

Choriocarcinoma in an Infantile Patient

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Abstract

Clinical diagnosis of choriocarcinoma may be difficult in post-menopause or children and ectopic origin. According to its histologic origin, it is classified as gestational or nongestational choriocarcinoma. Gestational choriocarcinoma its origin derived from placental trophoblast and nongestational choriocarcinoma-derived from a germ cell. However, DNA and genetic analysis can be used to define the origin of choriocarcinoma. Usually, the DNA examination and genetic analysis have not been used widely in clinical services. In this case the diagnosis to considered as a primary nongestational choriocarcinoma just based on clinical and laboratory finding. This article is aimed to remind the doctors who treat cases choriocarcinoma and is no doubt in deciding whether the origin of the disease from gestational or nongestational should carry out an investigation DNA and genetic analysis.

Keywords: Gestational; Nongestational; Choriocarcinoma; Genetic; DNA analysis; Infantile patient

Introduction

Choriocarcinoma is a malignant tumor that commonly occurs in the uterus during the reproductive period, and the diagnosis easily established due to the close relationship of pregnancy and high level of β -hCG. Clinical diagnosis of choriocarcinoma may be difficult in post-menopause, children, and ectopic origin.

According to its histologic origin, it is classified as gestational or nongestational choriocarcinoma. Gestational choriocarcinoma its origin derived from placental trophoblast and nongestational choriocarcinoma-derived from a germ cell. Choriocarcinoma rapid and accurate diagnosis is mandatory, β -Human chorionic gonadotrophin (β -HCG) levels in serum and urine are characteristically elevated in gestational choriocarcinoma owing to the tumor arises from trophoblastic cells.

Choriocarcinoma in children is extremely rare, and so far up to the year 2004 were reported is only 30 children [1]. Because of the rarity disease in children, the diagnosis and treatment are usually late. To differentiate the origin of the choriocarcinoma in children is important due to the nongestational choriocarcinoma had the poor prognosis and needed more excessive treatment. In our reported case, choriocarcinoma was diagnosed in a 13-month old girl after biopsy for the vaginal tumor with the history of recurrent vaginal bleeding. Her mother without evidence of suffering from choriocarcinoma.

Case Report

A 13-month old girl arrives at the Emergency Unit Dr. Sardjito Central Hospital with the main complaint of recurrent vaginal bleeding and unable to urinate. The history of urinary retention found since one-night before admission. The history found that patient had hematuria or bloody spot in her diapers since three weeks ago. The

patient was delivered through normal delivery, assisted by Obstetrician with body weight 2650 grams, crying spontaneously.

The mother did not have any histories of abortion, ectopic pregnancy, and hydatidiform mole. The girl is the second child from second pregnancy; the older child is 10-year-old. Physical examination reveals full urinary bladder, indicating urinary retention. The routine blood examination and kidney function test showed normal results. Renal ultrasound found cystitis and bilateral diffuse renal parenchymal inflammation. The dwelling catheter inserted and no blood stained urine found.

A confirmative ultrasound performed because cystography failed. The result found cystic and solid mass on left posterolateral aspect of the urinary bladder that probably from the gynecologic organ. The patient consulted with pediatric surgeon and gynecologist. Pediatric surgeon diagnoses patient with Botryoides sarcoma while the gynecologist suspected solid tumor of the ovary.

Multi-slice CT-scan of the abdomen with contrast showed solid and cystic heterogeneous mass in the uterus that pressed urinary bladder to right anterior cranialateral and infiltrated the posterior aspect of the bladder wall. The tumor suspected as embryonal rhabdomyosarcoma (Figure 1). Abnormalities not found in another organ. Vaginal swab found gram-negative bacteria and positive results for leucocyte and fungus. CEA was 1.18 ng/ml, and CA125 was 21.14 U/ml.

The patient then treated with antibiotics and anti-fungus. Surgical therapy planned would perform by the gynecologist and pediatric surgeon. During treatment, there was recurrent vaginal bleeding that caused anemia. Eleven days later, the hemoglobin was 8.5 gr/dl, and platelet count was 15.000/ml.

The patient received thrombocyte and packed red cell transfusion. Fourteen days after admission, laparotomy was performed. Uterus, fallopian tubes, ovaries and digestive tract were normal and no lymphadenopathy. A palpable mass found as nodule size 4 × 4.5 cm on the lower part of the cervix, suspected as tumor mass from the vagina. A biopsy performed and histopathological result mentioned as inconclusive vaginal mass (large necrotic mass).

