Case Reports

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
49(5) 1–7

DOI: 10.1177/03000605211014797
journals.sagepub.com/home/imr
SAGE

Mimics of malignancy caused by concurrent imperforate hymen and transverse vaginal septum: an instructive case and review of the literature

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Abstract

The coexistence of imperforate hymen and vaginal septum is rare and their ability to mimic malignant manifestations have not been frequently reported. This current case report describes a 13-year-old girl that presented with cyclic abdominal pain for 6 months. She was found to have a huge mass via abdominal plain film X-ray and sonography, with inexplicably high levels of serum carcinoembryonic antigen, cancer antigen (CA)-19-9 and CA-125. Pelvic computed tomography imaging disclosed two huge cystic lesions in the uterine and upper vaginal cavities. Surgical intervention conformed the diagnosis of a concurrent imperforate hymen and transverse vaginal septum, echoing the imaging findings of haematocolpometra. Her tumour marker levels gradually returned to normal after surgery. This rare case of concomitant imperforate hymen and transverse vaginal septum highlights that haematocolpometra, a benign disease that might mimic malignancy, should be taken into consideration in any adolescent females with an abdominal mass and amenorrhoea to ensure an early diagnosis and timely appropriate management.

Keywords

Haematocolpos, haematometra, imperforate hymen, neoplasms, primary amenorrhoea, transverse vaginal septum, tumour markers

Date received: 17 August 2020; accepted: 12 April 2021

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Introduction

Haematocolpos and haematometra are caused by blockage of the outflow of blood and the subsequent accumulation of blood in the vagina and uterus, respectively. Various aetiologies of congenital vaginal obstruction (CVO) have been well documented, including imperforated hymen, vaginal atresia and transverse vaginal septum,[1] but the reported cases with lesions occurring in combination are scarce.[2–4] Because patients with CVO are usually asymptomatic in childhood, the delayed diagnosis is often made in the setting of primary amenorrhoea and/or compression symptoms relating to the haematocolpometra.[1] This current case report describes a rare and instructive case with the coexistence of imperforate hymen and transverse vaginal septum. Her haematocolpometra contributed to an abdominal mass and amenorrhea together with inexplicably high levels of serum carcinoembryonic antigen (CEA), cancer antigen (CA)-19-9 and CA-125, mimicking malignancy. The malignant-like manifestation of haematocolpometra has not been widely addressed in previous published articles. It was effectively managed with surgical intervention after a prompt and precise diagnosis was made.

Case report

In June 2017, a 13-year-old girl was admitted to the Department of Paediatrics, Tri-Service General Hospital, National Defense Medical Centre, Taipei because of cyclic lower abdominal pain along with progressively enlarging abdominal mass for the previous 6 months. Her medical history was unremarkable. There was no fever, difficulty with bowel movements or dysuria.

Upon physical examination, she was ill-looking but without fever. Her height was 151 cm (25th–50th percentile) and she weighed 43 kg (15th–50th percentile). Her breast development was at Tanner stage V and the presence of axillary hair was noted, but there was no menstruation. Her abdomen was ovoid in shape with moderate distension and the bowel sound was hypoactive. Tympanic percussion over the epigastric region was noted and there was a non-tender palpable mass over the lower abdomen. In view of her abdominal mass and amenorrhoea accompanied by a normal Tanner stage, CVO was first considered. Although vaginal inspection is the most simple and important examination, her parents refused an examination of her genitalia in light of their strong traditional beliefs after our detailed explanation and education. Due to limited information from the physical findings, a series of examinations were conducted to clarify her underlying disease. Her blood tests and endocrine function were all within normal limits (Table 1). However, the tumour markers that were measured because of the abdominal mass disclosed inexplicably high levels of serum CEA, CA-19-9 and CA-125. An X-ray of the kidneys, ureters and bladder showed increased soft-tissue densities in the midline of the abdomen. Under abdominal sonography, two communicating cystic masses with debris deposition were found over the middle abdomen, 8.7×5.7 cm and 16.4×20.0 cm in size, respectively.

