Received: 7 January 2022 | Revised: 11 February 2022 | Accepted: 5 March 2022

DOI: 10.1002/jcla.24364

CASE REPORT

WILEY

A case of ovarian Teratoma with nephroblastoma presenting abdomen metastasis

Yinan Wu[1] | Chu Chu[2] | Jingyuan Zhang[1] | Beharee Nitish[3] | Jing Ni[3] | Xinyu Xu[1]

[1]Department of Pathology, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research, The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing, China

[2]Obstetrical Department, Lianyungang Maternal and Child Health Hospital, Lianyungang, China

[3]Department of Gynecological Oncology, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research, The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing, China

Correspondence
Xinyu Xu, Department of Pathology, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research, The Affiliated Cancer Hospital of Nanjing Medical University, Bai Zi Ting 42 Nanjing 210009, Jiangsu Province, China.
Email: xxuxy330@163.com

Abstract

Background: Teratoma with nephroblastoma (TWN) is an extremely rare condition. Since 1984, only 45 reported cases have been identified. To our knowledge, there have been only two cases of TWN of ovarian origin.

Case presentation: We described a case of ovarian TWN who presented to us with painless abdominal masses 6 months after undergoing right ovarian cystectomy. The tumor had spread to the abdomen due to spontaneous rupture of the ovarian cyst and failure to undergo chemotherapy. Microscopically, the ovarian mass exhibited the typical components of a mature cystic teratoma. The tumors found in both the ovary and abdomen contained the nephroblastoma components and were strongly positive for WT-1. The patient was advised to undergo chemotherapy and she was lost to follow-up.

Conclusion: A careful histological examination is necessary for an accurate diagnosis, which is based on morphology and extensive immunohistochemical studies. According to the literature, surgical excision alone seems reasonable as the prognosis of TWN is considered to be good. However, due to the spontaneous rupture of the ovarian cyst, chemotherapy of the patient after the first surgery was necessary in our case. Therefore, additional case studies are needed to clarify the standardized treatment of TWN.

KEYWORDS
case report, immunohistochemical, ovarian, Teratoma with nephroblastoma, therapy

1 | BACKGROUND

Nephroblastoma, also known as Wilms tumor, is a malignant neoplasm that typically accounts for more than 90% of renal tumors in children.[1] Classically, nephroblastoma frequently exhibits a polyphasic differentiation pattern with blastemal, stromal, and epithelial components.[2] Teratoma with nephroblastoma (TWN) is a rare variant of it, first described by Variend et al. in 1984.[3] According to Fernandas' criteria, the TWN should be defined as the triphasic tumor in which heterologous elements like cartilage, muscles, adipose tissue, glial tissue constituted more than 50% of the mass.[4] To the best of our knowledge, 45 cases of TWN have been reported in English literature, while only two of them were primary ovarian TWN.

We recently had an additional case of an adult ovarian TWN. Due to rupture and spillage of the tumor cells, dissemination to the

Yinan Wu and Chu Chu are the co-first author.

peritoneum occurred shortly after the first surgery. Hereunder, we present this particular case and review the literature.

2 | CASE PRESENTATION

A 38-year-old woman presented to our hospital with a painless abdominal mass for 1 week and was subsequently admitted. On physical examination and ultrasonic examination, two well-defined, firm, irregular, non-tender masses were found in the paraumbilical. Laboratory tests, including serum electrolyte levels, urinalysis, and complete blood counts were normal. Under general anesthesia, the patient underwent an exploratory laparotomy through a transverse abdominal incision. Two well-defined abdominal masses with a clear boundary were found intraoperatively. Macroscopically, the resected specimens were two irregular masses measuring 26*20*15 mm and 50*20*15 mm with a thin coating layer. The sections were tan in color and consisted mainly of solid areas and some focal cystic areas (Figure 1). Microscopically, the solid areas were composed of primitive small round blue cells with diffuse proliferation, similar to the renal blastemal components (Figure 2). Immunohistochemical results demonstrated strong positive for Wilms tumor antigen 1 (WT-1) and PAX-8 in the primitive areas, focally positive for CD56, CD99, and entirely negativity for AE1/AE3, Desmin, inhibin, CgA, EMA, CK7, CK20, and CR (Figure 2). The morphology and the findings were consistent with Nephroblastoma. According to the previous medical record, the patient had undergone a right ovarian cystectomy 6 months ago and was diagnosed with a mature cystic teratoma and a suspected ruptured ovarian mass. Subsequently, the case was referred to our institution for consultation. Histologically, the tumor showed components of a mature cystic teratoma, such as cartilage, adipose tissue, skin, and cutaneous adnexal structures. In addition, in the vicinity of the cystic teratoma, the tumor showed a diffuse proliferation of immature tumor cells, consisting of undifferentiated renal elements, mesenchymal renal stem cells, and blastemal cells (Figure 3). Immunohistochemical results showed positive for WT-1, CD56, AE1/AE3, partially positive for PAX-8 and negative for Desmin, E-cad, inhibin negative (Figure 3). These histological findings confirmed mature cystic TWN. Based on these results, the patient was diagnosed with TWN with intra-abdominal

