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Review Article

Unusual clinical presentations of choriocarcinoma: A systematic review of case reports

Mishu Mangla [a, *], Deepak Singla [b], Harpreet Kaur [a], Sushmita Sharma [a]

[a] Department of Gynecology and Obstetrics, GianSagar Medical College and Hospital, Banur, Punjab, India
[b] Department of Anesthesia, BPS Govt. Medical College, Khanpur Kalan, Sonipat, Haryana, India

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ABSTRACT

Choriocarcinoma (CC) is a highly malignant tumor originating in the trophoblastic tissue. The clinical presentation of CC is so much varied that every case may be one of its kinds and thus can be a diagnostic challenge. Numerous case reports have been published in various journals regarding the unusual clinical presentations of this cancer. Therefore, we conducted a systematic review of all case reports in English language on gestational CC published in PubMed-indexed journals from 1998 to 2015. The main aim was to provide a summary and critical analysis of all the data and evidence published regarding the atypical clinical presentations of CC in recent years. In total, 121 case reports pertaining to unusual clinical manifestations of gestational CC were analyzed. The age of patients in whom cases were reported ranged from 17 to 67 years, and the time period between the index pregnancy and development of CC varied from 4 weeks to as long as 25 years. Cardiopulmonary complaints (20.66%) followed by gastrointestinal (18.43%) and central nervous system manifestations (17.67%) were found to be the most common. Through this review, the authors have made an attempt to discuss various manifestations with which a patient with gestational CC can present to clinician so that early diagnosis and timely management can be initiated, thus improving clinical prognosis.

Introduction

Choriocarcinoma (CC) is a highly malignant tumor originating in the trophoblastic tissue. Majority of cases of CC arise due to malignant transformation of a complete molar pregnancy, although it has been reported following term pregnancy, spontaneous abortion, and even after ectopic pregnancy [1]. It is known to occur in 1 in 5333 tubal pregnancies and 1 in 1.6 million normal intrauterine pregnancies [2]. Although only 0.76–4 % cases of CC develop in ectopic locations, they are usually more aggressive and associated with distant metastasis [3,4]. It can develop anytime between 5 weeks and 15 years after gestation or even after menopause [5,6]. Cases have been reported to occur even 23 years after menopause [7].

Approximately 30 % cases of CC have metastatic disease at the time of diagnosis. Lungs (80%) are the most common site of metastasis, followed by vagina (30%) and liver (10%). Metastatic CC involves the brain in 3–28% of patients [8]. The clinical presentation of CC is so much varied that every case may be one of its kinds and thus can be a diagnostic challenge. Another problem leading to a delay in diagnosis is that sometimes the history of antecedent pregnancy may not be elicited or the presentation may be so delayed that the patient may not recollect such history. Such patients present advanced metastatic disease due to a delay in the diagnosis which can prove fatal.

Early diagnosis and prompt initiation of chemotherapy is a well-known determinant of prognosis of CC. A knowledge regarding the variations from its classic clinical presentation is, therefore, a must to any practicing clinician. The main aim of this systematic review was to provide a summary and critical analysis of all the data and evidence published regarding the atypical clinical presentation of CC in recent years and thus help the practicing clinicians in early diagnosis and timely treatment of CC, thus improving prognosis. A special emphasis was given to nongynecologic and atypical clinical manifestations which pose a real diagnostic challenge.

* Corresponding author. Department of Gynecology and Obstetrics, GianSagar Medical College and Hospital, Banur, Punjab 140401, India.
E-mail address: deepak10.4u@gmail.com (M. Mangla).

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Materials and Methods

An electronic search of Pubmed database was conducted for case reports regarding unusual clinical presentations of CC, published in English from 1998 to 2015, i.e., last 17 years. The electronic search strategy was done using keywords, such as "choriocarcinoma" and "clinical manifestation", "choriocarcinoma" and "unusual presentation", and "choriocarcinoma" and "case reports". Two authors independently analyzed the title and abstracts of all case reports found from the initial search. The data thus extracted was double checked to avoid duplication. Any disagreements between the two authors were resolved through discussion.

Clinical manifestation was defined as patient-level finding gathered during medical interview, physical examination, or through diagnostic studies. Patients reporting to health care practitioner with any clinical manifestation, other than the following common signs and symptoms [9], were regarded as unusual: (1) enlarged uterus; (2) abnormal uterine bleeding; (3) persistence of theca lutein cysts in the ovaries; and (4) plateau or rising serum human chorionic gonadotropin (hCG) concentrations measured during postmolar follow-up after uterine evacuation.

