





CASE REPORT

Sliding Inguinal Hernia with Ovarian Gangrene in an Infant of Minimal Age: A Case Report

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ABSTRACT

Background: Inguinal hernia is one of the common congenital conditions among pediatric age groups with an estimated incidence of 1 - 2% in mature infants and up to 30% in premature infants. The risk of incarceration of testis, bowel, or ovary in children with inguinal hernia is about 3–16%. Therefore, repair of the inguinal hernia is necessary to prevent such complications. However, only a few cases of the hernia sac contain both the ovaries and the uterus at the same time. If reduction of the hernia is not performed in a timely manner, the symptoms will worsen, tissue necrosis and gangrene will ensue.

Case presentation: Parents brought a 45 days old healthy baby to the emergency department for a history of sudden enlargement of the left inguinal swelling that forced the baby to cry continuously, the history, physical examination and investigations revealed incarcerated left inguinal hernia, emergency intervention was performed under general anesthesia, findings were left ovarian torsion, gangrene, and necrosis inside the indirect inguinal hernia sac, left salpingo-oophorectomy was done, histopathological result confirmed the diagnosis.

Conclusion: There is a strong likelihood that inguinal hernias containing the ovary in females pose a substantial risk of torsion and strangulation. Timely intervention should be recommended without delay.

Key words: Inguinal hernia incarceration; Ovarian gangrene; Sliding inguinal hernia; Ovarian torsion.



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INTRODUCTION

Inguinal hernia is one of the common congenital conditions among pediatric age groups [1]. Embryologically, the cause of indirect inguinal hernias is a variation of the inguinal canal throughout the period of intrauterine fetal development. Along the posterior abdominal wall and at six weeks of gestation, germ cells begin to differentiate into ovaries or testes. With the elongation of the fetus, the gonads migrate into the internal inguinal ring. The processus vaginalis is a diverticulum formed at the third month of intrauterine life when the parietal peritoneum protrudes through the abdominal wall at the internal inguinal ring. In male fetuses, the testes begin to move downward at about the seventh month of gestation by using gubernaculum, which is a mesenchymal cord that attaches to the gonad to the mesonephros, as a guide in the inguinal canal. When the testicles completely descend, the vaginal process is obliterated. Female fetuses undergo the same process, with a small difference compared to male fetuses, which is that the descent remains intraperitoneal.

The gubernaculum changes into round and ovarian ligaments, and the corresponding vaginal process, known as the Nuck diverticulum, finally enters into the labia majora. Normally obliteration of the vaginal processus occurs in the eighth month of intrauterine life, if this obliteration has not happened and the vaginal processus persists, it will lead to hydroceles and inguinal hernias that are present in childhood and infancy.[2]

The estimated incidence of inguinal hernia is 1–2% in mature [1] and up to 30% in premature infants [1, 3], this decreases to less than 5% in pediatric age groups [3]. In another study, the prevalence was estimated to be about 13% in infants delivered before 32 weeks of gestation [4].

In another study conducted in China, the prevalence of inguinal hernia was 9.02% in preterm infants and 4.07% in term infants. This rate was higher among males than among females [5]. Regarding the gender difference in the incidence of inguinal hernia, a study in Taiwan stated a ratio of 7: 1 male to female within the general population, but it was 3.5:1 in children. Additionally, gender differences were observed between age subgroups. It was higher in boys in ages 1–4 years old, while girls were higher in ages 5–9 years old. The sex ratio between preterm infants who underwent herniotomy was 3 males to 1 female [6].

Herniation of the ovary through the patent Processus vaginalis known as the canal of Nuck results in an ovary that contains inguinal hernia. However, fluid, fallopian tube, omental

fat, bowel, and rarely the urinary bladder and uterus can also be the content of the hernia sac [7], resulting in a differential diagnosis problem.

Incarcerated hernia is considered the most severe complication since these hernias can contain the ovary, a small bowel loop, a urinary bladder, undescended testicles, or appendix [1]. Approximately 20–35% of the hernia sac in female children contains an ovary and some may also contain a fallopian tube [8]. However, only a few cases of the hernia sac contain both the ovaries and the uterus at the same time [9]. The risk of incarceration of testis, bowel, or ovary in children with inguinal hernia is about 3–16%. So, inguinal hernia repair is necessary to prevent such complications [1, 3].

