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10.4103/jimr.jimr\_15\_24

# Cystica indeterminata – A novel intriguing pelvic pathology in a 9-year-old girl

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## Abstract:

Intra-abdominal cystic lesions are commonly associated with visceral locations such as renal, hepatic, pancreatic, ovarian/adnexal, and mesenteric. Rarely, nonvisceral locations such as retroperitoneum, free intra-peritoneum, prevertebral space, and pelvis harbor cystic lesions. In almost all these lesions, radiology, histopathology, immunostaining, and serology markers are able to assign a definite origin and pathogenesis. Very rarely a clear diagnosis is not possible, and these lesions have been designated as “indeterminate” lesions. We report the first case of “cystica indeterminata” with completely obscure origin and histopathogenesis in a 9-year-old female child. Clinical, radiological, seromarkers, histopathology, related differentials, and pathogenesis have been discussed. We hypothesize that aborted organogenesis or acquired degenerative/involuntary changes may lead to such indeterminate lesions.

## Keywords:

Cystica indeterminata, in childhood, indeterminate intra-abdominal cyst

## Introduction

Intra-abdominal cystic lesions have a wide spectrum of differential diagnoses mostly associated with visceral locations; very few arise in extra-visceral locations [Table 1]. Most of these lesions have a discernable histopathology. Rarely, the lesion has an obscure pathology, designated as indeterminate cysts in known viscera (renal, ovarian, adnexal, and pancreatic) locations.<sup>[1-3]</sup> Few indeterminate cysts have been reported in the literature at extra-abdominal locations such as pineal gland and thymus.<sup>[4-6]</sup> We report the first case of a unique intra-abdominal and extraperitoneal cystic lesion of obscure origin and histopathology in a 9-year-old female and coin it as “cystica indeterminata;” outlining its clinical, radiological, intraoperative, and histopathological characteristics. Based on histopathological

findings and literary background, we hypothesize the plausible genesis of such lesion. While encountering cystic lesions in clinical practice, a cognizance of this rare pathological entity should be kept in the list of differentials. A thorough systematic pathological and immunohistological analysis will establish the diagnosis after excluding all other possibilities.

## Case Report

A 9-year-old female had presented with recent onset, dull, intermittent, nonradiating lower abdominal pain, associated with precocious puberty and early menarche. She had been having irregular menstruation every 2–3 months. No complaints of dysuria, abnormal vaginal discharge, nausea, or constipation. Clinically, she was a healthy female, active, with nontender, nonmobile swelling palpable in the suprapubic area. Radiologically, USG showed a cystic lesion (measuring 6 cm × 5 cm × 5 cm) with mildly echogenic fluid supra vesical,

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**How to cite this article:** Pal K, El Bahtimi R, Pal A, Pal A. Cystica indeterminata – A novel intriguing pelvic pathology in a 9-year-old girl. J Integr Med Res 2024;2:174-8.

