

CASE REPORT

The Eyes Do Not See What the Mind Does Not Know: An Underreported Feature in Mature Cystic Teratoma of the Ovary

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ABSTRAK

Teratoma sista matang adalah tumor sel germa ovari yang paling biasa, menyumbang kepada 70% daripada semua neoplasma ovari jinak dalam kumpulan umur reproduktif. Sebagai tumor sel germa pluripotent, teratoma sista matang mempunyai sekurang-kurangnya dua daripada tiga komponen sel germa embrio yang matang: ektoderma, mesoderma dan endoderma. Kehadiran ruang sista berbilang di dalam dinding tumor, yang juga dikenali sebagai cystoides pneumatosis jarang dijelaskan tetapi merupakan salah satu ciri teratoma sista ovari. Pada masa ini, terdapat sedikit maklumat mengenai mekanisme pembentukannya. Di sini, kami menyifatkan satu kes teratoma sista matang ovari yang luar biasa yang kami temui di wanita hamil berusia 31 tahun dengan histologi ovarinya mengandungi kawasan menyerupai cystoides pneumatosis dalam usus. Pemeriksaan makroskopik dan mikroskopik ovari pesakit mendedahkan ciri-ciri diagnostik teratoma sista matang. Yang menariknya, terdapat pelbagai ruang sista yang berbeza-beza saiznya ditemui di dinding sista. Ruang-ruang sista tersebut dilapisi sebahagian atau sepenuhnya oleh makrofaj busa dan sel datia, yang menunjukkan immunoreaktiviti yang kuat terhadap CD68. Penanda immunohistokimia vaskular (CD31 dan CD34) dan penanda sel epitelium (cytokeratin AE1/AE3) adalah negatif. Diagnosis teratoma sista matang dengan ciri-ciri menyerupai pneumatosis cystoides telah dibuat. Pesakit dibenarkan pulang tanpa sebarang gejala atau tanda-tanda bersalin awal. Etiopatogenik ciri histologi yang menarik ini turut dibincangkan secara ringkas dalam artikel ini.

Kata kunci: cystoides pneumatosis, makrofaj busa, seperti-sista, teratoma kista matang

ABSTRACT

Mature cystic teratoma is the commonest ovarian germ cell tumour which accounts

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for 70% of all benign ovarian neoplasms in the reproductive age groups. Being a pluripotent germ cell tumour, mature cystic teratoma has at least two out of three mature embryonic germ cell components: ectoderm, mesoderm and endoderm. The presence of multiple cystic spaces within the tumour wall, also known as pneumatosis cystoides-like appearance is rarely described but a characteristic feature in cystic teratoma of the ovary. Currently, there is little information concerning the mechanism of its formation. Herein, we described an unusual case of ovarian mature cystic teratoma in a 31-year-old pregnant female with multiple sieve-like areas resembling pneumatosis cystoides of the intestine. Macroscopic and histological examination of the ovary revealed features diagnostic of mature cystic teratoma. Intriguingly, multiple cystic spaces of variable sizes were found within the cyst wall histologically. They were lined partially or completely by foamy histiocytes and foreign body type multinucleated giant cells, exhibiting strong CD68 immunoreactivity. Vascular endothelial markers (CD31 and CD34) and epithelial marker (cytokeratin AE1/AE3) were negative. A diagnosis of mature cystic teratoma with pneumatosis cystoides-like feature was rendered. The patient was discharged well with no signs and symptoms of early labour. The etiopathogenesis of this intriguing histological feature is briefly discussed in this article.

Keywords: cyst-like, foamy macrophage, mature cystic teratoma, pneumatosis cystoides

INTRODUCTION

Mature cystic teratoma is the commonest germ cell tumour of the ovary, which constitutes 70% of all benign ovarian neoplasms in the reproductive age groups (Sinha & Ewies 2016). Being a pluripotent germ cell tumour, mature cystic teratoma composed of various combinations of mature tissues that are derived from ectoderm (skin, skin appendages, glial tissue), mesoderm (bone, cartilages, fat, muscles) and endoderm (gastrointestinal and respiratory epithelium, thyroid tissue) (Sinha & Ewies 2016). The presence of multiple cystic spaces within the tumour wall, also known as pneumatosis cystoides-like appearance is rarely described

but is a characteristic feature of cystic teratoma of the ovary (Cierna & Danihel 2018). We present a case of ovarian mature cystic teratoma in a 31-year-old pregnant female with multiple sieve-like areas resembling pneumatosis cystoides of the intestine and briefly discussed its etiopathogenesis of this intriguing histological feature.