Computed tomography was arranged to elucidate the nature of the abdominal lesions. This showed an haematometra above a huge haematocolpos, which measured $13 \times 11 \times 14$ cm in size at the upper third of the vagina (Figures 1A and 1B). This cystic lesion had compromised the lower third of the right ureter leading to moderate hydronephrosis (Figure 1B). These images confirmed the diagnosis of haematocolpometra, which might be associated with distal vaginal agenesis or low transverse vaginal septum.

Table 1. Laboratory data for a 13-year-old girl that presented with cyclic lower abdominal pain along with a progressively enlarging abdominal mass for the previous 6 months.

Parameter	Patient's value	Reference range
White blood cell count, number/μl	9140	4500–11000
Haemoglobulin, g/dl	13.2	12.0–16.0
Platelet count, $\times 10^3$/μl	377	150–400
Creatine, mg/dl	0.6	0.5–0.9
Aspartate aminotransferase, U/l	11	0–40
Sodium, mmol/l	136	136–145
Potassium, mmol/l	3.5	3.5–5.1
C-reactive protein, mg/dl	0.3	0.0–5.0
Uric acid, mg/dl	4.8	2.3–7.0
Endocrine profiles		
Insulin-like growth factor 1, ng/ml	129.0	146–480
Cortisol, μg/dl	5.08	4.82–19.5
Thyroid-stimulating hormone, μIU/ml	3.8	0.25–5.00
Follicle-stimulating hormone, mIU/ml	8.46	3.5–12.5
Luteinizing hormone, mIU/ml	12.14	2.4–12.5
Oestradiol, pg/ml	277.20	12.4–233
Tumour markers before surgery		
Alpha-fetoprotein, ng/ml	3.52	0.0–20.0
Human chorionic gonadotropin, mIU/ml	0.62	0.0–5.3
Carcinoembryonic antigen, ng/ml	47.47	0.0–5.0
Cancer antigen 125, U/ml	1033	0.0–35
Cancer antigen 153, U/ml	22.46	0.0–30.0
Cancer antigen 19-9, U/ml	1691.9	0.0–37
Lactate dehydrogenase, U/l	323	240–271
Tumour markers 2 months after surgery		
Carcinoembryonic antigen, ng/ml	2.66	0.0–5.0
Cancer antigen 125, U/ml	21.24	0.0–35
Cancer antigen 19-9, U/ml	29.06	0.0–37

Based on a preliminary diagnosis of CVO causing haematocolpometra complicated with right obstructive uropathy, surgical intervention was performed and perineum examination showed a thickened and intact hymen under general anaesthesia (Figure 1C). After hymenectomy, a coexisting transverse vaginal septum was identified (Figure 1D); and 1200 ml of brown-coloured blood was drained until resection of the vaginal septum. The pathological report of the vaginal septum showed non-cancerous change. Immunohistochemical staining was performed to clarify the relationship between the benign haematocolpometra and the unusually elevated tumour markers. The results showed strongly positive staining for CEA, CA-19-9 and CA-125 in the vaginal septum tissue.

Following surgery, her abdominal pain completely resolved and her menstruation occurred naturally 10 days after the operation. Follow-up abdominal sonography showed that hydronephrosis was improved and intravenous urography disclosed resolving obstructive uropathy. The elevated levels of serum CEA, CA-19-9 and