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Submitted: 18-03-2024

Revised: 01-04-2024

Accepted: 02-04-2024

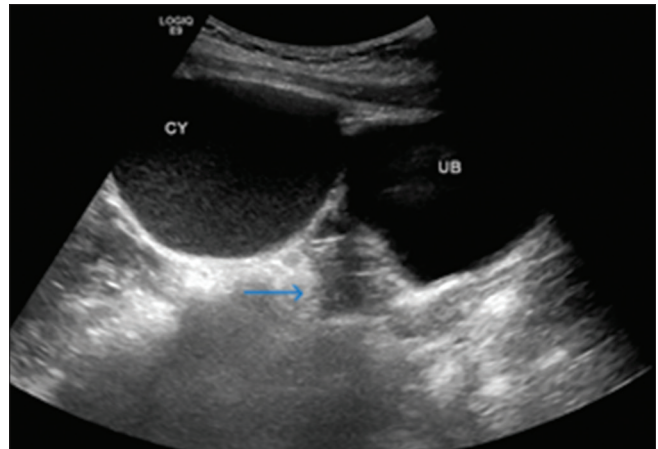
Published: 30-07-2024

**Table 1: Intra-abdominal cystic lesions in children**

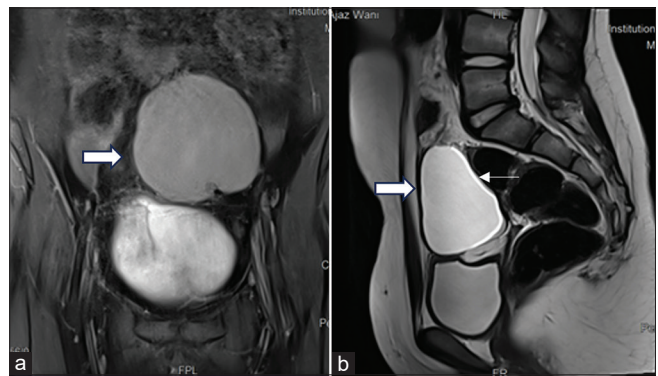
Visceral cystic lesions	Nonvisceral cystic lesions
Renal-hydronephrosis, renal cystic lesions, multicystic disease, cystic Wilms tumor	Cystic lymphangioma
Adrenal- hemorrhagic cyst	Abdominal abscess
Hepato-biliary - cystic lesions of liver, choledochal cyst	Parasitic cysts
Intestinal duplication cyst, mesenteric cyst omental cyst, Meckle's diverticulum	Resorbing hematoma
Pancreatic cystic lesions and pseudocyst splenic cysts	Cystica indeterminata (coined by the authors)
Ovarian cysts, follicular, luteal cyst, teratoma, dermoid cysts	
Hydrometrocolpos, Mullerian duct remnant, endometriosis	
Urachal cyst	
Sacrococcygeal teratoma	
Extra pulmonary sequestration cysts	

abutting the right adnexa, raising the possibility of a right ovarian cyst or urachal cyst [Figure 1]. Magnetic resonance imaging (MRI) showed cystic lesion (measuring 7 cm × 6 cm × 5 cm) in the supra vesical location extending to the left hemipelvis; hypointense on T1 and hyperintense on T2 with enhancing rim at its base [Figure 2]. Markers including alpha fetoprotein, beta human chorionic gonadotrophin (HCG), lactate dehydrogenase, and CA-125 were within normal limits. Laparoscopy revealed midline preperitoneal cystic lesion extending to the left hemipelvis. The cystic mass was separate from the adnexa, uterus, and rectum with a small area of proximity to the left lateral wall of the urinary bladder [Figure 3]. Only few pelvic lymph nodes were noted adjacent to the swelling, without any connections to the urinary bladder lumen or adherence to the dome of bladder or extension into presacral space or intervertebral extension, receiving vascular supply from internal iliac vessels. Complete laparoscopic excision of the swelling was performed. The cystic mass contained light greenish clear fluid with cholesterol crystals and hemosiderin pigments contained in a thick fibrous wall with fibro-fatty tissue and soft concretion [Figure 3d].

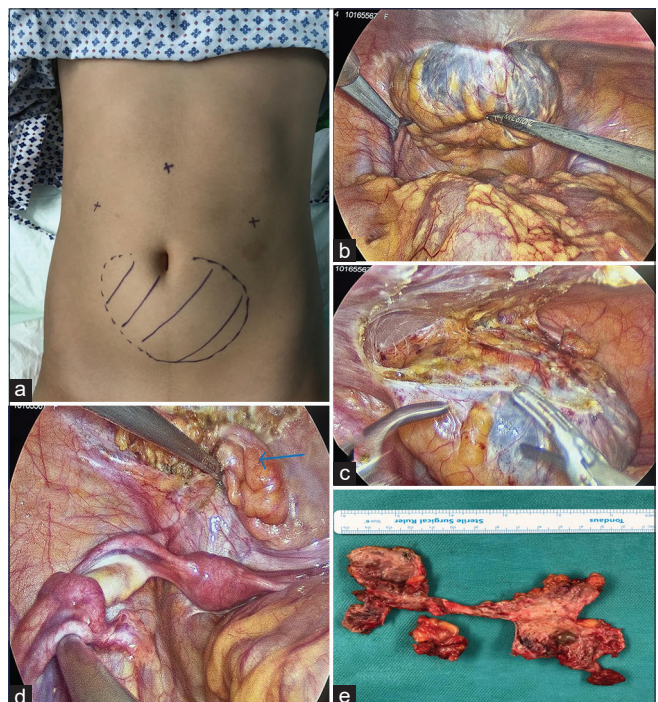
Histopathology showed the wall composed of fibro-fatty tissue with encapsulated cholesterol clefts surrounded by hemorrhage, hemosiderin pigments, and dystrophic calcification [Figure 4]. Smooth muscle actin (SMA) stain highlighted the smooth muscle in two layers [Figure 5a and b]. S100 and CD 34 were negative [Figure 5c and d]. Neither epithelial lining (urothelial, glandular, or squamous) nor ectopic functional rests could be identified in the whole cyst. No endothelial-lined lymphoid/vascular spaces, endometrial glands, or stroma were seen in the wall.



