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Primary rectal choriocarcinoma associated with rectal adenocarcinoma in a woman with a history of ulcerative colitis: Case report

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ABSTRACT

INTRODUCTION: Primary rectal choriocarcinoma is an extremely rare malignancy. The association of these neoplasms in patients with inflammatory bowel disease (IBD) has not been reported.
PRESENTATION OF CASE: A 34-year-old female with history of Ulcerative Colitis (UC) gave birth to a male fetus. She had postpartum bleeding and high level of beta-human chorionic gonadotropin (βhCG) was detected. Although initial investigations failed to confirm molar pregnancy, abnormal uterine bleeding and high βhCG level necessitate chemotherapy administration. She did not respond to chemotherapy sessions accordingly. Meanwhile, the patient experienced rectorrhagia and colonoscopy revealed a firm submucosal polypoid lesion 8–10 cm from the anal verge. The multidisciplinary team candidate the patient for total proctocolectomy and ileal pouch anal anastomosis. Although postoperative course was uneventful and βhCG level dropped but it showed a rising pattern in follow ups. Chemotherapy was planned but there was not suitable response. Unfortunately, the patient passed away 20 months after the initial diagnosis.
DISCUSSION: Pathology report indicated the coexistence of moderately differentiated tubular adenocarcinoma and choriocarcinoma. We assume previous history of UC might have put her at higher susceptibility to develop carcinoma and this poorly differentiated carcinoma has led to choriocarcinoma. Considering the fact that in most cases of colorectal choriocarcinoma, choriocarcinomatous differentiation was found alongside colonic adenocarcinoma made dedifferentiation theory to be the most acceptable explanation.
CONCLUSION: The adenocarcinoma of the colon and rectum in the setting of IBD may become so dedifferentiated that gain some characteristics of germ cell tumors.

1. Introduction

Gestational trophoblastic neoplasms (GTN) includes a spectrum of pregnancy-related disorders of either benign or malignant. The malignant disorders are invasive mole, choriocarcinoma, placental site trophoblastic tumor and epithelial trophoblastic tumor [1]. Another entity is non-gestational choriocarcinoma which usually arises in the gonads [2]. Rarely choriocarcinoma may originate from extragenital organs of midline structures, such as the pineal gland, third ventricle, mediastinum, and retroperitoneum but gastrointestinal tract origin is very scarce [3]. Choriocarcinoma can also occur in males, usually those between ages of 20 to 30 year-old. Choriocarcinoma coexisting with or after an otherwise normal, viable pregnancy is extremely rare, with an estimated occurrence of 1 in 160,000 pregnancies. No association has been reported between Inflammatory Bowel Disease (IBD) and any type of choriocarcinoma. Here we represent a case of gestational choriocarcinoma in a female patient with a previous history of Ulcerative Colitis (UC).

2. Case presentation

A 34-year-old Caucasian female was consulted with the department of colorectal surgery at Imam Khomeini Hospital Complex, Tehran University of Medical Sciences for rectorrhagia. She had a history of UC which was under control for the past 5 years taking mesalamine as Asacol 400 twice a day. The patient was prime-