The typical presentation of sliding inguinal hernias is intermittent swelling in the scrotum, labia, or groin region. It will become more obvious when intra-abdominal pressure increases, for example, while the patient is straining or crying. After undressing and in supine position, the examiner can usually observe inguinal mass or asymmetry. When swelling is not evident, the examiner can apply different maneuvers to increase intra-abdominal pressure. Infants can be allowed to cry or strain and the older child can be asked to stand upright and instructed to jump or cough, or to do a Valsalva maneuver. This will usually allow the bulge to appear through the external inguinal ring and present as a swelling. [2]. When the contents of the hernia cannot be pushed back into the intra-abdominal cavity incarceration of the hernias ensues. If reduction of the hernia is not performed in a timely manner, the symptoms will be worsen, tissue necrosis, and gangrene will ensue [3].

After excluding strangulation, the operation can be postponed for newborns; the presence of hernia containing an ovary in female children is an indication of urgent intervention, and surgery must be performed as soon as possible to prevent ovarian gangrene [1]. The timing of inguinal hernia repair is controversial. Delayed repair could be associated with hernia-related complications, whereas early repair has a high surgical risk and is technically challenging [10]. There is a paucity of data about the effect of the timing of inguinal hernia repair on the outcomes [10].

The purpose of this case report is the rarity of the case, the first case recorded in the Kurdistan region – Iraq and the advice for surgical consultation in the presence of an inguinal hernia in the female to prevent ovarian loss.

CASE PRESENTATION

A 45-day-old female, otherwise healthy, was brought to the emergency department of Ashti Hospital in Soran Town, Erbil city, Kurdistan region, Iraq, on 18 January 2015 by her parents for the appearance of swelling in her left groin region for approximately 10 hours.

The thorough history taken revealed that her mother had observed swelling while changing her diaper and while the infant cried since birth, from birth to presentation day, the parents neglected her to decide on the operation because they were afraid of the decision of surgery in such a newborn's age, at presentation time the mother commented that the infant became increasingly crying and the cry did not stop during the last several hours, and during changing the diaper she noticed the swelling increased in size and did not push back. The past history of medical diseases, surgeries, family history and drug history were unremarkable, no congenital anomalies were observed, the patient continued to urinate and defecate until the presentation time without obvious signs of septicaemia. She had been born by normal vaginal delivery without any obvious complications at normal gestational age and was full term, she received up to date vaccinations.

On examination the patient looked well, no signs of dehydration were observed, no colour change, no dyspnea, she was well hydrated, not lethargic and did not experience vomiting, but she was constantly crying, vital signs were normal (pulse 141 beats/min, respiratory rate 27 breaths/min, temperature 36.7°C, and SPO₂ 96% in room air). Her skin was unremarkable and her extremities were well perfused. Examination of the head, neck, lungs, and abdomen were normal. A firm, red, and hot solitary swelling sized about (1.5 × 2 cm) was noticed and palpable over the patient's left inguinal region. The patient became more irritable with palpation of the mass and the mass was irreducible. Ultrasonography of the inguinal and abdominal region was sent to exclude incarcerated inguinal hernia and other possible differential diagnoses.

The imaging result was a left indirect inguinal hernia containing a nonperistaltic bowel loop with decreased perfusion and suggesting an ischemic bowel loop inside the hernia sac; we considered the risk of gangrenous bowel to be high due to tenderness on examination and ultrasound features of decreased perfusion to the content of the hernia.

The pediatric surgeon was not available at that time, and we took consent from the parents for urgent surgical intervention with the possibility of the need for bowel resection and anastomosis in addition to the hernia surgery risks and complications.

Due to the urgent nature of the case, characterized by severe tenderness and heat surrounding the mass, we promptly proceeded with the intervention to mitigate the risk of septicemia. Without conducting a plain abdominal X-ray to assess air-fluid levels, we moved forward with the operation. On one hand, we were uncertain about the contents of the mass as there were no indications of vomiting or bowel obstruction. The operation was carried out under general anesthesia and endotracheal intubation, surprisingly the intraoperative finding was the hernia containing serosanguinous fluid with a firm mass that was black in colour, the mass rotated several times on its pedicle, derotation was done, 10 minutes we waited, but no colour change was noticed (**Figure 1**).



