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Pure nongestational ovarian choriocarcinoma: A scoping review

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Abstract

Choriocarcinoma of the ovary is a rare and highly malignant germ cell tumor. There are three ways in which an ovarian choriocarcinoma can arise: as a primary gestational choriocarcinoma that results from an ectopic ovarian pregnancy, as a metastatic choriocarcinoma that arises from a gestational choriocarcinoma, and as a germ cell tumor with differentiation into trophoblastic structures. Ovarian choriocarcinomas are therefore classified as *gestational* or *nongestational*. Recently, DNA polymorphism analysis has allowed investigators to determine the etiology of choriocarcinoma (gestational versus nongestational). Herein, in this scoping review, we detail the classification of, and clinical aspects of, pure ovarian choriocarcinoma.

Introduction

Choriocarcinoma is a very rare and highly malignant germ cell tumor that accounts for <1% of all malignant germ cell tumors [1]. There are three ways in which an ovarian choriocarcinoma can arise: as a primary gestational choriocarcinoma that results from an ectopic ovarian pregnancy, as a metastatic choriocarcinoma that arises from a gestational choriocarcinoma from another primary site in the female genital tract, and as a germ cell tumor with differentiation into trophoblastic structures [2].

Choriocarcinoma is classified as gestational or nongestational. Gestational choriocarcinoma is a form of gestational trophoblastic disease, which arises from a partial mole, a complete mole, or a normal pregnancy. Gestational choriocarcinoma is estimated to occur in about 2 to 7 pregnancies per 100,000 in the United States [3]. Nongestational choriocarcinoma does not arise from a pregnancy event and is an extremely rare occurrence. The incidence of primary ovarian nongestational choriocarcinoma is estimated to be 1 in 369,000,000 [4]. Differentiating gestational and nongestational choriocarcinoma can be difficult, as their clinical presentation and pathology can be identical. Traditionally, a definitive diagnosis of nongestational choriocarcinoma has been restricted to prepubescent females in whom the possibility of a pregnancy event can be eliminated with certainty.

Choriocarcinoma of the ovary can be pure choriocarcinoma or, more commonly, mixed with other germ cell components [1]. When examined histologically, if other germ cell components are present mixed with choriocarcinoma, a diagnosis of a nongestational origin can be made. However, if no other germ cell component is present, differentiating a nongestational from gestational origin is impossible using histologic means alone.

Recently, however, DNA polymorphism analysis has allowed investigators to determine the etiology of choriocarcinoma via analysis of the patient's DNA, her partner's DNA, and the DNA of the choriocarcinoma. By examining the DNA composition of the tumor and comparing it to the maternal and paternal DNA, the etiology of the choriocarcinoma can be determined. If the DNA of the tumor exactly matches the maternal DNA, the tumor is of non-gestational origin. However, if the tumor contains any alleles matching paternal DNA, the tumor is of gestational origin [5].

In 1982, Jacobs et al. published a comprehensive literature review on pure ovarian choriocarcinoma [6]. The study classified all published cases of pure ovarian choriocarcinoma at the time into three categories: gestational ovarian choriocarcinoma, pure nongestational ovarian choriocarcinoma, and choriocarcinoma of uncertain etiology. The pure nongestational ovarian choriocarcinoma category was assigned to all pure ovarian choriocarcinoma cases occurring in prepubertal females, and the uncertain etiology was assigned to all pure ovarian choriocarcinoma cases in postpubertal women who were said to be sexually abstinent or virginal. Since the publication of this review, several other literature reviews on this topic have been published; however, limitations exist, including lack of definitive categorization strategies. As a result, little is known about the incidence, clinical course, most effective treatment regimen, as well as outcomes for pure ovarian nongestational choriocarcinoma. The purpose of this scoping review is to provide a strict definition of pure ovarian choriocarcinoma that allows appropriate classification of nongestational and gestational origin in order to better understand this disease process.