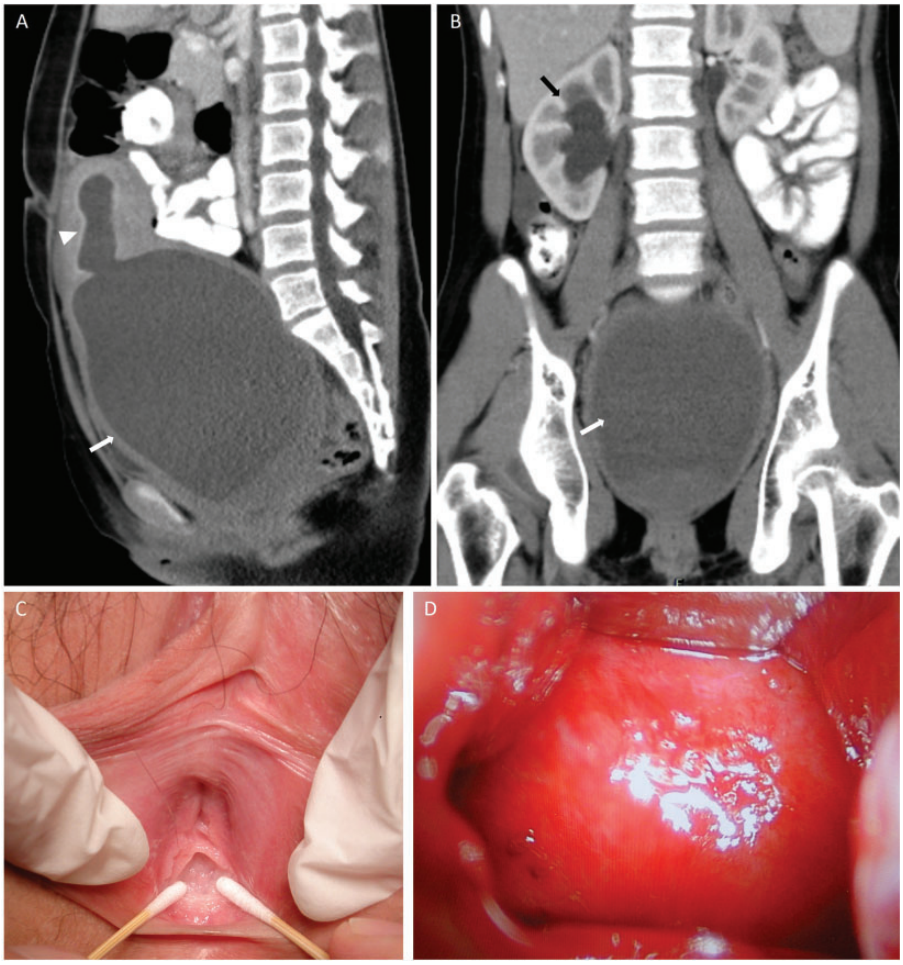

Figure 1. Computed tomography of the abdomen and pelvis of a 13-year-old girl that presented with cyclic lower abdominal pain along with a progressively enlarging abdominal mass for the previous 6 months showed marked dilatation of the uterine cavity (A, white arrowhead) and vaginal cavity (A and B, white arrow) along with right hydronephrosis (B, black arrow). Perineum examination under general anaesthesia revealed a thickened and intact hymen (C) and a blind vaginal pouch with a septum (D) was identified post hymenectomy. The colour version of this figure is available at: http://imr.sagepub.com.

CA-125 returned to normal within 2 months of the surgical intervention (Table 1).

This article was approved by the Ethics Committee of the Institutional Review Board of Tri-Service General Hospital, National Defense Medical Centre, Taipei (no. 2-108-05-054). The patient and her parents provided informed consent for publication of this case report.

Discussion

In light of the previous 6 months of cyclic abdominal pain with the normal development of secondary sexual characteristics and normal endocrine function, CVO was the most likely cause of the current patient's primary amenorrhoea. Genital examination is simple and decisive for providing a differential diagnosis of CVO, which can be

effectively corrected by surgery.[1] However, it was postponed for personal reasons until after the laboratory tests and imaging examinations had been completed. Although imperforate hymen is a clinical diagnosis, a retrospective review of 27 patients reported that approximately 70% of them and this current case had received imaging examinations prior to a confirmed diagnosis.[5] Further genital examinations of the current case might have resulted in professional misconduct and ethical issues. After a detailed explanation and education, this current patient and her parents fully realized the advantages and disadvantages of the examinations and still decided to receive the blood tests and imaging in light of their strong traditional beliefs. To reduce diagnostic uncertainty and avoid unnecessary investigation, the awareness of the common presentation and detailed genital examination should be emphasized in any possible CVO cases.

The abdominal mass that was found accidently in this current case along with the extremely high levels of CA-125, CA-19-9 and CEA warranted meticulous laboratory, imaging and pathology workups to exclude possible malignancy, such as ovarian epithelial stromal tumours. Eventually, the surgical intervention discovered a rare concurrent imperforate hymen and transverse vaginal septum, echoing the imaging findings of haematocolpometra. In the current case, the haematometra and haematocolpos were observed as a distended fluid-containing mass involving the vagina and uterus, with variable internal echotexture under ultrasound and heterogenous density under computed tomography. Associated Mullerian malformations might also be observed in patients, including Mullerian agenesis, obstructing vaginal septum, unicornuate uterus, bicornuate uterus, uterus didelphys and septate uterus.[1] These characteristic imaging findings might help clinicians to exclude a purely cystic mass in clinical practice.