Figure 1. Ten minutes waiting for color change of the mass

We suspected ovarian torsion and gangrene, no bowel loops found inside the sac, intraoperatively another verbal and written consent was taken from the parents for left salpingo-oophorectomy, left salpingo-oophorectomy was performed, hernia sac highly ligated at internal inguinal ring and excised, the wound was closed in layers, the excised specimen was sent for histopathological examination, the infant recovered without any complications, the mother was advised to start milk feeding 4 hours after the operation since bowel sound checked and was positive, after another 6 hour the patient followed up and she was completely comfortable without noticing vomiting or crying, since we considered the case as a day case surgery because there was no bowel loop resection and anastomosis and the infant passed smooth post-operative period, she has been discharged 12 hours after the operation, emergency contact number was provided to the parent of the

Slides No: 1

Microscopic Examination

Sections show ovarian tissue which reveal an edema, congestion of the blood vessels and full of red blood cells and clots, and numerous extra-vasated red blood cells was infiltrate within the parenchyma (interstitial).

No evidence of malignant elements within the received specimen.

Special staining:

Conclusion:

- **THE HISTOLOGICAL PICTURE IS COMPATIBLE WITH OVARY INFARCTION (RED INFARCTION), LEFT OOPHOROCYSTECTOMY.**
- **NO MALIGNANCY.**

Notes: **The red infarction is compatible with ovarian torsion.**

Figure 2. Histopathological report of the patient

patient, follow up of one week after the operation was uneventful, hence the skin stiches removed, the histopathological report was returned back 10 days following surgery and the result revealed ovarian infarction due to ovarian torsion (Figure 2).

DISCUSSION

Groin masses encompass a large number of differential diagnosis among pediatric age groups, inguinal hernias come at the top of the list [11]. Different reports estimated that the incidence of ovarian incarceration within inguinal hernia is approximately 15–30% [12]. The common presentation, as was found in our case, is the recurrent appearance of swelling in the groin region that can be visible only during increasing intra-abdominal pressure such as straining and crying, the same typical presentation was found in our infant case, despite the fact that the herniated ovary can be detected by palpation as a mobile mass, but it is better to send a colour Doppler ultrasound that provides valuable information on the state of ovarian perfusion and helps us to determine whether ischemia has developed or not [13], in our case also the ultrasound was sent but revealed ischemic bowel inside irreducible indirect hernia sac. The risk of torsion increases when the ovarian tubes are longer than normal; in this situation, the

ovaries become more mobile and the ovary is larger in size compared to its tubes [12, 14]. This arrangement may simulate the 'bellclapper' deformity, which is well known in spontaneous testicular torsion situations [15]. At the beginning, torsions can affect venous drainage, in turn leading to a decrease in arterial supply and end with ischemia and gangrene [16]. however, many pediatric surgeons stand against the view of the role of elective surgery for incarcerated herniated ovary based on its condition whether strangulated or reducible, but the fact imposes an urgent surgical intervention in case of ovarian prolapse in hernia sac due to the relatively narrow pedicle and extensively liable for incarceration and gangrene is to avoid losing a reproductive organ like the ovary or the fallopian tube [12].

The incidence of inguinal hernias is at its highest throughout the first year of life, with more than one third of cases seen in infants younger than six months of age [2]. This is in agreement with our 1.5 month age infant, The risk of incarceration of testis, bowel, or ovary in children with inguinal hernia is about 3–16%. [3] and in another study (15–30%) [12] On the other hand; ovarian torsion with or without fallopian tubes can develop in 2–43% of inguinal hernias. Adnexal torsion, with or without hernia, may be in the form of isolated fallopian tube torsion or in association with ovarian torsion. Isolated tubal torsion develops when the tube is prolapsing in

the hernia sac while the ovary is normally fixed in its place, which is called the bell-clapper deformity which is similar to the pathology in testicular torsion [12]. Therefore, inguinal hernia repair is necessary to prevent such complications [3], that's why we interfered within a few hours.