CASE REPORT

A 31-year-old pregnant woman at 14 weeks of gestation presented for antenatal follow-up and a left adnexal mass was detected incidentally by routine pelvic sonography. It was a 55 mm multiloculated cystic lesion with mixed echogenicity, suggestive

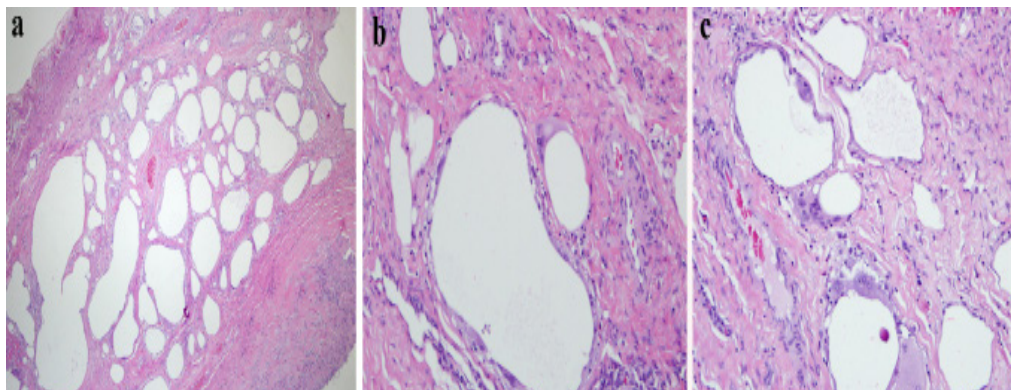


Figure 1: Histological features of pneumatosis cystoides-like appearance in ovarian cystic teratoma. (a) Multiple small cystic spaces of varying sizes are seen within the cyst wall, resembling vessels at low magnification (H&E, x40); (b) Most of the cystic spaces are lined partially or completely by foamy histiocytes and multinucleated giant cells (H&E, x200); (c) and some by mononucleated flat cells while some appear denuded, lacking that of epithelial lining (H&E, x200).

of an ovarian dermoid cyst. She was asymptomatic and was managed conservatively. However, three weeks later, she returned to us with two-day history of abdominal pain. Ultrasound examination of the pelvis showed the left adnexal mass had increased in size to 133 mm in diameter and extended to the left lumbar region. Left ovarian cystectomy was performed due to the suspicion of malignancy in a rapidly enlarging ovarian tumour.

Macroscopically, the ovarian mass was intact with glistening smooth outer capsule and it measured 130 x 80 x 40 mm. Cut section of the mass revealed a multiloculated cystic tumour filled with hair and soft greasy material. The cyst wall measured 2 to 5 mm in thickness with no apparent solid area. Histological examination of the ovarian cyst showed fibroconnective tissue partially lined by stratified keratinising squamous epithelium with hair follicles, sweat glands and sebaceous glands. Focally, mature cartilage and

glial tissues were identified. There was neither immature element nor malignancy.

Interestingly, there were multiple cystic spaces of variable sizes ranging from <1 to 3 mm within the cyst wall, (Figure 1a). Most of the cystic spaces were lined either partially or completely by foamy histiocytes and foreign body type multinucleated giant cells (Figure 1b). In some areas, the cystic spaces were lined by mononucleated flat cells while some appeared denuded (Figure 1c). Immunohistochemically, these lining cells, both flat and giant cells exhibited strong CD68 immunoreactivity (Figure 2a). They were negative for vascular endothelial markers (CD31 and CD34) (Figure 2b) and epithelial marker (cytokeratin AE1/AE3) (Figure 2c). A diagnosis of mature cystic teratoma with pneumatosis cystoides-like feature of the left ovary was made. The patient was discharged well on the 3rd postoperative day with no signs and symptoms of early labour.

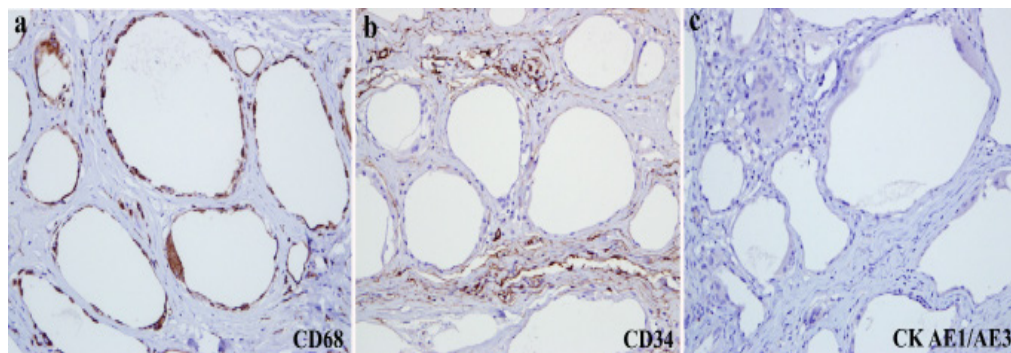


Figure 2: Immunohistochemical features of pneumatosis cystoides-like appearance in ovarian cystic teratoma. The cyst lining cells exhibit (a) strong CD68 immunoreactivity, consistent with the histiocytic nature of the cells; and show immunonegativity for (b) CD34 and (c) cytokeratin AE1/AE3.