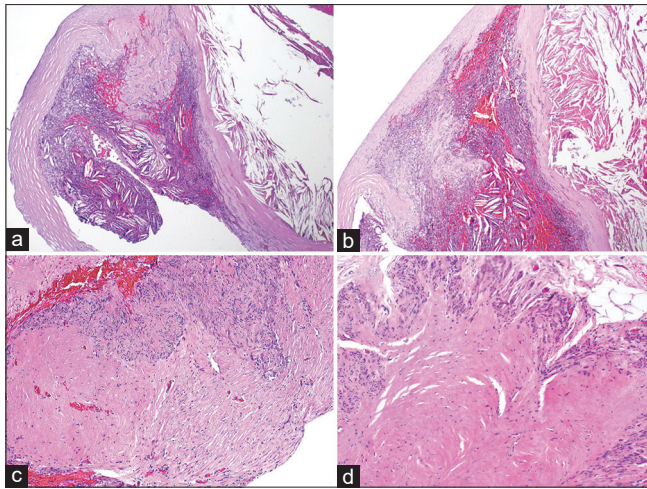
**Figure 1:** Ultrasound showing juxta vesical cystic lesion and right adnexa (blue arrow)



**Figure 2:** Magnetic resonance imaging showing cystic lesion, (a) hypointense on T1 (bold arrow), (b) hyperintense on T2 (bold arrow) with enhancing rim of tissue (thin arrow)



**Figure 3:** Clinical (a) and intraoperative view of cystic lesion (b-d) (e) excised specimen cut open



**Figure 4:** Hematoxylin and Eosin staining showing: (a and b) Cholesterol clefts with hemorrhage, and fibrosis, (H and E, ×10 and × 4). (c and d) Smooth muscle layer simulating muscularis propria, (H and E × 10 and ×4)

The child made an uneventful recovery and is symptom free at 6 months' follow-up.

### Discussion

Intra-abdominal cystic lesions have a wide spectrum of distinct pathologies in children. The most common differentials include visceral lesions originating from renal, adrenal, hepato-biliary-pancreatic, splenic, intestinal, omental, mesenteric, ovarian, mullerian, endometrial, urachal sources and nonvisceral cystic lesions from intraperitoneal, retroperitoneum, and pelvic sources [Table 1].