The most important step in the management of inguinal hernias in female patients is to focus on ovarian involvement. The uterus may be seen in the sac in very few cases. [3], while it was not found in our case, ovarian tissue can often be palpated as a small mobile mass, but it is usually better diagnosed by ultrasound, however in our case ultrasound could not notice the ovary within the hernia sac and misdiagnosed it as a small bowel loop and unfortunately the ovary was involved in incarceration and gangrene, which ended with oophorectomy. In elective cases, surgical intervention can often be postponed until a few weeks after presentation, and as on an outpatient basis, this includes those patients who have no suspicion of incarceration and who underwent careful manual reduction [2].

This reason in combination of neglecting the infant by parents may be the cause of their wish to wait some months for the decision of the operation on an elective basis, if reduction faced difficulties and requires sedation, emergency surgical repair may become necessary. [2], in our case we did not try for reduction, since there was high suspicion of sac content incarceration, situations in which surgery may need to be delayed include sepsis, premature birth, low birth weight, presence of congenital heart or pulmonary disease, and metabolic disease, all due to increased risks of anesthesia. [2], fortunately, the mentioned reasons for postponing the operation were not seen in our patient and the patient was fully fit for general anesthesia and the operation was successful. Irreducible inguinal hernia with ovarian content should prompt the surgeon to consider the risk of strangulation or torsion. Tenderness over the mass can give a clue about early signs of hypo-perfusion; here suspicion of ovarian torsion should be high. Based on the mentioned reasons, we performed the surgery without delay; however, prompt referral to a pediatric surgeon within a critical time for surgical repair is recommended to decrease the risk of torsion and eventually save viable reproductive tissue, but in our opinion, if the time and facility are not allowed for this referral, it was first unwise to waste time, and secondly emergency intervention by a general surgeon is also possible, as in our case report.

A 10-month old female infant reported in Canada treated by detorsion without the need for oophorectomy because she presented within a few hours [11], while due to neglect of our infant patient by the parents, she presented late and the case

eventually lost her left ovary. A 3-month-old woman case reported in Basrah – Iraq, diagnosis was confirmed by ultrasound for the right inguinal hernia containing the right ovary, oophorectomy was performed for her due to gangrene [17], the same fate and procedure faced our case with differences only in age (3 months vs 1.5 month), Thus, our case is the youngest female baby was reported to have developed ovarian gangrene in an indirect inguinal hernia, at least in our Kurdistan region and in Iraq. Tamer Fakhry et al. [18] concluded that indirect hernia with sliding ovary and fallopian tube inside it is not uncommon finding, and it is observed in approximately 30% of pediatric females affected by congenital inguinal hernia, so from clinical point of view, while the surgeons are dealing with hernia sac it is very important to keep this fact and incidence in their mind. For excluding the presence of sliding ovary and tube, the Hernia sac must be opened in all cases; If sliding ovary and tube are noticed, they must be dissected with caution and reduced prior to attempt of sac ligation to prevent their injuries.

However, male infants are affected more by congenital inguinal hernia than female infants, inguinal hernia is more on the right side and more affects preterm infants [5, 6, 19], but all the observed in our case were reverse, since our case was full-term female infant, and the hernia was on the left side of the groin.

One of the concerns about not early intervention to repair the inguinal hernia in newborns is the administration of different anesthetics and sedatives that increase the possibility of the risk of neurodegenerative disorders. [20] different pediatric and animal studies in humans have shown long-term adverse neurodevelopmental outcomes in the developing brain due to exposure to anesthetic agents. [19] Although only a few weeks difference was observed in this study for the delay in taking anesthesia and the timing of surgery between the 2 groups, but this short period of delay may be serious in preventing possible risks of anesthesia-related neurodegenerative complications, this concern was not applicable for our case, since the infant presented as emergency case and the operation could not be delayed and despite the well fitness of the patient for general anesthesia.

Non-torsion ovary found during an inguinal hernia operation for a full-term female newborn of 62 days old, which is diagnosed by ultrasound before the operation in Turkey. [13] that was treated by ovarian reduction of the ovary high ligation of the inguinal sac with fixation of the hernial sac. This case report differed from our recorded case in age (62 Vs. 45 days) and treatment approach since our case was not a candidate for ovarian reduction and isolated herniotomy due to gangrenous

ovary.