DISCUSSION

Pneumatosis cystoides intestinalis (PCI) was first coined by Mayer in 1825 describing a rare phenomenon with unknown aetiology occurring in the intestine. It is characterised by the presence of multiple gas-filled cysts containing hydrogen, nitrogen and carbon dioxide within the submucosal and subserosal region of the intestine (Gui et al. 2014). These optically "empty" cysts are typically lined by variable amount of foreign body type multinucleated giant cells, epithelioid macrophages and/or flattened cells of histiocytic in origin (Gui et al. 2014). The pathophysiology is not well understood.

These cystic structures were also observed in ovarian mature cystic teratoma. It was first described by Maudsley and Zakhour (1989) as sieve-like spaces in a cystic teratoma of ovary, incidentally discovered in a 29-year-old pregnant mother. Subsequently, Rubin and Papadaki (1990) reported the histochemical, immunohistochemical and ultrastructural features of 13 cases

of ovarian mature cystic teratoma with multicystic structures. They revealed that the cyst contents and cytoplasm of cyst lining cells were positive for oil red-O stain, indicated the cystic spaces contained lipid (Rubin & Papadaki 1990). Henceforth, the terms "pneumatosis cystoides-like", "sieve-like", "fat necrosis-like" areas were used interchangeably to illustrate these peculiar multicystic spaces in cystic teratoma. The cystic spaces were lined by macrophages which demonstrated strong CD68 immunoreactivity. Electron microscopic examination of the cyst wall showed lipid-laden lining cells with abundant intracytoplasmic lysosomes and sequestered collagen bundle fibres that are typically observed in macrophages (Rubin & Papadaki 1990). In addition, rare endothelial cells were found in close apposition to macrophages. This finding was supported by occasional immunoreactivity towards factor VIII-related antigen at the cyst wall lining in some cases. In our case, the vascular endothelial markers (CD31 and CD34) were negative. It could be

the endothelium was destroyed by local granulomatous response (Cierna & Danihel 2018).

The formation of multicystic pneumatosis cystoides-like structures in cystic teratoma was believed to be related to focal destruction of the lining epithelium and skin appendages, as a result of increased intratumoural pressure. Rubin and Papadaki 1990 proposed that the destruction of sebaceous gland released oleous material that would infiltrate through the cyst wall, and elicited a foreign body oleogranulomatous reaction. Eventually, after the removal of oleous material by macrophages, it would evolve to form multicystic sieve-like appearance devoid of any lining epithelium (Rubin & Papadaki 1990). On the other hand, some researchers believe the multicystic spaces are related dilatation of partially damaged lymphatic vessels (Canzonieri et al. 1994) due to the immunoreactivity for endothelial markers. However, this postulation was later disputed by the absence of D2-40 immunopositivity (Cierna & Danihel 2018).

The pneumatosis cystoides-like area could be easily regarded as blood vessels at low magnification, especially if little attention is paid to the cyst lining. In two case series consisted of 42 and 31 cases of mature cystic teratomas respectively, the authors concluded that these multicystic structures were not uncommon, it was observed in approximately one-third of the cases (Rubin & Papadaki 1990; Canzonieri et al. 1994). Intriguingly, despite it being a frequent feature seen in mature cystic teratoma, pneumatosis cystoides-like

area is underreported with less than 30 cases found in the literature (Mathew 2008). Rubin and Papadaki (1990) suggested that a careful search for such areas at the time of surgical dissection would increase its detection.

While PCI is notorious to cause complications related to the ruptured of its gaseous content including pneumoperitoneum, tension pneumoperitoneum and intussusception (Gui et al. 2014), little is known about the prognostic implication of these pneumatosis cystoides-like spaces within the tumour since it is an infrequently reported phenomenon. Whether it denotes a mere incidental histological finding with no prognostic value awaits further study.

CONCLUSION

In summary, pneumatosis cystoides-like area is a relatively common, but under-reported feature in mature cystic teratoma. These multicystic structures are thought to be a feature characteristic of ovarian cystic teratoma and may potentially be helpful in its diagnosis.

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Received: 7 Jun 2018

Accepted: 15 Oct 2018