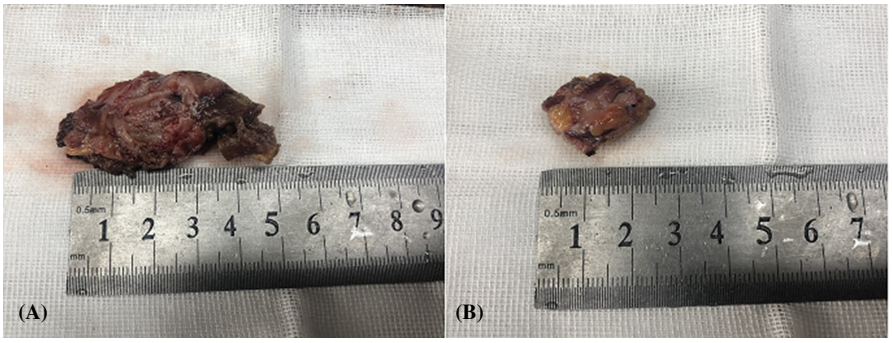

FIGURE 1 Gross findings. The 50 mm size (A) and 26 mm size (B) tumors were well circumscribed and encapsulated solid mass with cystic area

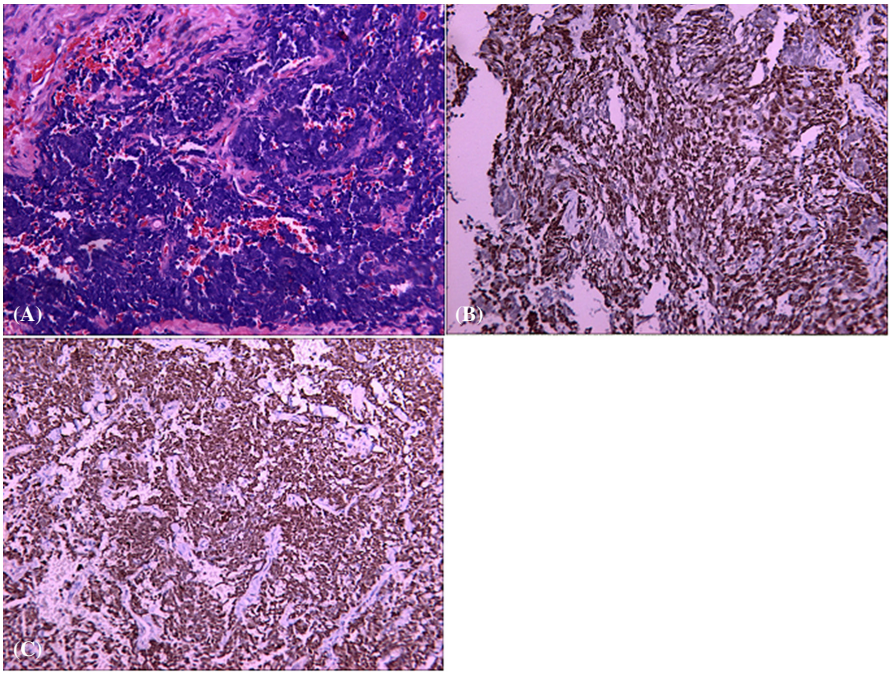

FIGURE 2 The dissemination lesion consisted mainly of blastermal foci (A). Tumor cells were strongly positive for WT-1 (B) and PAX-8 (C). Magnification 200×