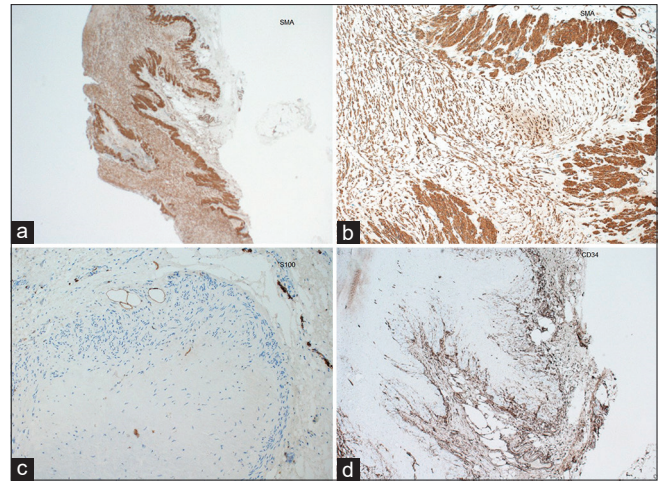
Seldom, a clear histopathological diagnosis is elusive, in such cystic lesions, these are designated as indeterminate lesions, mostly reported in renal, pancreatic, and ovarian-adnexal locations in the literature.<sup>[1-3]</sup> Indeterminate cystic lesions are also infrequently reported in extra-abdominal locations such as the pineal gland and thymus.<sup>[4-6]</sup>

We attempted to derive a possible diagnosis of the cystic lesion based on radiological, intraoperative, serology markers, histopathological, and immunostaining findings compared with the following commonly described differentials.

Possibility of ovarian/adnexal, endometrial, rectal duplication, and neuro-enteric cysts were ruled out at the outset due to lack of anatomical proximity and lack of typical histological findings.

#### Urachal cyst

The urachus is a connection between the primitive bladder and the umbilical cord. If it does not obliterate, several remnants are possible. The urachus can stay



**Figure 5:** Immunostaining showing. (a and b) Diffuse SMA positive showing smooth muscle arranged in two layers in the wall (×4 and × 20). (c) S-100 negative, (×0). (d) CD 34 negative, highlighting the stroma, (×10)

open, allowing urine to escape through the umbilicus. The most common remnant is a diverticulum on top of the bladder. It is also possible that a part of the urachus persists as a cyst in the course of the urachus. Pathologic examination typically shows an urothelium-lined cyst, compatible with a urachal remnant.

In our case, the cystic lesion was located in the preperitoneal midline but was separate from the bladder dome and midline ligament and lacked any urothelial lining, thereby negating the possibility of an urachal cyst.

#### Dermoid cyst

They are congenital ectodermal inclusion cysts and tend to occur in the midline, classically described as T1-hyperintense lesions due to proteinaceous thick content.<sup>[7]</sup> Histology demonstrates a cystic lesion delineated by a keratinizing squamous epithelium with a granular layer, sebaceous glands, and keratin. In our case, the cyst was thin-walled, clear liquid content, hypointense on T1, having no lining epithelium or other ectodermal tissue.

#### Lymphangioma

Intra-abdominal lymphangiomas consist of dilated lymphatic channels, comparable to the cystic lesions in the neck; they typically involve mesentery, omentum, and retroperitoneum (sometimes the term omental cyst or mesenteric cyst is used). On ultrasound cystic masses are seen, which can be clear or cloudy, unilocular or multilocular, and vary in size from small to very large. Computed tomography will demonstrate masses with water density. Septa are less well seen on ultrasound. After hemorrhage, they can even appear solid. The MRI characteristics depend on the absence or presence of bleeding or infection. Uncomplicated cysts are low on

T1 and high on T2, but these signals are variable after bleeding.<sup>[8]</sup>

Lymphangiomas are thin-walled cystic masses with a smooth gray, pink, tan, or yellow external surface. On the cut section, they vary in appearance and may contain large macroscopic interconnecting cysts (often referred to as cystic hygroma or cystic lymphangioma) or microscopic cysts (cavernous lymphangioma). Histologically, it consists of variably sized, thin-walled, dilated lymphatic vessels lined by flattened endothelium. Frequently, surrounded by lymphoid aggregates, sometimes with reactive germinal centers. Lumina may contain eosinophilic and amorphous proteinaceous fluid with occasional lipid-laden macrophages and lymphocytes. Longstanding lesions may show interstitial fibrosis. The wall of larger vessels may contain smooth muscle. Stromal mast cells and hemosiderin deposits are frequently seen. The cyst lining may rarely form papillary projections. Lymphangiomatosis frequently shows an anastomosing growth pattern, dissecting around normal structures. Extensive granulation tissue and inflammation may obscure the lymphatic nature.<sup>[9]</sup> Immunohistochemical expression of D2-40 (Podoplanin), PROX1,<sup>[10]</sup> vascular endothelial growth factor receptor 3, lymphatic endothelial hyaluron receptor 1 (LYVE1), CD31 and variable FVIII and CD34,<sup>[9]</sup> SMA is positive in smooth muscle in the larger vessels. Negative stains include GLUT1, HHV8, and CMYC.<sup>[9,10]</sup>