Imperforate hymen is the most common congenital malformation of the female genital tract and its sporadic occurrence rate is 0.05–0.1% at term.[6] Embryologically, the hymen is a mucous layer of epithelized connective tissue that separates the lumen of the vagina from the urogenital sinus. This membrane is ruptured and partially reabsorbed in the 8th week of gestation. However, the failure of this process results in imperforate hymen. In contrast, transverse vaginal septum is comparatively less common and occurs in approximately 1 in 70000 female births.[7] It is a developmental defect in the embryogenesis of the vagina that leads to incomplete canalization and fusion between the Müllerian duct and the urogenital sinus. To date, the simultaneous occurrence of these two congenital anomalies has rarely been reported.[2–4]

The present case is the first in the literature to show that the coexistence of imperforate hymen and transverse vaginal septum can be one of the benign conditions resulting in increased levels of CA-19-9, CA-125 and CEA. Although tumour markers are not routinely required for diagnosis, it has been reported that patients with CVO in premenarcheal age might exhibit increased CA-125 and C-19-9 levels (Table 2),[7–14] but CEA was not measured. The mechanism of haematocolpos causing high CA-19-9 and CEA levels might be either proliferation of the noncancerous mucinous tissue or obstruction of their secretion pathways.[15] In addition, high CA-125 levels in patients with CVO might be explained by increased expression of CA-125 in endocervical epithelium and desquamation of this epithelium into the contents of the haematocolpometra.[16] However, the precise mechanisms underlying the pathological association between haematocolpometra and these tumour makers merits further research.

Table 2. Summary of reported cases of patients with congenital vaginal obstruction with haematocolpometra and increased levels of tumour markers.[7–14]

Author	Age, years	Diagnosis	CA-19-9, U/ml	CA-125, U/ml	CEA, ng/ml
Buyukbayrak et al., 2008[8]	13	Imperforate hymen	>1000	457	1.3
Kalmantis et al., 2009[9]	15	Imperforate hymen	NA	70	NA
Partsinevelos et al., 2009[10]	12	Imperforate hymen	960	277	NA
Sak et al., 2013[11]	13.8 (14 girls)	Imperforate hymen	162 ±189	84.0 ± 23.7	NA
Celik et al., 2015[12]	Term newborn	Distal vaginal atresia	110.1	278.7	NA
Kaya et al., 2012[7]	15	Transverse vaginal septum	40.9	80.2	NA
Deligeoroglou et al., 2012[13]	13.3	Transverse vaginal septum	1552	195	NA
Unal et al., 2016[14]	13	Uterus didelphys with unilateral obstructed hemivagina and ipsilateral renal agenesis (HWW Syndrome)	234.6	N/A	NA
Present case	13	Imperforate hymen and transverse vaginal septum	1691.9	1033	47.47

CA-19-9, cancer antigen 19-9; CA-125, cancer antigen 125, CEA, carcinoembryonic antigen; NA, not available; HWW, Herlyn–Werner–Wunderlich.

In conclusion, this current rare case of concurrent imperforate hymen and transverse vaginal septum highlighted that haematocolpometra should be taken into consideration in any adolescent female with chronic abdominal pain and amenorrhoea. Furthermore, haematocolpometra may mimic malignancy together with increased serum CEA, CA-19-9 and CA-125 levels, but it can be managed effectively with surgical intervention.

Acknowledgements

We would like to thank two anonymous (unknown) reviewers and the editor for their comments.

Author contributions

Ying-Fu Wang conceptualized the study, collected data, drafted the initial manuscript, and reviewed and revised the manuscript; Shih-Ming Kuo, Chun-Hao Chu, Yu-Chun Lin and Hong-Hsiang Fang collected data, carried out the initial analyses, and reviewed and revised the manuscript; Chien-Ming Lin conceptualized the study, coordinated and supervised data collection, and provided critical editing and revision to the final drafts of the report. All authors were involved in the editing and review of the final manuscript, and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

Funding

This study was supported in part by a grant from the Research Fund of Tri-Service General Hospital (no. TSGH-E-110187).

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