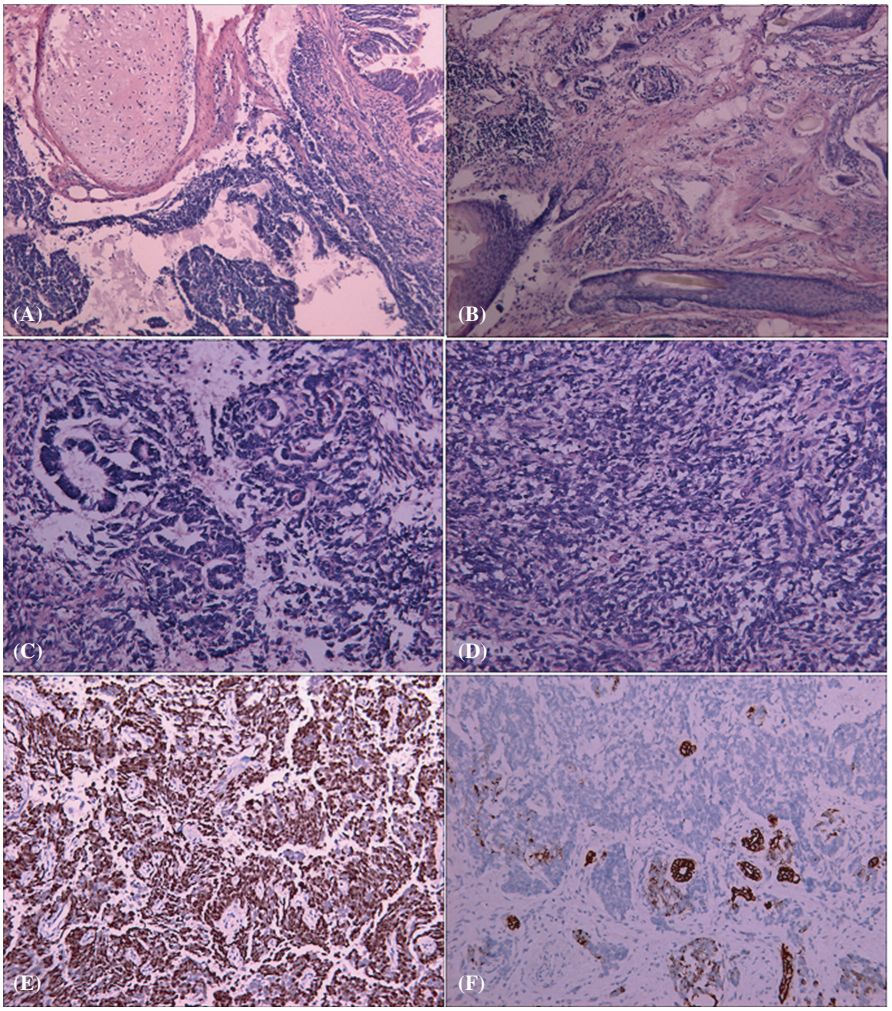

FIGURE 3 Heterologous elements and typical histological pattern of the tumor from ovarian (A) hyaline cartilage tissue, (B) mature adipose tissue and cutaneous adnexal structures, (C) and (D) triphasic pattern of nephroblastoma with blastematous, epithelial and stromal components, (E) WT1 is strongly positive in epithelial and blastemal cells, (F) AE1/AE3 is strongly positive in epithelia component. Magnification 200×

dissemination. As the mass had ruptured, the patient was counseled to receive chemotherapy. However, we had any follow-up information since February 2020.