Another case of right inguinal hernia was reported in London [21] for a 15 day preterm (36 weeks gestation) female infant and presented as a mass on the right side of the groin and anterior labium major, which was diagnosed preoperatively by ultrasound which showed heterogeneous hypoechoogenicity containing small cysts. without evidence of visible fat or peristalsis within the mass, suggesting a lymph node or bowel with no blood flow within the mass, hence suspected strangulation, treated by oophorectomy due to intraoperative finding of incarceration, and the case discharged at the third postoperative days. This case was similar to our reported case in the treatment approach since both underwent oophorectomy, but it differed in many other points such as age (15 vs. 45 days), (preterm vs. full term), (pre-operative sonographic diagnosis Vs. intraoperative diagnosis), (right vs. left side). 20-year-old female [22] also underwent an operation for right side inguinal hernia that had been discovered since birth but was neglected by parents, intraoperatively right ovary has been observed and reduced to the intra-abdominal cavity followed by herniotomy and modified bassini repair, the same neglect has been observed in our case but not at such an age of 20 years, however, the fate of the ovary of this 20-year-old lady was good compared to our case that was ovarian loss, in our opinion the age of presentation has impact on the fate of the ovary, since any appearance of mass or feeling of any pathologies in a 20-year-old lady can be felt easier and seeking for consultation is faster before the development of possible complications.

CONCLUSION

It must be highly suspected that the inguinal hernia containing the ovary in females carries a significant risk of torsion and strangulation and intervention should be offered as soon as possible. Our case is the least age female infant who developed ovarian gangrene in a sliding indirect inguinal hernia, at least in the Kurdistan Region and Iraq as well.

RECOMMENDATION

Surgical consultation in the presence of an inguinal hernia in a female is crucial to prevent ovarian loss.

ETHICAL DECLARATIONS

• Acknowledgements

None.

• Ethics Approval and Consent to Participate

Ethical approval for this case study was approved by Koya University – Faculty of Medicine.

• Consent for Publication

The parent of the patient provided written consent for the publication of this case report and any accompanying images.

• Competing Interests

The authors declare that there is no conflict of interest.

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• Authors' Contributions

All stated authors contributed significantly, directly, and intellectually to the work and consented it to be published.

REFERENCES

- [1] Alrzoq RA, Alhaji AMA, Alolayt IYI, Almulhim AI, Althobaiti SA, Alzahrani IA, et al. The incidence of inguinal hernia among children. The Egyptian Journal of Hospital Medicine 2018;70(3):483–486. <https://doi.org/10.12816/0043492>.
- [2] Palmer LS. Hernias and hydroceles. Pediatrics in review 2013;34(10):457–464. <https://doi.org/10.1542/pir.34-10-457>.
- [3] Dreuning K, Maat S, Twisk J, van Heurn E, Derikx J. Laparoscopic versus open pediatric inguinal hernia repair: state-of-the-art comparison and future perspectives from a meta-analysis. Surgical endoscopy 2019;33:3177–3191. <https://doi.org/10.1007/s00464-019-06960-2>.
- [4] Olesen C, Mortensen L, Öberg S, Rosenberg J. Risk of incarceration in children with inguinal hernia: a systematic review. Hernia 2019;23:245–254. <https://doi.org/10.1007/s10029-019-01877-0>.
- [5] Fu YW, Pan ML, Hsu YJ, Chin TW. A nationwide survey of incidence rates and risk factors of inguinal hernia in preterm children. Pediatric surgery international 2018;34:91–95. <https://doi.org/10.1007/s00383-017-4222-0>.
- [6] Chen YH, Wei CH, Wang KWK. Children with inguinal hernia repairs: age and gender characteristics. Global