In our case, the cyst was thin-walled, and mildly echogenic, with similar MRI characteristics as a typical lymphangioma, the wall had smooth muscle, but it was devoid of endothelial lined lymphatic spaces/lymphoid aggregates and was CD 34 negative.

### Sacroccygeal teratoma

A sacroccygeal teratoma is composed of solid tissue, cysts, and calcifications. They are often detected at prenatal ultrasound and can be huge. It ranges from completely external (no presacral component) to completely internal (pelvic and presacral without any external component).

Completely internal tumors can escape detection at birth and present later with constipation. The alpha-fetoprotein level is usually elevated. Diagnosis is generally made on physical examination and confirmed on ultrasound. An MRI is often made to document the exact extension of the tumor, especially to depict intraspinal extension, although ultrasound can demonstrate this in newborns and infants.

In our case, there was no intraspinal extension, and alpha-fetoprotein was negative.

### Ancient cystic schwannoma

Schwannoma, one of the most common soft-tissue tumors, is a benign tumor that arises from the Schwann cells of the nerve sheath and present with symptoms of pain or paresthesia. Ancient schwannoma, a degenerative neurilemmoma, is a subtype of schwannoma that can grow to a large size and show degenerative changes, appearing as a cystic lesion.<sup>[11]</sup> Intra-abdominally, it could present as a palpable mass with a long-term clinical course, symptoms of a neurogenic tumor such as local pain, positive Tinel's sign and distinct radiologic features that include an adjacent nerve visualized on sonography, a circumference of a degenerative area and fibrous tumor capsule enhanced on MRI, and positive accumulation seen on a bone scan but not on a gallium scan.<sup>[12]</sup> Lesion would be positive for neural markers S100 and calretinin.

In our case, an enhancing rim of the capsule was seen on the deep pelvic portion of the lesion however, the mass was negative for S 100 ruling out neural/neurilemmal origin.

### Parasitic cyst (echinococcal cyst)

These parasitic cystic lesions can occur in visceral and nonvisceral locations without true epithelial/endothelial/or mesothelial lining. Protoscolices and refractile hooklets are often present. Serologic test for *Echinococcus* is frequently positive. Our case did not have any findings suggestive of parasitic cysts.

### Mesothelial cyst

These lesions have clear mesothelial lining; positive for cytokeratin and calretinin, and negative for CD31. In our case, there was no mesothelial lining.

### Indeterminate cyst genesis

Hypotheses proposed to explain the genesis of an indeterminate cystic lesion in visceral or solid tissues with obscure histopathology include physiological involution, ischemic degeneration followed by necrosis and cavitation.<sup>[5]</sup> Intralesional bleeding, inflammation, and presence of calcification, hemosiderin, and/or fibrosis may obscure the origin of the lesion.<sup>[6]</sup> Secondary involution or degenerative changes over a period of time may alter the histopathology in terms of cyst lining, and other wall features making a clear diagnosis difficult.

However, in nonvisceral location, obscure histopathology could be a result of aborted or dys-organogenesis as seen in twinning, or a result of secondary involution.

### Conclusion

Cystic lesions in the abdomen are mostly visceral in origin with clear histopathological characteristics. Rarely, indeterminate cystic lesions may be encountered in

visceral locations with obscure histopathology, possibly due to secondary degeneration, intralesional bleeding, or reactive inflammation. Cystica indeterminata is a rare entity in nonvisceral location, reported for the first time in this case report. Dys-organogenesis or secondary involution is purported to cause obscure histogenesis in this lesion. Further study is advocated to discern accurate etiopathogenesis of such lesions.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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