Methods

The search strategy was developed in collaboration with a librarian at Penn State Hershey College of Medicine. We searched PubMed for articles published in English using the following

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search string: ((("choriocarcinoma"[MeSH Major Topic] OR choriocarcinoma [Title/Abstract]) AND (nongestational[Title/Abstract] OR non-gestational[Title/Abstract])) AND ((ovary[Title/Abstract] OR ovarian[Title/Abstract]) OR gonad[Title/Abstract])) AND english[Language] which resulted in 66 titles. Additionally, we searched Web of Science using All Databases with the following search string: (ts=(choriocarcinoma AND (nongestational OR non-gestational)) OR ti=(choriocarcinoma AND (nongestational OR non-gestational))) AND LANGUAGE: (English), which yielded 57 titles for a sum total of 123 titles. The final search in PubMed and Web of Science was performed on January 6, 2016. Duplicates (n=43) were excluded.

We included case reports and retrospective chart reviews. Review articles and book chapters were excluded (n=7). Review articles and those articles included in the analysis were cross-referenced to identify additional studies missed in initial database search (n=6). Included articles were limited to those dealing with pure non-gestational choriocarcinoma of the ovary.

Criteria used to define a non-gestational origin of the tumor were cases occurring in prepubertal girls or a cases establishing a diagnosis of non-gestational origin via DNA analysis. All other cases were excluded from the results and discussion. Some literature described young G0 females without mention of their history of sexual activity. In these cases, if the patient was <20 years of age, these cases were included (unless nongestational origin was confirmed upon DNA analysis). Because Jacobs et al published an exhaustive literature review on pure choriocarcinoma of the ovary of cases occurring prior to 1981; we included only studies published after 1980. Those articles not meeting this criteria (n=49) were excluded, see Table 4. Additionally, nine articles were inaccessible to us despite multiple requests for full-text articles, and so these were excluded [6-14]. The total number of articles included in this review is 21 (Figure 1).

Results

Classification

Since 1980, a total of 22 possible cases of pure nongestational ovarian choriocarcinoma have been published in the English language. Of these, nine occurred in premenarchal females [12-18], 11 occurred in postmenarchal females but were confirmed by DNA analysis [18,19-25], and eight were considered possible cases of pure NGOC according to the strict criteria described above in the methods section [18,26-32] (Tables 1-3).

Age

In the premenarchal group, the average age at diagnosis was 13.6 years. One study did not include the age of the patient at presentation [20]. Another case occurred in a 39 year-old female with a history of gonadal dysgenesis and primary amenorrhea [19].

In the DNA confirmed group, the average age at diagnosis was 24.5 years. One study that reported on three of these cases did not include the age at diagnosis [21].

In the possible cases group, the average age at diagnosis was 14.0 years.

FIGO Stage

In the premenarchal group, the FIGO stage of eight of the cases did not state the FIGO stage. For the one case that did, the FIGO stage was reported as IC [16].

For the DNA confirmed group, the FIGO stage of five cases was not reported. The remaining cases had FIGO stages of IA [26], IIIC [23], and IV [25].

For the possible cases group, the FIGO stage of five cases was not reported. The remaining cases had FIGO stages of IA [31], I [32], and III [35].

Surgery performed

In the premenarchal group (n=9), surgical therapy was reported for five of the cases but not stated for four cases. Of the five cases which reported surgical therapy, two had a unilateral oophorectomy performed [15], one had a unilateral salpingo-oopherectomy performed [17], one had a unilateral salpingo-oopherectomy and partial omentectomy performed [16], and one had a bilateral salpingo-oopherectomy, hysterectomy, omentectomy, and thoracoscopy and wedge resection for pleural lesions [19].

For the DNA confirmed group (n=11), surgical therapy was reported for all but five of the cases. Of the 11 cases which reported surgical therapy, one had a total abdominal hysterectomy, bilateral salpingo-oopherecotmy, and omentectomy performed two months after completion of chemotherapy [22]; one had an initial removal of the ovarian mass and two rounds of chemotherapy which were followed by followed by a total abdominal hysterectomy, bilateral salpingo-oopherecotmy, omental resection, pelvic lymph node dissection, and appendectomy [23]; one had a total abdominal hysterectomy, bilateral salpingo-oopherecotmy, omentectomy, and pelvic lymph node dissection performed [24]; two had a left salpingo-oopherectomy and partial omentectomy performed [25,26]; and one had a right salpingo-oopherectomy performed [27].

