

# Silver sulfadiazine as the topical treatment for giant omphalocele - a case report

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## ABSTRACT

36 **Introduction:** Major omphalocele is defined as an abdominal defect greater than 5 cm with the  
37 presence of liver and most parts of bowel in the sac. The management remains challenging for  
38 pediatricians and surgeons with remarkably high mortality. Clear consensus explaining the  
39 standard of care is still unavailable. Current methods are staged surgical closure, defined as  
40 multiple staged operation before final fascial closure and non-operative delayed closure, which  
41 involves a neoeptelialization attempt by applying a topical escharotic agent directly onto the  
42 omphalocele membrane followed by interval repair of the remaining ventral hernia. Reports about  
43 topical agents/dressing use as escharotic therapy such as silver sulfadiazine, povidone-iodine,  
44 topical antibiotics, or honey have been published with different results. Continue application of a  
45 thick layer of silver sulfadiazine on the omphalocele surface is needed to promote eschar formation  
46 and neoeptelialization.

47 **Case description:** A term, 2700-gram newborn male infant presented with abdominal defect and  
48 herniated abdominal contents covered by a membranous sac and contains liver that widely known  
49 as omphalocele. A thick layer of silver sulfadiazine was applied repeatedly onto the omphalocele  
50 sac to promote epithelialization and successfully reduces the sac diameter.

51 **Conclusion:** Conservative treatment with silver sulfadiazine is safe and showed satisfying results.

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53 Keywords: omphalocele, conservative treatment, sulphadiazine

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70 **INTRODUCTION**

71 Omphalocele is one of the major congenital abdominal wall defects leaving abdominal  
72 content eviscerated into the umbilical cord through the umbilical ring and exposed to the  
73 environment. The disease's incidence is 1/4000-7000 live births and is affects 10-30% of cases of  
74 chromosomal anomalies with a high mortality rate. Approximately 60% of children with such  
75 defects survive their first year of life.<sup>1</sup> The well-established risk factors contributing to the  
76 prognosis include the defect's size, antenatal rupture of the sac, low birth weight, gestational age,  
77 related malformations, and prenatal respiratory distress. Omphalocele is a deformity in the ventral  
78 abdominal wall caused by the failure of the four embryonic folds to meet in the midline and create  
79 an umbilical ring before the 10<sup>th</sup> week of gestation.<sup>2</sup>

80 The ideal route of delivery is still the subject of debate. Clinicians must evaluate the defect  
81 size, herniated organs in the sac, the sac's integrity, and any other related abnormalities.<sup>3</sup>  
82 Congenital cardiac disease, chromosomal, renal genitourinary fascial, skeletal, and gastrointestinal  
83 defects are among the associated malformations.<sup>4</sup> The omphalocele ranged in size from 4 to 12  
84 centimeters. Omphalocele major has a defect of more than 5 cm diameter while minor has a defect  
85 less than 5 cm diameter. The omphalocele and abdominal cavity sizes are crucial to surgical  
86 planning. Therapy aims to close the abdominal wall defect after decreasing abdominal content and  
87 stabilizing the patient. Treatment strategies are generally categorized as immediate (primary),  
88 staged repair with delayed primary closure, and delayed repair (paint and wait) with secondary  
89 closure of abdominal hernia. In recent years, the most prevalent treatment has been non-operative  
90 delayed closure, which entails the preservation of the sac with topical medicine and frequent  
91 dressing, followed by epithelization and delayed surgery to close the ventral hernia. Infants with  
92 large omphalocele and/or a significant degree of abdominal-visceral disproportion often get this  
93 procedure.<sup>5</sup>

94 Here we present one omphalocele case, that successful decrease of the size defect with  
95 non-operative treatment, use Silver sulfadiazine topical. Informed consent was obtained from  
96 parental consent.