3 | DISCUSSION

TWN, an extremely rare histological variant of Wilms' tumor, shows a predominance of teratoid elements. The literature search identified 45 cases of TWN (Table 1), of which only 11 occurred outside the kidney: 4 in the retroperitoneal space, 2 in the ovarian, and 1 in the uterus, mediastinum, vaginal, testis, and sacrococcygeal region. In 2017, Alexander et al. reported a 26-year-old female patient with a right ovarian cyst that was removed and, upon pathological examination, was found to be composed of an immature component of nephroblastoma.[4] Nakabayashi et al. in 2019[5] described a 33-year-old patient with ovarian TWN who presented with spontaneous rupture. The current case is the third case of ovarian TWN.

By searching the literature, we found 45 previously reported cases of TWN involving 26 males and 19 females, with a male-to-female ratio of 1.37:1. The mean of the patients was 95.5 months (range 0–744 months). Except for six adults, the majority of TWN were young adults. Of these six cases, two were in the ovaries and one in the uterus, kidney, testes, and abdomen. The most frequent clinical signs are the presence of an abdominal mass, abdominal distension, or abdominal pain.

Currently, the pathogenesis of TWN is still controversial. Some researchers believe that majority of these tumors are pure nephroblastomas, but that only a small part of it originates from teratomas or germ cell neoplasms,[6] while some other investigators favor that TWN is thought to be aroused from extensive metaplasia of metanephric blastema.[7] Moreover, TWN has been presented in various locations. However, it is important to note that 34 of 45 reported cases were identified in the kidney. It is well known that the ovaries and the mediastinum are the most common site for the occurrence of teratomas. Considering the rarity of renal teratomas and the absence of organogenesis in TWN, it can be presumed that TWN is unlikely to arise from renal teratoma.[8] The presence of nephroblastoma-like tissue in germ cell tumors outside the kidney suggested that the combination of teratoma and nephroblastoma might be the intersection of two distinct neoplasms that originate from pluripotent cells.[9–11] Further research is needed to evaluate and verify the speculations to gain more insight into the biological origin of TWN.

TABLE 1 Summary of clinicopathological features of 45 cases of TWN

No.	References	Reported year	Age	Sex	Location	Operation	Chemotherapy	Follow-up	Metastasis
1	Variend et al.	1984	3y	F	Left kidney	+	+	Unknown	No
2	Fernandes et al.	1988	2y	F	Bilateral kidney	+	+	Dead	No
3	Fernandes et al.	1988	2y	F	Bilateral kidney	+	+	7y	No
4	Fernandes et al.	1988	2y	F	Bilateral kidney	+	+	Unknown	No
5	Gorden M. Vujanic	1991	1.1y	F	Right kidney	+	+	2y	No
6	J F Magee	1992	2.5y	M	Left kidney	+	+	4y	No
7	J F Magee	1992	9m	M	Right kidney	+	+	1y	No
8	Kotiloglu et al.	1994	3y	F	Right kidney	+	+	23m	No
9	Williams	1994	3y	F	Bilateral kidney	+	+	Unknown	No
10	Ashworth MT	1996	3y	F	Left kidney	+	+	Unknown	Lung
11	Pawel	1998	7y	M	Right kidney	+	+	18m	No
12	Karaca	2000	2.5y	M	Right kidney	+	−	Dead	Lung
13	Paterson	2000	2y	F	Left kidney	+	+	Unknown	No
14	Bakshi et al.	2003	1.5y	M	Left kidney	+	+	3y	No
15	Cacchetto et al.	2003	4y	F	Right kidney	+	+	32m	No
16	Park	2003	4y	F	Left kidney	+	−	Unknown	No
17	Inoue M	2006	4m	M	Right kidney	+	−	3y	No
18	Myers JB	2007	4.5y	F	Right kidney	+	+	4y	No
19	Koksal Y	2007	2.5y	M	Right kidney	+	+	16m	No
20	García-Galvis O F	2009	62y	F	Uterus	+	+	16m	No
21	Gupta R	2009	4y	M	Right kidney	+	−	5m	No
22	Seo J et al.	2009	50y	M	Right kidney	+	−	0.5m	No
23	Kajbafzadeh A	2010	4y	M	Left kidney	+	+	9.5y	No
24	Sultan I	2010	2y	M	Left kidney	+	+	20m	No
25	Sultan I	2010	5y	F	Thorax	+	+	20m	Brain
26	Sultan I	2010	11m	F	Bilateral kidney	+	+	9m	No
27	Song	2010	13y	F	Vagina	+	+	7y	No
28	Song	2010	1d	M	Coccyx	+	+	2.5y	No
29	Treetipastit	2011	9m	M	Bilateral kidney	+	+	20m	No
30	Mukhopadhyay B	2011	4y	F	Right kidney	+	+	7y	No
31	Chowan AK	2011	15m	M	Abdomen	+	+	6m	No
32	Keskin S	2011	19y	M	Testes	+	+	Dead	Liver
33	Yadav	2012	2y	M	Right kidney	+	−	Unknown	Lung
34	Ishida M	2012	2m	F	Abdomen	+	−	3m	No
35	Okur A	2012	10m	M	Bilateral kidney	+	+	Unknown	No
36	Baskaran D	2013	3y	M	Abdomen	+	+	1y	No
37	Sinha A	2013	2y	M	Right kidney	+	+	1y	No
38	Karakus E	2015	8y	M	Right kidney	+	+	Unknown	No
39	Alexanden VM	2017	26y	F	Ovary	+	−	11m	No