For the possible cases group (n=8), surgicial treatment was not reported for one case. Surgery was not performed in one case [3]. Unilateral salpingo-oopherectomy was performed in two cases [30,34]. The remaining cases were treated surgically with a left salpingo-oopherectomy, total omentectomy, and inversion appendectomy [29]; a left salpingo-oopherectomy and partial omentectomy [31]; a left salpingo-oopherectomy and right ovarian cystectomy [32]; and a right salpingo-oopherectomy, left ovarian cystectomy and omentectomy [35].

Chemotherapy

In the premenarchal group, one case did not state whether chemotherapy was used [21]. Two cases were treated with surgical therapy alone [15]. Two cases were treated with PVB (cisplatin, bleomycin, and vinblastine) therapy [16, 18]. One case was treated with vincristine, methotrexate, leukovorin, bleomycin, Adriamycin, and cyclophosphamide [14]. One cases was treated with multiple rounds of various chemotherapeutic agents, see Table 1 [19]. One case was treated with "radiotherapy and chemotherapy," but the study did not describe any further details [20]. One case was treated with "three drug chemotherapy," but the study did not expound upon what these three drugs were [20].

For the DNA group, five cases did not include information of chemotherapy treatment. The BEP chemotherapy regimen was used in two cases for four and five cycles, respectively [22] and [23]. One patient was treated with the MAC regimen for four cycles [16]. One patient was treated with the EMA regimen for four cycles [27]; and one patient was treated with one course of EMA followed by 7 cycles of just etoposide and actinomycin due to methotrexate-toxicity [26].

For the possible cases group, chemotherapy treatment was not reported in two cases. Chemotherapy was not given in one case [33]

Table 1: Pure NGOC cases in premenarchal females since 1980

Case	Age (years)	Menarchal Status	hCG	Surgery	FIGO Stage	Chemotherapy	Outcome
[15]	6	Premenarchal	NS*	RO	NS	None	NED at 10 years
[15]	11	Premenarchal	NS	RO	NS	None	DOD—"attributed to immediate postoperative complications"
[16]	10	Premenarchal	7957 mIU/L at 7 days postop	LSO, partial omentectomy	IC	PVB x 5 cycles	NS
[17]	11	Premenarchal	Not performed prior to surgery; negative postop	RSO	NS	Vincristin, methotrexate, leukovorin, bleomycin, adriamycin, cyclophosphamide	NS
[18]	9	Premenarchal	NS	NS	NS	PVB x 3 courses	NED at 6 months
[19]	39	History of gonadal dysgenesis and primary amenorrhea 45XO/46XY karyotype	26392 mIU/ml at postop referral	Hysterectomy, BSO, omentectomy Thoracoscopy for pleural lesion resection and wedge resection of lung nodules	NS	Cisplatin and etoposide x 4 courses BEP x 1 course Cisplatin, etoposide, ifofsamide x 2 course Oral etoposide x 7 days Carboplatin, vinblastine, Adriamycin x 1 course High-dose CTx + autologous BMT	NED at 17 months
[20]	NS	Presented with precocious puberty	"precocious puberty 2/2 tumor production of hCG"	NS	NS	"Radiotheray and chemotherapy"	DOD
[20]	11	Premenarchal	"increased"	NS	NS	"3 drug CTx"	NED at 1 year
[21]	12	Premenarchal	Elevated	NS	NS	NS	NS