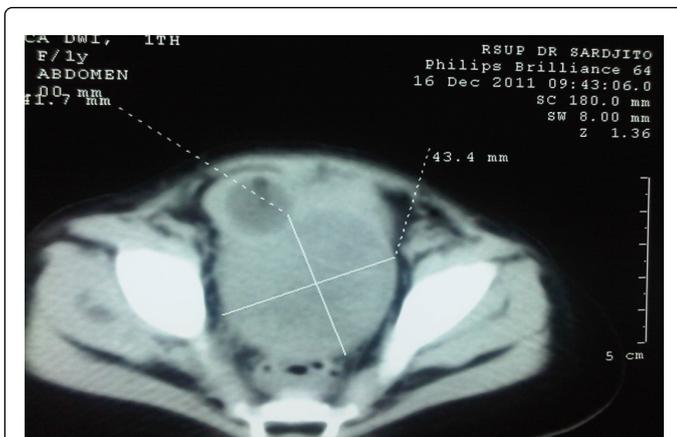


Figure 1: CT-scan found heterogeneous mass with solid and cystic parts in uterus (oval shape, distinctive border, $41.7 \times 43.3 \times 82 \text{ mm}^3$ size) that pushed urinary bladder to right anterior craniolateral and infiltrated the posterior aspect of the bladder wall.

A biopsy was repeated and found large necrotic mass with solid tumor foci infiltrating surrounding stroma. The lesion composed of two types of cells: medium and large-size atypic, polymorphic, oval hyperchromatic nucleus. Some of the areas infiltrated with polymorphonuclear leukocytes. Cytochromatin and vimentin staining were positive, indicating choriocarcinoma (Figures 2 and 3).

From repeated ultrasound, the uterus was enlarged and pushed distal part (ureters-bladder junction) of bilateral ureters that caused hydronephrosis. However, after the laparotomy surgery the patient discharged from the hospital on family request. β human chorionic gonadotropin (β -HCG) examination was $<1 \text{ mIU/ml}$.

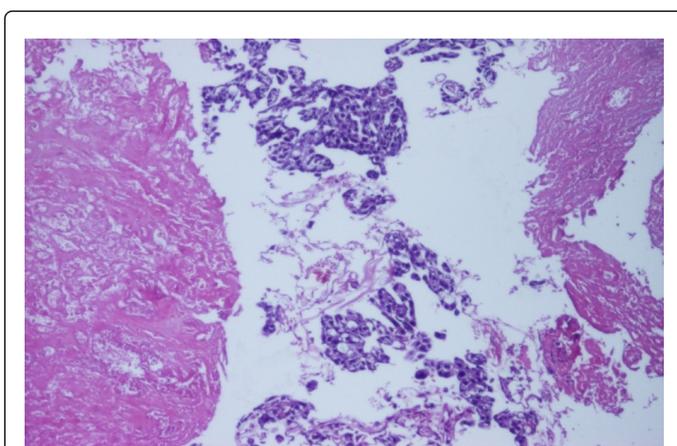


Figure 2: Large necrosis with the solid infiltrative tumor.

One week later patient arrived for a revisit with chief complaints of fever and bloating. After getting antibiotics and free of fever, the patient was treated as nongestational choriocarcinoma patient and planned to give 4-cycles chemotherapy following germ cell tumor protocol (Bleomycin, Etoposide, Cisplatin). Unfortunately, the patient passed away after one cycles of chemotherapy. The patient passed away due to sepsis, pneumocystis carinii pneumonia and diarrhea without dehydration. The condition most likely was caused by side effects of

chemotherapy that is myelosuppression. There was no sign of choriocarcinoma on her mother by clinically and laboratory finding. According to a reported case of occult choriocarcinoma, positron emission tomography/computed tomography can detect choriocarcinoma lesion that cannot detect by another radiologic methods [2].

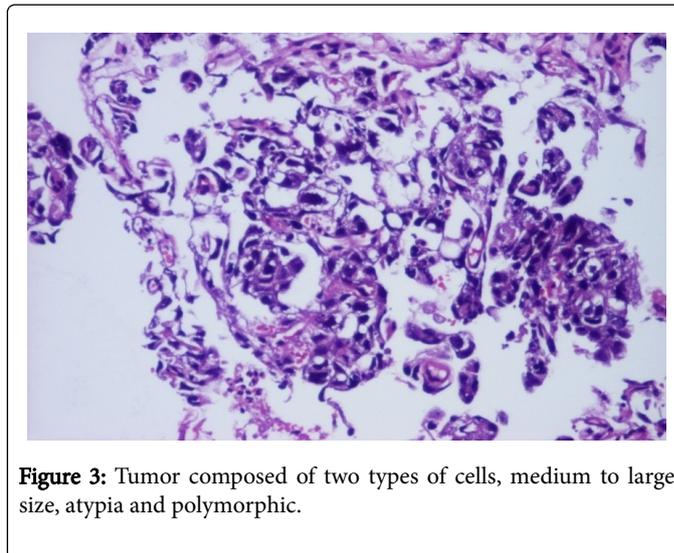


Figure 3: Tumor composed of two types of cells, medium to large size, atypia and polymorphic.