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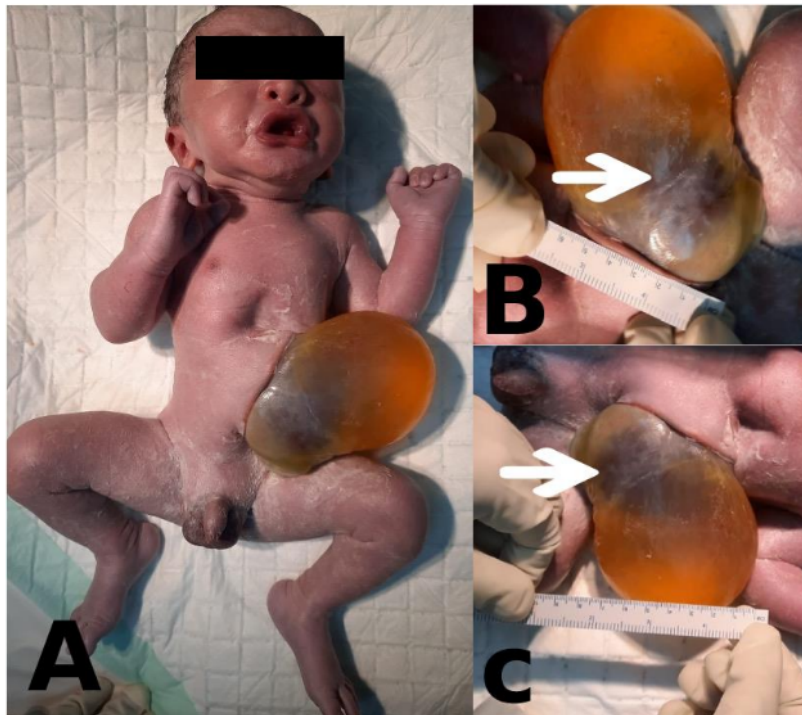
## 98 CASE DESCRIPTION

99 A 2700 grams male newborn was born by caesarean section from a 25-year-old mother at  
100 38-39 weeks of gestation. General activities of the baby were normal with spontaneous crying and  
101 7-8 of APGAR score and normal hemodynamic status. The patient has an initial heart rate of 126

102 beats per minute, a respiratory rate of 42 breaths per minute, and a temperature of 36.7° Celcius.  
103 A herniated-out bowel on an 8 cm sac protruding from his umbilical cord with liver apparent on  
104 the sac (Figure 1A-C). Complete blood count reported hemoglobin 11.8 mg/dl, leukocytes 16,820,  
105 hematocrit 36.2%, platelets 294,000. The abdominal x-ray revealed a cavity with tissue intensity  
106 on the anterior abdominal wall (Figure 2).

107

108 On the 7<sup>th</sup> day of life, the echocardiography result was Patent Ductus Arteriosus (PDA),  
109 0,27 mm diameter, right to left shunt. Ibuprofen drop was given for PDA management (Figure 3).  
110 The management aims to maintain the sac and avoid membrane rupture. A thick layer of silver  
111 sulfadiazine was applied topically onto the omphalocele sac, reapplying as its needed. The layer  
112 was applied repeatedly if the prior layer was completely absorbed. The surrounding omphalocele  
113 is wrapped with sterile gauze. After nine days, the patient was discharged from the hospital with a  
114 decrease of omphalocele diameter (4x6 cm) (Figure 4).



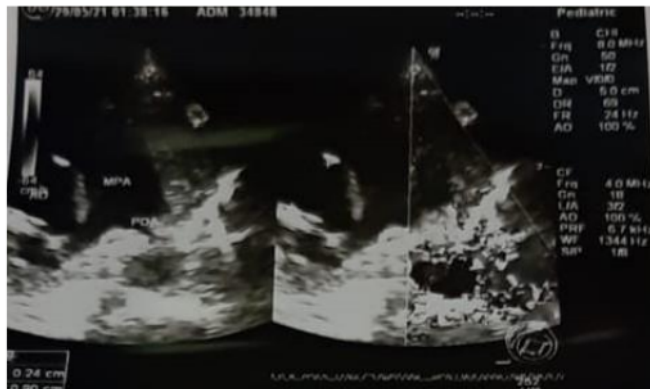
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116 Figure 1. Omphalocele size of  $\pm 5$  cm and  $\pm 8$  cm with a liver appearance on the sac (White arrow)