* Abbreviations: NS: Not Stated, AAW: Alive and Well, DOD: Dead of Disease, NED: No Evidence of Disease, TAH: Total Abdominal Hysterectomy, R: Right, L: Left, B: Bilateral, S: Salpingectomy, O: Oophorectomy, MAC: Methotrexate, Actinomycin, Alkylating Agent, BEP: Bleomycin, Etoposide, Cisplatin, PVB: Cisplatin, Bleomycin, Vinblastine, EMA: Etoposide, Methotrexate, Actinomycin, EMA/CO: Etoposide, Methotrexate, Actinomycin, Cyclophosphamide, Oncovin

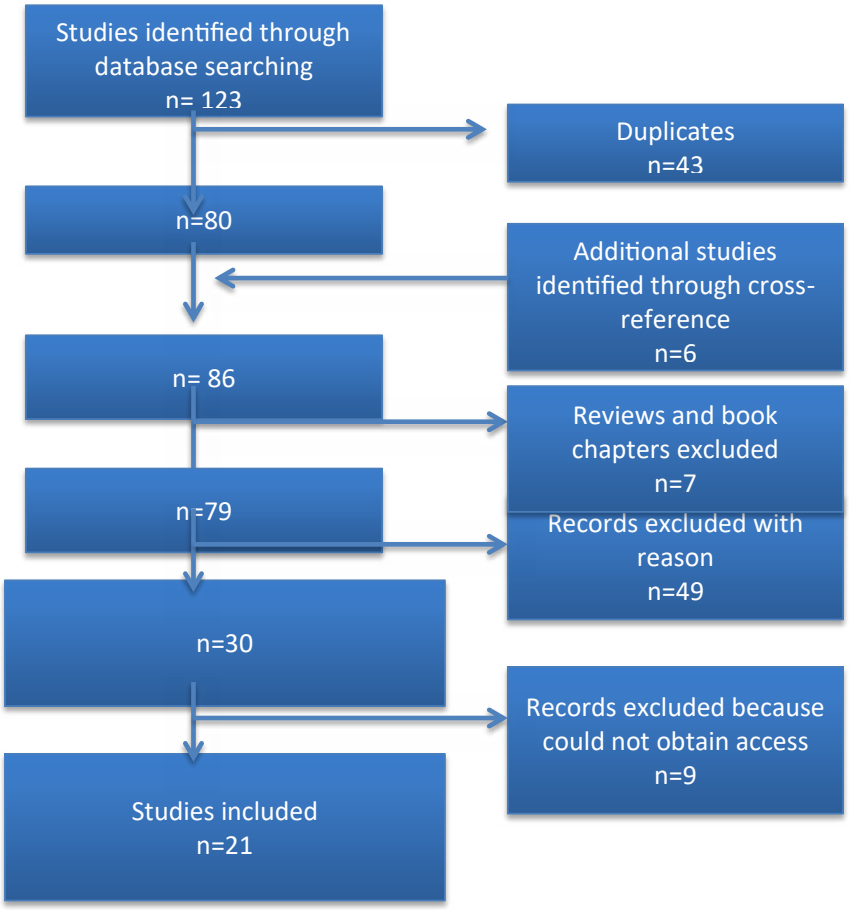

Figure 1: Flow diagram of included studies

Table 2: Pure NGOC cases confirmed by DNA analysis

Case	Age (years)	Reproductive Status	hCG	Surgery	FIGO Stage	Chemotherapy	Outcome	DNA analysis
[22]	24	G1P0A1	675,713 mIU/mL	TAH, BSO, omentectomy 2 months after completion of CTx	NS	BEP x 4 cycles	NED at 1 month	DNA polymorphism analysis at 8 loci
[23]	23	G3P1	26,516 mIU/mL	Initially, removal of mass and omental biopsy TAH, BSO, omental resection, pelvic lymph node dissection, appendectomy following 2 courses of BEP CTx	IIIC	BEP x 5 cycles	NED at 30 months	Histo: ovarian CC and some immature seminiferous tubulues DNA polymorphism analysis with 5 STR loci Karyotype analysis of peripheral blood 46XX FISH confirmed absence of SRY hybridization signal in tumor; all nuclei of ovary and tumor hybridized with two XX signals In testicular tissue both two XX signals (75%) and one X signal (25%)
[24]	33	G0	185,000 mIU/mL	TAH, BSO, omentectomy, pelvic lymph node dissection	NS	MAC x 4 courses	NED at 18 months	DNA polymorphism analysis using eight microsatellite markers
[25]	19	G0, virgin		LSO, partial omentectomy, R ovarian biopsy	IV	EMA/CO x "multiple courses"	NS	DNA polymorphism analysis of two loci