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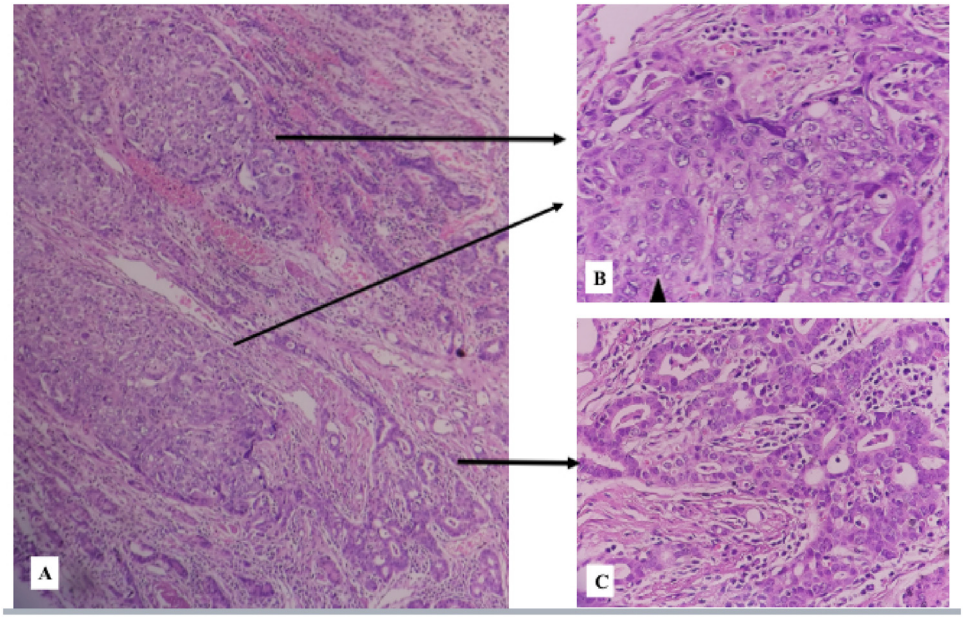

Fig. 1. A) Microscopic examination (100X) of Hematoxilin and Eosin stained slides show neoplastic tissue composed of B) choriocarcinoma component with biphasic proliferation of atypical cytotrophoblasts and syncytiotrophoblasts (arrow head) (400X) adjacent to C) adenocarcinoma component showing infiltration of irregular glandular structures with overlying atypical epithelial cells (400X).

gravid and gave birth to a male fetus through natural vaginal delivery with consequent postpartum vaginal bleeding 5 months prior to referral to colorectal surgery. On the forth postpartum day, she had a beta-human chorionic gonadotropin (βhCG) level of 417 mIU/mL and a primary diagnosis of a retained product of gestation (RPG) or GTN was proposed. A trans-vaginal ultrasonography evaluation was done which reported a 4.5×9 mm intrauterine echogenic mass suggestive for RPG. Intra-uterine dilation and curettage was performed for the patient which was not completely compatible with pathological features of molar pregnancy. However, obstetricians at our center decided to initiate chemotherapy as uterine bleeding and high βhCG level dictated presence of molar pregnancy. The patients underwent 2 courses of Methotrexate (MTX) within a week. Consecutive monitoring of the βhCG level showed that not only it was not fallen but also had risen to 1500 mIU/mL one month after the cessation of MTX. In this step, an abdominal and pelvic computed tomography scan was ordered which showed a 20×20 mm lesion located in the left side of the uterine. MTX, Vinblastin and Actinomycin were given for 3 sessions within a two-month period, but the βhCG level never reached below 300 mIU/mL. Etoposide, MTX, Dactinomycin/Cyclophosphamide, Vincristine (EMA/CO) regimen was started and followed by Bleomycin, Etoposide, Cisplatin (BEP) regimen but the patient did not respond to either of these regimens. Eventually, Etoposide, Ifosfamide, and Cisplatin were tried, but the βhCG level was 880 mIU/mL one month later. Meanwhile, the patient experienced rectorrhagia and a subsequent colonoscopy revealed a firm submucosal polypoid lesion 8–10 cm from the anal verge and a 2 cm ulcer just above the previous lesion. Other parts of the colon showed multiple superficial erosions which were also taken biopsies. The pathology report indicated high grade infiltrating carcinoma with trophoblastic differentiation and mild chronic colitis in the rest of the colon. The Immuno-histochemical (IHC) study was positive for CK7, CK20, CDX2 and PLAP. Based on the World Health Organization and International Federation of Gynecology and Obstetrics criteria, the tumor was stage IV [4]. The cumulative score was 8 and it was considered high risk. The multidisciplinary team (MDT) including colorectal surgeons, obstetricians, pathologists, gastrointestinal specialists and oncologists, referred the patient for surgery. She underwent a total proctocolectomy, ileal pouch anal anastomosis, trans-abdominal hysterectomy and bilateral salpingo-oophorectomy. Also, unilateral iliac and aortic lymphadenectomy was done. Gross pathology showed a polypoid mass in the sigmoid and upper rectum with an adjacent large necrotic lymph node. Microscopic examination of the colon revealed an infiltrative tumor composed of choriocarcinoma component with biphasic proliferation of atypical cytotrophoblasts and syncytiotrophoblasts adjacent to adenocarcinoma components (Fig. 1). There was no tumor detected in uterine specimen. Post-operative course was uneventful and she was discharged on fourth post-operative day. βhCG level had fallen to 20 mIU/mL one week after surgery. However, 4 months after surgery the βhCG level raised to 2000 mIU/mL, chemotherapy was planned and Gemcitabine and Cisplatin were initiated. After 3months, βhCG level continued to rise and reached 30,000 mIU/mL. Brain magnetic resonance imaging and thoracic-abdominal-pelvic CT scan were requested which was negative unless for a solitary tumor in the left lower lobe of the lung. Another 6 cycles of Gemcitabine and Cisplatin was administered for the patient but the βhCG level reached 20,000 mIU/mL 3 months later. Unfortunately, the patient abandoned the treatment for 5 months and she returned with a significant weight loss later to our center. The patient was discussed in the MDT again and the possibility of lobectomy of the left lower lobe was considered but the thoracic surgeons advised against the surgery based on her general condition and prognosis. Thus the chemotherapy was continued. The patient passed away 20 months after the initial diagnosis with acute respiratory distress syndrome and an underlying cause of severe hospital-acquired pneumonia. This study has been reported in line with the SCARE 2018 criteria [5].