TABLE 1 (Continued)

No.	References	Reported year	Age	Sex	Location	Operation	Chemotherapy	Follow-up	Metastasis
40	Rajaian S	2018	36y	F	Ovary	+	–	Unknown	No
41	Kromka JJ	2018	27y	F	Abdomen	+	+	5y	No
42	Rathod SG	2019	4y	F	Right kidney	+	+	1y	No
43	AL Ghamdi D	2019	2y	M	Right kidney	+	Unknown	7m	No
44	AL Ghamdi D	2019	20m	M	Right kidney	+	+	Unknown	No
45	AL Ghamdi D	2019	11y	F	Right kidney	+	Unknown	2y	Regional lymph nodes

The preoperative diagnosis of TWN is not easy to obtain accurately due to its diverse presentation and lack of imaging features. In the literature, the diagnosis of TWN is based on biopsy to determine the typical triphasic pattern.[10] Microscopically, the tumor is predominantly a teratoma interspersed with areas of nephroblastoma. Different heterogeneous tissues, including adipose tissue, cartilage, and skeletal fibrovascular can be observed in the teratomas areas. The composition of nephroblastoma is composed of undifferentiated tubular structures, mesenchymal elements, and blastemal dells.

The differential diagnosis should be differentiated from extrarenal nephroblastoma and sacrococcygeal yolk sac tumor. Extrarenal nephroblastoma is extremely rare. Sacrococcygeal nephroblastoma, especially sacrococcygeal teratoma, may sometimes include some differentiated tissue, embryonic cells, and primitive glomeruli and tubules, and there is some morphologic overlap between sacrococcygeal nephroblastoma and sacrococcygeal teratoma with a nephroblastic component.[12]

Ultrasonography of the pelvis and abdomen is a very helpful test for determining the extent of ovarian tumors spread without exposing the patient to ionizing radiation.[13] Ultrasonography is utilized to determine the extent of the lesion and to classify it as a solid, simple cyst, or complicated cyst based on its gross morphologic state.[14] At the time of diagnosis, a CT scan of the pelvis and abdomen is deemed necessary for accurate staging of any pelvic malignancy. An MRI of the pelvis and abdomen can be used instead of a CT scan in some circumstances.[13]

Histopathologic diagnosis of TWN is challenging as it can present monophasic or biphasic variants rather than the typical triphasic pattern. The differential diagnosis of TWN includes Primitive Neuroectodermal tumor (PNET), Alveolar Rhabdomyosarcoma (ARMS), and Immature teratoma.[10,11,15] PNETs consist of sheets or nodules of densely packed primitive cells with small-sized, round to ovoid nuclei, small nucleoli, and scant cytoplasm. PNETs may also contain Homer-Wright rosettes. However, they lack epithelial differentiation and show immune reactivity to FLI-1 and CD99. FISH analysis may detect EWSR1 rearrangement. ARMS consist of round cells with a large nucleus, prominent nucleoli, and eosinophilic cytoplasm. They lack glomerular or tubular differentiation, and a few cells may be arranged in an alveolar pattern. In general, tumor cells show a strong positive response to vimentin, Myo-D1, Myogenin, Desmin, and a rearrangement at FKHR locus.[16,17] Immature teratoma contains tissues from three embryologic layers and immature neuroepithelium. Although teratomas and TWN may have similar histologic features, the most distinct feature of TWN is the presence of nephroblastomas, and in occasional cases of TWN, the serum AFP levels may be elevated. Neglecting the areas of nephroblastoma, this case could be easily misdiagnosed as mature cystic teratoma. Furthermore, the potential for misdiagnosis as angiomyolipoma is real in cases with predominant smooth muscle and adipose elements.