[26]	19	G0, virgin	206,949.7 mIU/mL	LSO, partial omentectomy	IA	EMA x 1 course Etoposide, actinomycin x 7 courses	NED at 12 months	DNA polymorphism analysis at 15 loci
[21]	NS	G0, virgin						DNA polymorphism analysis at 12 loci
[21]	NS	"married"						DNA polymorphism analysis at 12 loci
[21]	NS	"married"						DNA polymorphism analysis at 12 loci
[27]	26	G0	64,000 IU/L	RSO	NS	EMA x 4 courses	DOD at 4 months	DNA polymorphism analysis at 9 loci
[28]	25	G0	NS	NS	NS	NS	NS	DNA polymorphism analysis at 11 loci
[28]	27	G0	NS	NS	NS	NS	NS	DNA polymorphism analysis at 11 loci

*See Table 1 for explanations of abbreviations.

Table 3: Possible pure NGOC cases since 1980

Case	Age (years)	Reproductive Status	hCG	Surgery	FIGO Stage	Chemotherapy	Outcome
[29]	15	G0, virgin	Urine positive x 2 Blood negative x 3	LSO, total omentectomy, inversion appendectomy	NS	NS	NS
[30]	10	Menarche 6 months prior to presentation	6,600 ng/mL	RSO	NS	BEP x 3 courses	NED at 62 months
[31]	12	G0, virgin	20,257 mIU/mL	LSO, partial omentectomy, multiple peritoneal biopsies	IA	BEP x 6 courses	NED at 14 months
[32]	18	G0, virgin	Urine positive	LSO, R ovarian cystectomy, omental and peritoneal biopsies	I	MAC x 4 courses	NED at 5 months
[33]	16	G0, virgin	NS	Not performed	NS	Not given	Cardiac arrest during imaging, all resuscitating measures unsuccessful
[34]	13	G0, virgin	Urine positive	RSO	NS	MAC x 5 courses	NED at 9 months
[21]	16	G0, virgin	NS	NS	NS	NS	NS
[35]	12	G0	1,100,000 IU/L after initial surgery	RSO, L ovarian cystectomy, omentectomy	III	BEP x 4 courses High-dose CTx with carboplatin, etoposide, ifosphamide followed by BMT	NED at 3 years

*See Table 1 for explanation of abbreviations.