3. Discussion

This is a rare case of rectal choriocarcinoma in a female patient with previous history of IBD. There is a dilemma about what should be this tumor named, gestational or non-gestational choriocarcinoma. Given the occurrence of tumor so close to a previous pregnancy, we assume this should be considered pregnancy related

Table 1
Characteristics of patients with previous IBD and choriocarcinoma. EMA/CO: etoposide, methotrexate and dactinomycin alternating with cyclophosphamide and vincristine.

First author of the study	age	gender	presentation	IBD type	Tumor location	Metastatic sites	IHC study positive for	Treatment
Ragam et al. [13]	46	male	fever and bloody diarrhea	UC	Rectosigmod	Liver and Kidney	βhCG, CK 7, p63, CD10, and CD30	Chemotherapy with bleomycin, etoposide and cisplatin
Pezzuto et al. [14]	47	male	abdominal pain and melena	Crohn's disease	Cecum	Lung and Brain	β-hCG CK-pool, CK-19 and Vimentin	Total colectomy with lymph-nodes dissection
Bircher et al. [15]	25	Female	Abdominal pain and vaginal bleeding	Crohn's disease	Not found	Lung	Not performed	Chemothera py started with methotrexate and folinic acid and continued with EMA/CO

as the patient was completely symptom free before getting pregnant. This phenomenon could have occurred in three different scenarios. First, simply it might be the metastasis of choriocarcinoma to GI tract. Second, it might be the result of extragonadal choriocarcinoma occurring in colon as primary site. Third, as the patient had previous history of UC it might be the result of higher susceptibility to develop carcinoma and this poorly differentiated carcinoma has led to choriocarcinoma.

Typically, gestational choriocarcinoma represents as primary lesion of uterus with great invasion. Approximately in 30% of cases, hematogenous dissemination causes distant metastases, preferably to the lungs, liver and brain [1]. Although modified World Health Organization (WHO) prognostic scoring system as adopted by the International Federation of Gynecology and Obstetrics (FIGO), considered 2 point for GI metastasis but it is extremely rare entity [2]. Thus it is unlikely that first scenario could explain our case.