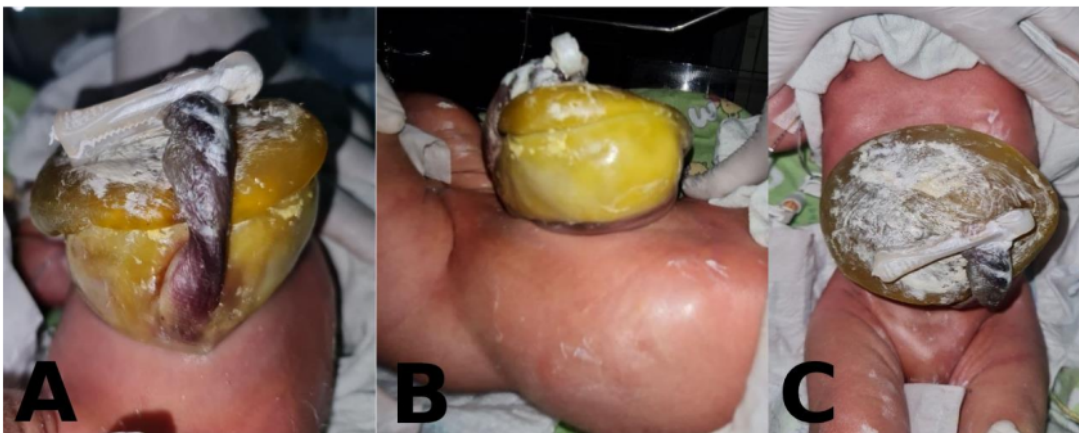
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118 Figure 2. Babygram showed cavity with tissue intensity within the anterior abdominal wall



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120 Figure 3. Echocardiography on seven days old showed Patent Ductus Arteriosus



121

122 Figure 4A-C. Omphalocele care using sulphadiazine cream

123



124 **DISCUSSION**

125 Maldevelopment of midline abdominal wall in early embryonic development (ED) is the  
126 etiology of omphalocele. The normal development of the primitive intestine allows at six weeks  
127 of embryonic development a normal physiologic herniation of the primitive mid-gut after  
128 undergoing the 90 degrees counterclockwise rotation back into the umbilical cord.<sup>6,7</sup> Omphalocele  
129 occurs caused by two events: (i) an incomplete embryonic lateral plicature between 4 and 8 weeks  
130 of embryonic development. (ii) an incomplete migration and differentiation of mesodermal  
131 somites into myotomes originate cutaneous tissue and abdominal wall muscle.<sup>7,8</sup> The incomplete  
132 mechanism causes midline defect of the abdomen where the abdominal organs and especially the  
133 bowel segments were herniated out.

134 The optimal route of delivery is still controversially discussed. The extent of the defect, the  
135 organs affected, the integrity of the sac, and any concomitant anomalies must be considered when  
136 deciding the delivery method.<sup>3</sup> Prenatal screening is important for the early detection of  
137 omphalocele and associated malformations and increases the incidence of elective abortions.<sup>9</sup> Due  
138 to omphalocele, the patient in this case was delivered through cesarean section. Children's Hospital  
139 of Orange Country (CHOC Children's) indicates that small omphaloceles may be acceptable for  
140 vaginal birth. Cesarean section was recommended for giant omphalocele to prevent omphalocele  
141 membrane rupture and enclosed organs trauma (specifically liver). Full-term delivery was  
142 encouraged, but the latter depends on fetal and/or maternal indications.<sup>10,11</sup>