Table 4: Excluded citations

Reason for Exclusion	Title	Authors
Gestational choriocarcinoma	Primary choriocarcinoma of the ovary. Report of two cases	Gangadharan VP, Mathew BS, Kumar KS, Chitrathara K
	Intra-operative cytodiagnosis of primary ovarian choriocarcinoma with ki67 immunoexpression	Kar A, Kar T, Mahapatra S, Dehuri P
	Pure ovarian choriocarcinoma: a report of two cases	Mood NI, Samadi N, Rahimi-Moghaddam P, Sarmadi S, Eftekhar Z, Yarandi F
	Ovarian choriocarcinoma arising from partial mole as evidenced by deoxyribonucleic acid microsatellite analysis	Namba A, Nakagawa S, Nakamura N, Takazawa Y, Kugu K, Tsutsumi O, Taketani Y
	Pure choriocarcinoma of ovary diagnosed by fine needle aspiration cytology	Naniwadekar MR, Desai SR, Kshirsagar NS, Angarkar NN, Dombale VD, Jagtap S
Not ovarian choriocarcinoma	Genotyping Diagnosis of Nongestational Choriocarcinom Involving Fallopian Tube and Ligament: A Case Study	Buza N, Rutherford T, Hui P
	Extraovarian nongestational choriocarcinoma in a postmenopausal woman	Dilek S, Pata O, Tok E, Polat A
	Endometrial carcinoma in elderly women	Hoffman K, Nekhlyudov L, Deligdisch L
	Primary non-gestational choriocarcinoma of the uterine cervix: a case report	Maesta L, Michelin OC, Traiman P, Hokama P, Rudge MVC
	Fallopian tube choriocarcinoma presenting as ovarian tumour: a case report	Mundkur A, Rai L, Hebbar S, Guruvare S, Adiga P
	Concurrent ovarian-type primary peritoneal adenocarcinoma and peritoneal choriocarcinoma. A case report and review of the literature	Pentheroudakis G, White J, Davis J, Brown I, Vasey P
	Primary omental gestational choriocarcinoma ascertained by deoxyribonucleic acid polymorphism analysis	Sakumoto K, Nagai Y, Inamine M, Kanazawa K
	Testicular choriocarcinoma metastatic to the skin: an additional case and literature review	Tinkle LL, Graham BS, Spillane TJ, Barr RJ
	Primary renal artery choriocarcinoma causing secondary renovascular hypertension	Usta TA, Karacan T, Ozyurek E, Naki MM, Omeroglu SN, Demirkiran F
	Pure nongestational uterine choriocarcinoma in a postmenopausal Chinese woman confirmed with short tandem repeat analysis	Wang YM, Yang YF, Teng F, Zhang HY, Xue FX
	Primary choriocarcinoma of the vulva	Weiss S, Amit A, Schwartz MR, Kaplan AL
Not pure choriocarcinoma	Ovarian nongestational choriocarcinoma mixed with various epithelial malignancies in association with endometriosis	Hirabayashi K, Yasuda M, Osamura RY, Hirasawa T, Murakami M
	Serous carcinoma of the endometrium with choriocarcinomatous differentiation: A case report and review of the literature indicate the existence of 2 prognostically relevant tumor types	Horn LC, Hanel C, Bartholdt E, Dietel J
	Malignant mixed ovarian germ cell tumor with embryonal component	Moniaga NC, Randall LM
	Nongestational choriocarcinoma arising from a primary ovarian tumour	Oladipo A, Mathew J, Oriolowo A, Lindsay I, Fisher R, Secki M, Yiannakis D
	Nongestational choriocarcinoma of the ovary—a case report	Pai MR, Naik R