There have been reports of primary extragondal choriocarcinoma originating from distal colon and rectum. The total number of known cases of this tumor have reached just to eighteen cases [6]. These patients ranged from 29 to 74 years old and the median survival period was 4 months ranging from 0.3 to 60 months. Distant organ metastasis was found at the time of colorectal choriocarcinoma diagnosis in over 70% of cases [7]. Previous literature emphasized on the role of surgical resection with lymph node dissection but recently systemic chemotherapy proposed to have a great role in the prognosis. However, no standard chemotherapy regimen has been dedicated to the treatment of non-gestational choriocarcinoma as these tumor rarely occur [8]. Colorectal choriocarcinoma is considered pathologically similar to choriocacinoma of GTN, thus almost all previously used chemotherapeutic regimens were based on those designed to treat GTN [25].

Few mechanisms have been introduced to explain development of primary choriocarcinoma of colorectal origin, including dedifferentiation of carcinoma [10], origin from an underlying teratoma, metastasis from a latent primary lesion in the genitalia, ectopic primordial chorion in the wall of digestive tract, and histomorphologic imitation of carcinoma. In this regard, the dedifferentiation theory is considered to be the most acceptable. The reason that this hypothesis became more popular is the fact that in most cases of colorectal choriocarcinoma, choriocarcinomatous differentiation was found alongside colonic adenocarcinoma. Pathology report in our case indicated the coexistence of moderately differentiated tubular adenocarcinoma and choriocarcinoma. Harada et al. [9], reported that they were able to recognize the borderline between the choriocarcinomatous and adenocarcinomatous components in the pathology specimen. In contrast, Le et al. [10], and Kubosawa et al. [11], claimed that direct malignant change in ectopic chorion or totipotent cells result to this tumors as in their reported case common colon carcinoma was alongside the choriocarcinoma, but metastatic tumors were composed solely of choriocarcinoma [4]. The absence of adenocarcinoma in some cases might be explained by the extent of dedifferentiation as the more aggressive choriocarcinomatous component, get the adenocarcinoma components diminish [12]. From clinical point of view, the importance of such tumorogenesis is that chemotherapy response of colorectal choriocarcinoma is much worse than choriocarcinoma of GTN [7].

There were only three cases of IBD association with choriocarcinoma in the literature. Each case is summarized in Table 1. These three investigations used the same diagnostic approach and utilized abdominopelvic CT scan and colonoscopy. IHC study confirmed choriocarcinoma in two studies. However, Ragam et al. [13], used chemotherapy with bleomycin, etoposide and cisplatin and Bircher utilized methotrexate and folinic acid while the patients was still pregnant and continued with high-risk protocol with etoposide, methotrexate and dactinomycin alternating with cyclophosphamide and vincristine, (known as EMA/CO, this is a regimen widely used in metastatic choriocarcinoma) after child birth. Pezzuto et al. [14], did colectomy with lymph-nodes dissection. Although initial treatment was accompanied with β-hCG level reduction patients passed away in less than 2 years of initial treatment in Ragam et al. [13] and Pezzuto et al. [14] subjects. However, Bircher et al. [15] case was alive and could gave birth to another child 7 years later of termination of treatments.

4. Conclusion

The interesting fact about these cases is that adenocarcinoma of the colon and rectum in the setting of IBD may become so dedifferentiated that gain some characteristics of germ cell tumors. This would be clinically important whenever surgeons and pathologists encounter a colorectal carcinoma with invasive behavior. Also, if there is an increase in tumor markers of any kind in an IBD patient, surveillance colonoscopy is warranted.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

Ethic committee of Tehran University of Medical Sciences approved this study.

Consent

The patient gave written consent about her willingness to participate in the study after she was completely informed about study.

Author contribution

Seyed Mohsen Ahmadi Tafti M. D.: Conception and Design of the study, Writing the paper.

Amirsina Sharifi. M. D.: Data collection and/or processing, Writing the paper.

Amir Keshvari. M. D.: Critical review.

Fatemeh Nili. M. D.: Writing the paper, Critical review.

Masoomeh safaei. M. D.: Writing the paper.

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