143 Omphaloceles are classified as 'minor' or 'major' depends on the sac's contents and the  
144 defect's diameter. Most 'minor' cases have diameters less than 5 cm and contain small portion  
145 loops of the small bowel. There are usually no other major congenital anomalies. The description  
146 of omphalocele major includes a defect larger than 5 centimeters, the presence of liver, and a  
147 significant amount of bowel in the sac.<sup>12,13</sup> Primary surgical closure can be performed in small  
148 omphaloceles cases, and on the contrary, the surgery should not be attempted on giant  
149 omphaloceles.<sup>11,14</sup> Among the life-threatening problems caused by a rapid increase in  
150 intraabdominal pressure include respiratory failure, hemodynamic instability, compression or  
151 distortion of the inferior vena cava, acute renal failure, bowel obstruction, and intestinal  
152 ischemia.<sup>14</sup> Fifty-80% may have multiple congenital defects, which may raise infant death, and the  
153 condition appears to be more common in males. Depending on the cause, these other abnormalities  
154 may impact any organ, including neural tube defect, cleft palate, single umbilical artery, and

155 amniotic fluid abnormality (oligoamnios or polyhydramnios). Cardiovascular defects were the  
156 most common associated disorder in up to 40-60% of cases.<sup>7,10,15</sup> Our patient is a male with major  
157 omphalocele with 8 cm sac diameter and liver involvement. He also suffers from 0,27 mm Patent  
158 Ductus Arteriosus (PDA) right to left shunt.

159 The omphalocele must be stabilized throughout resuscitation and transport to prevent  
160 bleeding from the liver or obstruction of the liver veins. During primary stabilization, be aware of  
161 the hypothermia, establish vascular access to achieve and maintain the euolemia but avoid the  
162 umbilical vessels, and avoid mask ventilation in case of respiratory distress, early intubation may  
163 be indicated. Children's Hospital of Orange country recommends maintaining sac integrity by  
164 using 1) utilized sterile gloves when handling, 2) placing neonate in bowel bag lined with small  
165 amount of warm sterile saline solution, and 3) positioning neonate sideline while supporting the  
166 omphalocele with blanket rolls to optimized perfusion and prevent compression of blood  
167 vessels.<sup>3,11</sup>

168 Omphalocele treatment aims to reduce the abdominal content followed by the closure of  
169 the abdominal wall defect.<sup>16</sup> The current primary treatment is divided into two basic categories: 1)  
170 non-operative delayed closure (involves the maintenance of the sac with topical medications and  
171 regular dressings, providing epithelization, also known as Paint and Wait methods), 2) removal of  
172 the graft and primary closure after ensuring epithelization with the graft in the early period. The  
173 topical medications used in non-operative delayed closure are the topical antimicrobial or  
174 escharotic agents. Conservative management of omphaloceles allows wound contraction and  
175 epithelization by eschar formation, leaving a ventral hernia that may be repaired at the following  
176 time at adequate age to avoid the risk of major neonatal surgery. It has been reported that this  
177 method yields better results than early surgery in terms of a shorter duration of hospitalization,  
178 early enteral feeding, and reduced mortality due to fatal complications (such as abdominal  
179 compartment syndrome, wound dehiscence, intestinal obstruction and perforation).<sup>13,17</sup> The choice  
180 of an escharotic agent depends on the local availability, cost, ease of application and low risk of  
181 adverse effects.<sup>17</sup>

182 Some topical agents that have been well established to have positive outcomes include  
183 silver sulfadiazine, povidone-iodine, *A. nilotica* paste, topical antibiotics, or honey.<sup>5,18</sup> A  
184 combination of povidone-iodine and antibiotic powder (polymyxin B sulfate, bacitracin zinc, and  
185 neomycin) shows faster escharization in infants with GO than povidone-iodine alone.<sup>16,19</sup> In the