Postmenopausal patient	Choriocarcinoma of the ovary in a postmenopausal woman	Babu MK, Kini U
	A case of non-gestational choriocarcinoma arising in the ovary of a postmenopausal woman	Park SH, Park A, Kim JY, Kwon JH, Koh SB
Patient ≥20 years old	Primary pure ovarian choriocarcinoma mimicking ectopic pregnancy: a report of fulminant progression	Balat O, Kutlar I, Ozkur A, Bakir K, Aksoy F, Ugur MG
	Primary ovarian choriocarcinoma mimicking ectopic pregnancy managed with laparoscopy--a case report	Chen YX, Xu J, Lv WG, Xie X
	Pure nongestational choriocarcinoma of the ovary: a case report	Choi YJ, Chun KY, Kim YW, Ro Dy
	Pure nongestational choriocarcinoma of ovary	Corakci A, Ozeren S, Ozkan S, Gurbus Y, Ustun H, Yucesoy I
	Pure primary non-gestational ovarian choriocarcinoma: a diagnostic dilemma	Gon S, Majumdar B, Barui G, Karmakar R, Bhattacharya A
	Management of non-gestational ovarian choriocarcinoma: laparoscopy can be essential. Report of two cases	Gremeau AS, Bourdel N, Kondo W, Jardon K, Canis M
	Primary pure choriocarcinoma of the ovary	Grover V, Grover RK, Usha R, Logani KB
	Leydig cell tumor, mature teratoma, and nongestational choriocarcinoma in a single ovary	Jain T, VanKessel K, Reed S, Paley P
	Pure choriocarcinoma of the ovary: a case report	Lv L, Yang K, Wu H, Lou J, Peng Z
	Ovarian choriocarcinoma: a difficult diagnosis of an unusual tumor and a review of the hook effect	Wheeler CA, Davis S, Degefu S, Thorneycroft IH, O'Quinn AG
	Developing retroperitoneal anaplastic carcinoma with choriocarcinoma focus after ovarian nongestational choriocarcinoma: a case report	Nikolic B, Ljubic A, Terzic M, Arandjelovic A, Babic S, Vucic M
	Primary pure choriocarcinoma of the ovary in reproductive ages: a case report	Simsek T, Trak B, Tunc M, Karaveli S, Uner M, Sonmez C
	Primary ovarian nongestational choriocarcinoma. Report of a case in a young woman of childbearing age	Vogler C, Schmidt WA, Edwards CL
Case labeled as nongestational choriocarcinoma, but no further information of clinical context provided	Primary chemotherapy and the role of second-look laparotomy in non-dysgerminomatous malignancies of the ovary	Pippitt CH Jr, Cain JM, Hakes TB, Pierce VK, Lewis JL Jr
Patient <20 years old but with history of sexual activity	Pure choriocarcinoma of the ovary in Silver-Russell Syndrome	Haruma T, Ogawa C, Nishida T, Kusumoto T, Nakamura K, Seki N, Katayama T, Hiramatsu Y
Animal study	Immunohistological Description of Nongestastional Ovarian Choriocarcinoma in Two Female Mice with Conditional Loss of Trp53 Driven by the Tie2 Promoter	Castiglioni V, Ghahremani MF, Goosens S, Maglie MD, Ardizzone M, Haigh JJ, Radelli E
	Non-gestational malignant placental site trophoblastic tumor of the ovary in a 4-year-old rhesus monkey	Marbaix E, Defrere S, Duc KH, Lousse JC, Dehoux JP
Cell line study/bench research/no human case study	Limitation of differential expression of HLA-A,B,C antigens on choriocarcinoma cell lines by messenger RNA for HLA heavy chain but not by beta 2-microglobulin	Kawata M, Sizer K, Sekiya S, Parnes JR, Herzenberg LA
	Epidermal growth-factor receptors in human corpora-lutea during the menstrual cycle and pregnancy	Khandawood FS, Ayyagari RR, Dawood MY
	Localization of the cellular expression of inhibin in trophoblastic tissue	McCluggage WG, Ashe P, McBride H, Maxwell P, Sloan JM
	Establishment and properties of a human choriocarcinoma cell line of ovarian origin	Sekiya S, Kaiho T, Shirotake S, Iwasawa H, Inaba N, Kawata M, Higaki K, Ishige H, Takamizawa H, Minamihisamatsu M, Kuwata T
	Usefulness of intraoperative imprint cytology in ovarian germ cell tumors	Abe A, Sugiyama Y, Furuta R, Matoda M, Takeshima N
	The impact of molecular genetic diagnosis on the management of women with hCG-producing malignancies	Fisher RA, Savage PM, MacDermott C, Hook J, Sebire NJ, Lindsay I, Secki MJ
Published prior to 1980	Nongestational choriocarcinoma of ovary—report of a case	Dehaan QC
	Primary non-gestational choriocarcinoma of the ovary. Report of a case	Panayotou PP
Author published two studies that described same case (excluded one of studies from review)	Ovarian neoplasms in children and adolescents in Papua New Guinea	Sengupta SK, Everett VJ
Review articles/book chapters	Diagnostic dilemma: non-gestational or gestational choriocarcinoma of the ovary	Bhatia K, Vaid AK
	Hormonally Active Organ Tumors in Children and Adolescents	Hicks ML, Danzey TJ
	Gestational Choriocarcinoma	Hui P
	Recent advances in the pathology and classification of ovarian germ cell tumors	Roth LM, Talerman A
	Clinical syndromes associated with ovarian neoplasms: a comprehensive review	Shanbhogue AK, Shanbhogue DK, Prasad SR, Surabhi VR, Fasih N, Menias CO
	Germ Cell Tumors of the Ovary	Talerman A, Vang R
	Pathology of Germ Cell Tumors	Zaloudek CJ