This systematic review was planned according to PRISMA guidelines. The articles pertaining only to unusual clinical manifestation of gestational CC were included in the present review. Only female patients with cases reported by authors as gestational CC, which they confirmed by beta hCG or histopathology, were included in the review. Studies and reports of fatal cases were also included if the condition causing death was attributed to CC or its related complications. Case reports with nongestational CC, case reports of male patients with CC, and articles focusing predominantly on the management of CC were excluded. Any article that was not a case report, i.e., review article, original article, clinical trial, or commentary was also excluded from the present review.

Of all the case reports finally included in the review, one author extracted information such as geographical distribution or country of occurrence of the case, year of publication, age of the patient at the time of presentation, relationship with pregnancy or abortion, diagnostic modality used to confirm CC, and its final prognosis. The details regarding the antecedent pregnancy event and the time interval between index pregnancy and detection of choriocarcinoma was also extracted. The data thus collected was entered in an excel sheet and organized into system-wise manifestations of CC cases. Descriptive statistics was used to calculate simple frequency, percentage, and proportion out of the total case reports.

Results

Data collection

In total, 750 case reports pertaining to the unusual clinical manifestations of CC were found on electronic data search of PubMed database from 1998 to 2015. After excluding the duplicates and case reports on nonhuman subjects, we were left with a total of 722 articles. Furthermore, 572 articles were excluded as they were pertaining to either testicular CC, nongestational CC, or were not in English language. Additionally, 29 articles were excluded as they focused mainly on the management of CC, newer treatment options available for the same, and did not highlight the clinical manifestation. Considering all the inclusion and exclusion criteria, a total of 121 case reports were finally analyzed (Figure 1).

Case distribution

Cases have been reported from all over the world. Geographical distribution of the cases has been shown in Figure 2. Majority of cases have been reported from Asia (47.1%) and Europe (26.44%). Additionally, 14.04% cases were from North America and 3.3 % from South America. Two cases have been reported from Australia, three cases from Africa, and six cases from Eurasia. The distribution of articles according to the year of publication has been shown in Figure 3. It is interesting to note that the number of cases being reported has increased from 2006 onward as shown in Figure 3. Maximum number of cases were reported in 2006 (13 cases), followed by 2009 (12 cases). In 2011 and 2013, 10 cases each were reported (Figure 3).

The age of the patients in whom CC was reported varied from 17 to 67 years, with the majority of patients (84.29%) aged 20–40 years. There were two patients aged < 20 years and five patients aged > 50 years.

Antecedent pregnancy

In 50 out of 121 case reports, antecedent pregnancy was full term pregnancy, 18 cases followed abortion, 8 followed molar pregnancy, 7 ectopic gestations, and 1 case followed partial mole. In 10 case reports, the details regarding antecedent pregnancy were either not available or not mentioned; however, as the authors had reported them to be gestational CC, they were included in the present review. The time period between the index pregnancy and development of CC varied from 4 weeks to as long as 25 years.

Out of all the reported cases, 15 patients succumbed to disease, mainly because of late presentation or delay in diagnosis, whereas 106 patients showed remission. The diagnosis of CC in these case reports was made by authors on the basis of histopathology in majority of patients (73.55%), by fine needle aspiration cytology in one patient, after autopsy in one patient, and on clinical grounds in the remaining patients.

Clinical manifestations

Maximum number of patients (20.66%) in the reported cases came to clinical attention due to cardiopulmonary complaints, followed by gastrointestinal (18.43%) and central nervous system manifestations (17.67%). Furthermore, 9.91% cases were detected due to feto maternal hemorrhage and 5.28% and 4.95% cases due to renal and ocular manifestations, respectively. Other manifestations that brought the patient to clinical attention are shown in Figure 4. A brief summary of the various clinical presentations of this great clinical masquerader has been shown in Figure 5.

Atypical gynecologic and obstetric manifestations

Abnormal vaginal bleeding is known to be the most common gynecological presentation of CC [8]. Gestational CC has been reported to present as both primary as well as secondary postpartum hemorrhage [10]. It can present any time after the termination of index pregnancy, but patients who present early have a better prognosis. Other symptoms included severe pelvic pain, isolated vaginal nodule [11], and vulvovaginal swelling mimicking an infected and neglected Bartholin cyst or a hematoma [12]. It also presents itself as necrotic and hemorrhagic cervical mass [13]. Although there are not many cases reported in literature, cervical CC is thought to arise from either a malignant transformation of a cervical ectopic pregnancy or from cervical metastasis of a primary tumor of uterine origin which later spontaneously regressed or by transport of malignant chorionic cells to the cervix after a dormant period following previous pregnancy [14–16].

Interestingly, a few cases of spontaneous uterine rupture due to CC have also been reported in literature [17]. Okamoto et al [18] have even reported a case of spontaneous rupture of the uterus