186 study of giant omphalocele management using povidone-iodine shows complete epithelialization  
187 of sac at  $10.0 \pm 2.5$  weeks, and the surgical procedure was performed between the ages of 4 and 9  
188 months.<sup>17</sup> The application of *A. nilotica* paste twice a day shows epithelialization in the mean  
189 period of  $7.83 \pm 4.82$  weeks. The mechanism of action in *A. nilotica* paste is inducing coagulation  
190 of the protein contents of the sac, changing the sac consistency into a rigid structure, which  
191 prevents fluid loss and acts as a barrier against microorganisms.<sup>20</sup> The epithelialization by  
192 application of Manuka honey was achieved in the median of 63 days (48-119).<sup>21</sup>

193 Silver sulfadiazine is low cost and provides a moist wound healing environment, promoting  
194 early granulation with good broad-spectrum antibiotics properties. It is also had antifungal  
195 coverage. It is commonly used for burn treatment and has had positive therapeutic results.<sup>10,22</sup>  
196 Three to five layers of a silver sulfadiazine dressing create a moist wound environment that  
197 promotes angiogenesis and minimizes wound deterioration.<sup>23</sup> In our center, silver sulfadiazine  
198 cream is used repeatedly, applying silver sulfadiazine if the previous layer has been absorbed while  
199 using sterile gloves and gauze. The application may be continued at home with the same routine  
200 with a clean technique.<sup>10</sup> The NOC score assessment on severe burn patients shows NOC 35.20 in  
201 the mean duration of wound healing of 25.4 days, indicating a significant process in the wound  
202 healing (85.7% granulation tissue growth and 75-100% epithelialization).<sup>24</sup> The length of  
203 hospitalization and time to enteral feeding was also shorter (20 days and four days, respectively).<sup>14</sup>  
204 Ein and Langer have explained the omphalocele management technique using silver sulphadiazine.  
205 About 20 g of silver sulphadiazine cream were applied onto the omphalocele sac and then wrapped  
206 with sterile gauze using a clean method once a day. The granulation tissue often appears by the  
207 end of the third or fourth week. It is replaced by an epithelialized scar during the next four to  
208 twelve months, leaving behind a massive ventral hernia. If the neck of the sac was narrow (less  
209 than 5 cm) and blocked viscera from returning to the peritoneal cavity, the sac was removed, and  
210 the narrow neck was converted to a broad base (for later reduction and closure), and a Silon pouch  
211 or Op-site was applied. The subsequent surgery is a repair of the ventral hernia, which started  
212 approximately one year old.<sup>10</sup>

213 It has been reported that silver sulfadiazine can disrupt the granulation tissue. Other  
214 reported risks related to silver toxicity such as convulsions, peripheral neuropathy, ocular  
215 pathologies, nephrotic syndrome, elevated transaminases, argyria, and leucopenia. However, there

216 is no clear report regarding the duration of exposure, dosage, and silver serum level leading to this  
217 complication.<sup>16,20,25</sup>

218 Our patient showed a positive outcome as reduced the omphalocele size after nine days.  
219 The patient family has been educated about the continued application of silver sulfadiazine.  
220 Although the non-operative delayed treatment provides lower mortality rates and better clinical  
221 results, the patients should wait for the reconstruction surgery for a long time. The wound care  
222 during this waiting period is challenging to the family and the clinician.<sup>16</sup> The family should be  
223 trained to apply silver sulfadiazine and suggested for weekly monitoring to primary health care.  
224 The patient should be taken to the emergency room immediately if intestinal malrotation signs  
225 occur (e.g., recurrent vomiting or abdominal distention).<sup>17</sup>

226 The limitation this case only presents one case. In the future, it is very necessary to present  
227 more cases with another treatment, to increase the success of non-operative treatment in  
228 omphalocele cases.

## 229 CONCLUSION

230 Conservative treatment with silver sulfadiazine is safe and showed satisfying results by  
231 reducing the omphalocele size.

232

## 233 DISCLOSURES

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235 No funding or grant support

### 236 Conflict of interest

237 None

### 238 Author Contribution

239 NLPHM involved in writing the manuscript. RE, MTU, DA, KDH supervising and revising the  
240 manuscript. All authors prepare the work and consent to its submission to this journal in its final  
241 form.

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