The BEP regiment was used in two cases for three and six cycles, respectively [30,31]. The BEP regimen was also used on another patient for four cycles, followed by high-dose CTx with carboplatin, etoposide, ifosphamide with subsequent bone marrow transplantation [35]. Finally, two patients were treated methotrexate, actinomycin, and an alkylating agent (MAC) regimen for 4 cycles [32] and 5 cycles [34].

Survival

In the premenarchal group, survival outcomes were not reported for three cases [16,17,21]. One patient was reported to be alive and well at ten-year follow-up [15], one patient had no evidence of disease at six-month follow-up [18], one had no evidence of disease at 17-month follow-up [19], and one had no evidence of disease at one year follow-up [20]. One patient died from immediate postoperative complications [15], and one patient was reported dead of disease [20].

For the DNA-confirmed group, outcome was not reported in six cases. Four patients had no evidence of disease at varying follow-up intervals: one month [22], 12 months [26], 18 months [24], and 30 months [23]. One patient was reported dead of disease at 4 months [27].

For the possible cases group, outcome was not reported in two cases. Five patients had no evidence of disease at varying follow-up intervals: 5 months [32], 9 months [34] 14 months [31], 36 months [35], and 62 months [30]. In one case, the patient arrested during initial imaging and all resuscitation efforts were unsuccessful [33] (Tables 1-3).

Discussion

This study highlights several features of pure nongestational ovarian choriocarcinoma. First, this study emphasizes the rarity of pure nongestational ovarian choriocarcinoma. Nine cases of premenarchal pure nongestational ovarian choriocarcinoma and eight cases of possible pure nongestational choriocarcinoma have been reported since 1980. Just twelve cases of pure ovarian nongestational ovarian choriocarcinoma have been confirmed by DNA polymorphism analysis. Because of the rarity of this disease process, stricter diagnostic criteria should be used in order to correctly categorize nongestational origin from gestational origin, as unless confirmed by DNA analysis or the disease occurs in a patient who is premenarchal, one cannot with absolute certainty classify an ovarian choriocarcinoma. Recently, DNA analysis has been used to successfully determine nongestational versus gestational origin of ovarian choriocarcinoma. This technology will allow for appropriate classification of this disease process which will ultimately lead to improved therapeutic strategies as more information is learned about pure nongestational ovarian choriocarcinoma.

Secondary to the rarity of this disease process, no standard therapy has been established. Treatment is often extrapolated from treatment strategies for gestational choriocarcinoma and germ cell tumors, thereby leading to significant heterogeneity in treatment strategies for pure nongestional ovarian choriocarcinoma. In reviewing the clinical outcomes of those with pure ovarian suspected choriocarcinoma (confirmed and suspected), it is difficult to make definitive treatment recommendations secondary to heterogeneity in, and inconsistent reported of, relevant clinical factors, including disease classification, patient age, stage, surgery, adjuvant therapy and outcomes, combined with the rarity of this particular entity. For those reported cases in which outcomes were reported (n=16), at a follow-up ranging from one month to ten years, 12 were reported as NED, a majority (n=11) were treated with adjuvant chemotherapy (Tables 1-3). Commonly used adjuvant combinational treatment regimens include BEP and EMA.

Herein, in this scoping review, we have detailed the classification of, and clinical aspects of, pure ovarian choriocarcinoma. Secondary to its rarity and variability in reporting, conclusive recommendations regarding ideal therapy is lacking. Going forward, definitive categorization, via DNA polymorphism analysis, and creation of an international tumor registry is warranted for rare disease entities such as pure ovarian choriocarcinoma, in order to facilitate better comprehension of its etiology and standardization of therapy with optimization of outcomes.

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