocol using a plastic bag, head covering, and the American Academy of Pediatrics neonatal resuscitation protocol. She was dusky in color and had irregular breathing with heart rate less than 100 beats/minute. Apgar scores were 4, 7, and 9 at 1, 5, and 10 minutes, respectively. The baby was intubated and treated with supplemental oxygen as needed per saturations/blood gas evaluations. A GO was noted; the membranes were intact and parts of the liver could be seen inside it. A right microtia was noted.³¹ Echocardiography showed a patent

foramen ovale and an apical ventricular septal defect, all are known associations.³¹

The abdominal herniation was covered with a transparent perforated silicone adhesion wound-contact dressing. The perforated design of these dressings allows the drainage of exudates. Per the manufacturers' guidelines, we can keep these dressings in place for up to 14 days. On the 2nd postnatal day, the surgeon began applying povidone-iodine over the omphalocele followed by nonadherent dressings. The peripheral edges of the dressing were supported using dry gauze. Similar protocols have been previously described from other neonatal units.³² The baby received assisted ventilation for respiratory support and intravenous fluids per our protocol at 80 mL/kg/day through a peripheral line. On the 2nd postnatal day, the surgeon began applying povidone-iodine over the omphalocele followed by a nonadherent dressing. The infant remained intubated for 2.5 months and was then weaned gradually to nasal cannula.

Serum thyroid stimulating hormone (TSH) and free T4 levels were followed over time (Figs 1 and 2). The first and second thyroid screens were normal, but the third screen showed a high TSH at 17 mU/L. The repeat TSH level was 26.9 mU/L and free T4 levels of 11.1 pM. Daily levothyroxine supplementations were initiated, and repeat tests in 10 days showed a good response with TSH levels of 2.45 mU/L and free T4 of 22.5 pM. The infant had feeding intolerance, and an upper gastrointestinal contrast study showed a hiatal hernia with gastroesophageal reflux.

The iodine levels were also monitored. The levels at 35 weeks' corrected gestational age suddenly rose to 33,917 µg/L (normal 40–100 µg/L). The infant was still receiving daily povidone-iodine



Figs 2A and B: Serial serum levels of (A) TSH and (B) free T4 from postnatal days 39 until 251

dressings at this time. These dressings were stopped immediately, and the serum iodine levels dropped to 97 µg/L in 2 months.

DISCUSSION

Thyroid dysfunction, commonly with hypothyroidism, can occur when infants with giant hemangioma, umbilical stump, or complex open wounds are exposed to exogenous povidone-iodine.³³ This issue needs to be considered, and TSH should be monitored carefully in these patients.^{34,35} Exposure to exogenous iodine can cause transient suppression of endogenous thyroid hormone production; this is a well-recognized autoregulatory protective mechanism known as the Wolff–Chaikoff effect (WCE).^{36,37}

The WCE is a safety mechanism that prevents thyroid overactivity following exposure to high levels of circulating iodine and typically resolves in 48 hours.^{37,38} However, this normalization of thyroid function may take longer in premature infants, ranging from several days to weeks.^{39,40} Such delays in thyroid recovery can also be seen in infants with GOs who are treated with topical povidone-iodine solutions that can prevent infections and also promote epithelialization.²³ Repeated exposures over days to weeks can alter thyroid function, particularly in premature neonates; these patients may be at higher risk, as the thin epidermal layer might predispose them to higher iodine absorption and their thyroid axis may be more sensitive to inhibitory effects of iodine overload.^{30,41} Term neonates also share this risk, but possibly to a lesser extent and have relatively more transient hypothyroidism.⁴²

Thaker et al.⁴³ reported a rise in TSH in infants following cardiac catheterization and surgical repair for congenital heart defects following exposure to a large amount of iodine from intravenous iodinated contrast studies and topical applications of iodine-containing antiseptic formulations. Many of these infants needed treatment with levothyroxine for up to 10 months.⁴³ We still do not have sufficient information about the lowest amounts/duration of topical iodine that will likely suppress thyroid function. In addition, the impact of gestational age/birth weight/genetics/ethnicities/geographical origins needs to be explored.³⁹ Based on the available literature, close monitoring of thyroid function during and shortly after frequent topical use of povidone-iodine is recommended for early detection of secondary thyroid suppression to prevent developmental sequelae from undiagnosed hypothyroidism.^{39,44,45}

Our infant was treated with povidone-iodine for a GO and was noted to have developed hypothyroidism during a routine 3-week newborn screening. These findings are important because even though hypothyroidism secondary to exposure to topical povidone-iodine has been reported in the literature, our own center (and most in our region, as evident in a telephonic survey) has not routinely monitored thyroid levels in these patients. Giant omphalocele is not a very frequently-seen condition and so (a) our experience with/anticipation of iatrogenic transient hypothyroidism is limited; (b) premature infants might be at an enhanced risk of suppression of thyroid function due to developmental factors, and possibly of consequent neurodevelopmental delays; (c) there is a need to establish screening protocols in high-risk infants; and (d) there is a need to study the amount and duration of exposure to iodine in infants.^{39,46–48} We were fortunate that our patient was diagnosed in routine newborn screens. This might not have been the case in every patient/unit/region.

We conclude that infants, especially preterm, who are exposed to repeated topical exposure to iodine-containing antiseptic solutions over a large surface area may be at risk of developing transient hypothyroidism. There is a need to remain cognizant of these complications and be aware of the need for close monitoring of thyroid function in high-risk infants. Early detection, timely treatment, and possibly, prevention of hypothyroidism can be helpful.⁴⁹ Once thyroid hormone supplementation is established, close coordination with endocrinologists will be needed for close monitoring.⁵⁰ We also need to evaluate alternatives for iodine-containing topical cleansing solutions in these infants.⁵¹

ORCID

Aimen EB Ayad  <https://orcid.org/0009-0007-5229-6455>

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