- pediatric health 2018;5:2333794X18816909. <https://doi.org/10.1177/2333794X18816909>.
- [7] Sarkar S, Panja S, Kumar S. Hydrocele of the canal of Nuck (female hydrocele): a rare differential for inguino-labial swelling. *Journal of Clinical and Diagnostic Research: JCDR* 2016;10(2):PD21. <https://doi.org/10.7860/JCDR/2016/16710.7284>.
- [8] Cascini V, Lisi G, Di Renzo D, Pappalepore N, Chiesa PL. Irreducible indirect inguinal hernia containing uterus and bilateral adnexa in a premature female infant: report of an exceptional case and review of the literature. *Journal of Pediatric Surgery* 2013;48(1):e17–e19. <https://doi.org/10.1016/j.jpedsurg.2012.09.065>.
- [9] Takezoe T, Sato K, Watanabe T, Ohno M, Takahashi M, Migita M, et al. A female infant with an inguinal hernia containing the uterus and bilateral ovaries. *Journal of Pediatric Surgery Case Reports* 2015;3(2):46–47. <https://doi.org/10.1016/j.epsc.2014.11.021>.
- [10] Khan FA, Zeidan N, Larson SD, Taylor JA, Islam S. Inguinal hernias in premature neonates: exploring optimal timing for repair. *Pediatric surgery international* 2018;34:1157–1161. <https://doi.org/10.1007/s00383-018-4356-8>.
- [11] Lee J, Scampoli N. Incarcerated ovarian inguinal hernia in a 10-month-old girl. *CMAJ* 2015;187(8):596–598. <https://doi.org/10.1503/cmaj.140823>.
- [12] Volkan Sarper Erikci AST Cemal Bilir, GK. Ovarian Torsion Associated with Strangulated Inguinal Hernia: A Case Report and Review of Literature. *ECronicon* 2018;7(5):478–482.
- [13] Kaya O, Esen K, Gulek B, Yilmaz C, Soker G, Onem O, et al. The inguinal herniation of the ovary in the newborn: ultrasound and color Doppler ultrasound findings. *Case Reports in Radiology* 2014;2014. <https://doi.org/10.1155/2014/281280>.
- [14] Marinković S, Kantardžić M, Bukarica S, Grebeldinger S, Pajić M. When to operate nonreducible ovary? *Medicinski Pregled* 1998;51(11-12):537–540.
- [15] Aihole JS. Bell clapper deformity in female? *International Journal of Surgery Case Reports* 2022;92:106879. <https://doi.org/10.1016/j.ijscr.2022.106879>.
- [16] Aydin S, Ergün E, Fatihoğlu E, Durhan G, Koşar PN. Ovarian torsion within an incarcerated inguinal hernia; Ultrasound and color Doppler findings. *Cumhuriyet Medical Journal* 2017;39(1):449–452. <http://dx.doi.org/10.7197/cmj.v39i1.5000198898>.
- [17] Abdulla MA. STRANGULATED OVARIAN INGUINAL HERNIA IN A FEMALE INFANT—CASE REPORT. *Basrah Journal of Surgery* 2022;28(2):49. <https://doi.org/10.33762/bsurg.2022.134714.1026>.
- [18] Fakhry T, Albatany A, Sabry A, Fawzy A. Incidence of sliding ovary and fallopian tube in congenital inguinal hernia among female children. *The Egyptian Journal of Surgery* 2017;36(1):1–5. <https://doi.org/10.4103/1110-1121.199899>.
- [19] Boyer T, Kritzmire S, Neonatal anesthesia. StatPearls. Treasure island (FL). StatPearls Publishing StatPearls Publishing LLC; 2019.
- [20] Habre W, Disma N, Virag K, Becke K, Hansen TG, Jöhr M, et al. Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe. *The Lancet Respiratory Medicine* 2017;5(5):412–425. [https://doi.org/10.1016/S2213-2600\(17\)30116-9](https://doi.org/10.1016/S2213-2600(17)30116-9).
- [21] Choi KH, Baek HJ. Incarcerated ovarian herniation of the canal of Nuck in a female infant: Ultrasonographic findings and review of literature. *Annals of medicine and surgery* 2016;9:38–40. <https://doi.org/10.1016/j.amsu.2016.06.003>.
- [22] Saini R, Bains L, Kaur T, Lal P, Pal V, Beg MY, et al. Ovarian inguinal hernia—a possibility in MURCS syndrome. *Journal of Ovarian Research* 2021;14:1–6. <https://doi.org/10.1186/s13048-021-00869-y>.