It is known that TWN is less aggressive than conventional nephroblastoma and prognosis is generally more positive if the tumor is excised completely.[18] According to previously published statistics, metastasis occurred in 6 of 45 cases, or 13.3%. Among them, three cases showed lung metastasis, one case showed regional lymph node metastasis, one case metastasized to the liver, and one case metastasized to the brain. Due to its rarity and varying tumor components, currently, there is no standardized therapy for TWN. Surgical resection appears to be the best option. It is yet uncertain if fetal TWN requires surgical procedures in utero. TWN are typically indolent, and metastases are quite rare.[12]

The histological evaluation may be significant in guiding treatment and prognosis. According to some published reports, chemotherapy is recommended for TWN regardless of the tumor size, stage, histology, age at diagnosis.[19] However, TWN may be resistant to chemotherapeutic agents due to the presence of a high proportion of mature heterologous tissues, unlike typical classical.[20] Of the reported cases, all 45 patients with TWN underwent surgical resection and 32 of them received adjuvant chemotherapy with all but one being resistant to the therapy. The mean follow-up time was 26.09 months (0–7 years). Three of 45 patients died at the last follow-up (6.67%). Of the three deaths, one was due to liver metastasis, one to lung metastasis, and one to postoperative complications. Of the two reported cases of ovarian TWN, one was treated with surgery but no chemotherapy, while the other patient received three cycles of bleomycin, etoposide, and cisplatin followed by three cycles of vincristine and actinomycin due to rupture. No recurrence was reported in either patient. Therefore, to determine the optimal treatment, clinical and histopathological characteristics must first be taken into account. If the tumor is completely excised without rupture or distant spread, surgical excision alone seems reasonable.

However, the management experience with long-term follow-up of TWN is underreported in the literature. In our current case, metastases occurred within 6 months after the first operation. Furthermore, histologically, the metastatic lesion had only a nephroblastoma component and consisted of blastemal foci with no teratoid. We suspected that the metastatic tumor behaves more like a nephroblastoma and is perhaps sensitive to chemotherapy. After standard chemotherapy, the prognosis and outcome were promising. However, we need long-term follow-up and more case studies to clarify the clinical features and appropriate treatment of TWN.

The probability of recurrence is determined by the original location, histological grade of immaturity, and the extent of primary resection. In young individuals with mature tumors (bilateral or multiple), there is a 2%–3% chance of developing germ cell cancers later in life.[21,22]

4 | CONCLUSION

TWN is very rare, especially primary ovarian TWN, and can be a challenge to diagnose. Careful histological examination is necessary for accurate diagnosis, which is based on morphology and extensive immunohistochemical studies. The prognosis of TWN is considered to be good. In routine clinical practice, surgical resection appears to be the best option. However, additional case studies are required to verify whether chemotherapy is necessary for fully resected TWN.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ORCID