Discussion

Choriocarcinoma is a rare malignant tumor from syncytiotrophoblast and cytotrophoblast that may found after pregnancy. The incidence in normal pregnancy is about one every 50,000 deliveries. Choriocarcinoma that occurs in both the mother and the baby was extremely rare. β -Human chorionic gonadotropin (β -HCG) levels in serum and urine characteristically elevated because the tumor arises from trophoblastic cells. In the absence of a known maternal choriocarcinoma, the diagnosis is frequently incorrect because of the rarity of the lesion and the non-specific MRI findings [3]. Choriocarcinoma in children only reported in 30 cases [1]. Latest concept of choriocarcinoma mentioned that choriocarcinoma in children is also originated from the placenta as well [1,4]. Reviewed find that the symptom of children suffering from infantile choriocarcinoma become symptomatic at a median age of 1 month (range 0 days–5 months) [1]. Typical early symptoms of decreasing incidence are anemia, failure to thrive, hepatomegaly, hemoptysis or respiratory failure; there may be signs of precocious puberty. The tumor affected more than one organ in most cases; organs involved were liver, lung, brain, or skin [1,5]. β -Human chorionic gonadotropin universally elevated in 19/19 tested infants. Maternal choriocarcinoma reported in 17 of the 30 cases. The natural disease course is rapidly fatal. Without appropriate antineoplastic treatment, infantile death occurs on average within three weeks from the first presentation.

Non-gestational Choriocarcinoma is one of germ cell malignancy. Based on the histogenesis, primitive germ cell migrates from yolk sac wall to gonadal ridge. Therefore, most germ cell tumors occur on gonad. Germ cell tumor rarely found outside of gonads, such as central nervous system, mediastinum or retroperitoneum. Embryonic carcinoma consists of multipotent cells with differentiation ability. Differentiation is a dynamic process that may cause tumor with different elements that represent their different stages of development. This lesion is the precursor for several extraembryonic germ cell

tumors (yolk sac tumor, choriocarcinoma) or embryonic tumor (teratoma). Several histogenetic mechanisms have been proposed since the last of the twentieth century to explain extragonadal choriocarcinoma in men [6]. The remnant of germ-cell that failure migration has been postulated for embryologically related to the urogenital ridge (mediastinum, retroperitoneum, urinary bladder, and prostate or pelvic region) [7]. Mediastinal nongestational choriocarcinoma reported in nulligravid 22-year-old, the diagnosis was confirmed by histopathology of biopsy specimen and genotype of the tumor was strictly identical with the patient's genotype without any paternal features [8]. These results were as the confirmation the diagnosis of the non-gestational choriocarcinoma. DNA and genetic analysis can be used to define the origin of choriocarcinoma. Detection of Y chromosome using fluorescent in situ hybridization (FISH) can be used to differentiate two types of choriocarcinoma [9]. Human leukocyte antigen typing for the paternal antigen of trophoblast element can be used to determine etiology of gestational choriocarcinoma [10]. DNA polymorphism analysis can be utilized to distinguish pure nongestational choriocarcinoma of the ovary from gestational choriocarcinoma [11,12]. The genetic analysis thus can be a useful modality in determining the origin of the choriocarcinoma. Diagnosis of pure nongestational choriocarcinoma is uncertain without the DNA analysis and genetic analysis, it can be a useful tool in to determine the origin of the choriocarcinoma. If scans identify a lesion consistent with malignancy, then this should be excised for histological examination. If gestational trophoblastic neoplasia (GTN) reported by the pathologist, then genetics should be used to determine whether the tumor is gestational or nongestational in origin that will assist to provides therapeutic and prognostic significance [13].

In an adult woman, gestational choriocarcinoma commonly occurs with the history of pregnancy, hydatidiform mole, abortion and ectopic pregnancy. Highly elevated levels of serum human chorionic (hCG) levels more frequently associated with gestational tumors. From histopathologic examination, nongestational choriocarcinoma may also have another germ cell component because 60% of the tumor consists mixed of two or more histologic findings, known as mixed germ cell tumor. Tumor marker of germ cell tumors that should examine are AFP and β -HCG [14]. Unfortunately, the level of tumor marker AFP of this case was not examined. Elevation of β -HCG usually found in choriocarcinoma. In this patient β -HCG level was within normal limit, whether it was true or it may be caused by commercial β -HCG kit that is not able to detect certain degradation product of human chorionic gonadotropin. Inability to detect certain products of HCG degradation by many common HCG testing kits leads to the error of diagnosis. Only three of the seven common commercial serum HCG tests appropriately detects nicked HCG and its free [15]. They report their case a choriocarcinoma patient with urinary and serum β -HCG negative either.

From 30 choriocarcinoma cases in children, seven children were treated with cisplatin and tumor resection where five children survived. Resection after chemotherapy may be safer than primary tumor resection. Single chemotherapy with methotrexate is beneficial for gestational choriocarcinoma in the mother, but not improve the outcome in children [16]. In this case, the patient treated with BEP

regimen due to the diagnosis tend to the nongestational choriocarcinoma. As usual treatment of malignant ovarian germ cell tumor was BEP. Neeyalavira and Suprasert (2014) reported their studied on malignant ovarian germ cell tumor found that most frequent chemotherapy used was BEP and the complete respond was 73.3%, and partial respond was 11.1%. Compare to the VAC regimen BEP becomes as the preferred regimen and represents the current standard after cytoreductive surgery [17].

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