Xinyu Xu https://orcid.org/0000-0002-1730-1462

REFERENCES

1. Dome JS, Mullen EA, Dix DB, et al. Impact of the first generation of children's oncology group clinical trials on clinical practice for wilms tumor. *J Natl Compr Canc Netw*. 2021;19(8):978-985.
2. Sinha A, Phukan JP, Bandyopadhyay G, et al. Teratoid Wilms' tumor in a child: a report of a rare case. *Int J Appl and Basic Med Res*. 2013;3(1):72-74.
3. Variend S, Spicer RD, Mackinnon AE. Teratoid Wilms' tumor. *Cancer*. 1984;53(9):1936-1942.
4. Fernandes ET, Parham DM, Ribeiro RC, et al. Teratoid Wilms' tumor: the St Jude experience. *J Pediatr Surg*. 1988;23(12):1131-1134.
5. Alexander VM, Meisel J, O'Brien S, et al. Wilms' tumor of the ovary. *Gynecol Oncol Rep*. 2017;19:18-21.
6. Nakabayashi A, Kanno T, Takahashi N, et al. A case of ovarian teratoma with nephroblastoma presenting spontaneous rupture. *J Obst Gynaecol Res*. 2019;45(5):1079-1083.
7. García-Galvis OF, Stolnicu S, Muñoz E, et al. Adult extrarenal Wilms tumor of the uterus with teratoid features. *Hum Pathol*. 2009;40:418-424.
8. Chu H, Deng Q-F, Liu X, Peng BO, Cao Y-S. Kidney teratoma: a case report and literature review. *Urol Case Rep*. 2018;20:83-84.
9. Kim YW, Park YK, Oh SM, et al. Retroperitoneal teratoma with predominance of nephroblastic elements—a case report. *J Korean Med Sci*. 1990;5:237-242.
10. Al Ghamdi D, Bakshi N, Akhtar M. Teratoid Wilms tumor: report of three cases and review of the literature. *Turk J Pathol*. 2019;35(1):061-68.
11. Cheng CH, Yang SH, Su B. Nephroblastic elements in a retroperitoneal immature teratoma with elevated serum alpha-fetoprotein. *J Case Rep Images Pathol*. 2016;2:15-19.
12. Ma Y, Zheng J, Zhu H, et al. Sacrococcygeal teratoma with nephroblastic elements: a case report and review of literature. *Int J Clin Exp Pathol*. 2014;7(11):8211-8216.
13. Stanton AE III. Pediatric Teratomas and Other Germ Cell Tumors. Available at: http://emedicine.medscape.com/article/939938-medication Access date June 26, 2020.
14. Skiadas VT, Koutoulidis V, Eleytheriades M, et al. Ovarian masses in young adolescents: imaging findings with surgical confirmation. *Eur J Gynaecol Oncol*. 2004;25:201-206.
15. Karakuş E, Senayli A, Özcan F, et al. Teratoid Wilms' tumor exhibiting extensive squamous differentiation. *Fetal Pediatr Pathol*. 2015;34(1):70-72.
16. Ananthaneni A, Kuberappa PH, Srinivas GV, Kiresur MA. Alveolar rhabdomyosarcoma of maxilla. *J Oral Maxillofac Pathol*. 2016;20(1):164-169.
17. Ioannou M, Perivoliotis K, Zaharos NM, Tsanakas A, Tepetes K, Koukoulis G. Alveolar rhabdomyosarcoma with unusual cytogenetic findings: one more case and review of the literature. *Oxf Med Case Rep*. 2019;10:447-450.
18. Inoue M, Uchida K, Kohei O, et al. Teratoid Wilms' and apos: a case report with literature review. *J Pediatr Surg*. 2006;41:1759-1763.
19. Mukhopadhyay B, Shukla RM, Mukhopadhyay M, et al. Teratoid Wilms′ tumor - A rare renal tumor. *Urol Ann*. 2011;3(3):155-157.
20. Gahine R, Srivastava S, Siddiqui RP, et al. Teratoid Wilms tumour with chemotherapy resistance. *Arch Med Health Sci*. 2015;3(2):326.
21. Cass DL, Hawkins E, Brandt ML, et al. Surgery for ovarian masses in infant, children, and adolescents: 102 consecutive patients treated in a 15-year period. *J Pediatr Surg*. 2001;36:693-699.
22. Templeman CL, Hertweck SPaige, Scheetz JP, Perlman SE, Fallat ME. The management of mature cystic teratomas in children and adolescents: a retrospective analysis. *Hum Reprod*. 2000;15:2669-2672.

How to cite this article: Wu Y, Chu C, Zhang J, Nitish B, Ni J, Xu X. A case of ovarian Teratoma with nephroblastoma presenting abdomen metastasis. *J Clin Lab Anal*. 2022;36:e24364. doi:10.1002/jcla.24364