AN AGGRESSIVE COURSE OF DE NOVO ULCERATIVE COLITIS AFTER RENAL TRANSPLANTATION: COLONIC ADENOCARCINOMA WITH CHORIOCARCINOMATOUS DIFFERENTIATION

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RÉSUMÉ

But : Rapporter une observation du carcinome colique se développant sur une colite ulcéreuse de NOVO après transplantation rénale chez une femme âgée de 42 ans.

Observation : La patiente présentait une colite ulcéreuse de huit ans après une transplantation rénale. Sur ce terrain, un cancer colique s'est développé avec métastases hépatiques deux ans après et décédé un mois après intervention.

Histologiquement, la pièce opératoire était composée de deux éléments un adénocarcinome et choriocarcinome. La métastase hépatique était exclusivement un choriocarcinome. L'identification du choriocarcinome s'est basé sur l'aspect histologique et immunoistochimique en montrant de HCG élevé non en rapport avec une maladie du troplobaste.

Conclusion : L'évolution des colites ulcéreuse de NOVO après transplantation rénale reste encore un sujet de débat. D"autres investigation sont nécessaires pour comprendre la tumorigenèse sur ce terrain.

SUMMARY

Aim : A rare case of colonic carcinoma arising in de novo ulcerative colitis after renal transplantation in a 42-year-old woman is reported.

Case : Clinically, the patient presented ulcerative colitis 8 years after renal transplantation, developed colonic cancer with liver metastasis 2 years later and died one month post operatively. Histologically, the removed tumor was composed of two distinctive elements consisting of adenocarcinoma and choriocarcinoma. The metastatic foci in the liver were composed exclusively of choriocarcinoma. Identification as choriocarcinoma was made on the basis of typical histological appearance, immunohistochemical demonstration of human chorionic gonadotropin (hCG) in the tumor cells and the high serum hCG level, unrelated to trophoblastic disease. In this report, pathogenesis is briefly discussed and clinical conditions are reviewed.

Conclusion : In conclusion, the issue of de novo UC after organ transplantation is still a matter of debate. Further investigations are necessary to understand the tumorogenesis of colorectal cancer in de novo UC after renal transplantation,

MOTS-CLÉS

Adenocarcinome, choriocarcinome, côlon, colite ulcéreuse, la transplantation.

KEY-WORDS

Adenocarcinoma, choriocarcinoma, colon, ulcerative colitis, transplantation.

تطور خطير لآلتهاب القولون المتقرح لنوفو بعد عملية زرع الكلى : سرطانة غدية في القولون

الباحثون : كوردا . ن - بالطيب . إ - بلال . أ - زغلامي . أ - بدوي . ر - ناجح . ن - بلطجي بن جيلاني . س - زرماني . ر.

تستعرض دراستنا حالة سرطان في القولون تكون بسبب آلتهاب متقرح في القولون لنوفو وذلك بعد عملية زرع الكلى عند آمرأة عمرها 42 سنة . ظهر هذا الإلتهاب المتقرح 8 سنوات بعد عملية الزرع وتكون السرطان بعد سنتين مع وجود نقيلات على مستوى الكبد توفيت المريضة شهرا بعد إجراء عملية جراحية . التحليل التشريحي المرضي الذي أجري للقطعة المستأصلة أثبت أنها تتكون من عنصرين سرطانة غدية وسرطانة مشيمائية نستنتج أن تطور آلتهاب القولون المتقرح لنوفو بعد عملية زرع الكلي موضوع نقاش ويجب إجراء بعض البحوث الأخرى لفهم التكون الورمي في هذه الظروف.

الكلمات الأساسية : قولون - سرطانة غدية - سرطانة مشيمائية - آلتهاب متقرح

The risk of developing malignancy is increased after transplantation. This high incidence of cancer is believed to be related to the use of immunosuppressive agents. Since ulcerative colitis (UC) is itself a strong risk factor for the development of colonic carcinoma, de novo UC after renal transplantation might be at higher risk for colonic carcinoma. Colorectal carcinomas presenting with choriocarcinomatous differentiation are exceedingly rare; only six prior cases have been reported. All reported patients have had a poor clinical outcome [1]. We report a new case of colonic carcinoma developed in de novo ulcerative colitis after renal transplantation in a 42-year-old woman.

CASE REPORT

A 42-year-old woman had undergone renal transplantation in 1991 for end-stage renal disease of unknown cause. She was treated with immunosuppressive agents. In 2000, the patient presented with diarrhea and lower gastro-intestinal bleeding. Colonoscopy with histological examination of the colonic mucosa biopsy specimens confirmed the diagnosis of ulcerative colitis. She reunderwent colonoscopy in 2002 due to rectal bleeding, revealing a 6cm mass of the sigmoid colon with 80% luminal occlusion.

Histological examination of the biopsy specimen showed a well differentiated adenocarcinoma. The patient underwent laparotomy for total colectomy. Grossly, the resected colon measured 80cm. On opening, there was a tumor involving the whole circumference of the sigmoid colon and measuring 4,5cm a cross. It was sessile, polypoid, pinkish and soft. On cut section, it showed hemorrhagic necrosis and invaded the pericolic fatty tissue. 18 lymph nodes were found along the paracolic fatty tissue of the mesentery.

Histologically, the removed tumor was composed of two distinctive elements consisting of an adenocarcinoma and choriocarcinoma (figure 1): the main tumor was the adenocarcinoma arising from the colonic epithelium, invading the muscularis and extending into the adjacent pericolic fatty tissue; the hemorrahagic component of the colonic tumor showed a classic choriocarcinoma with irregular nests of cytotrophoblasts and syncytiotrophoblasts. In several areas, the adenocarcinomatous elements showed transition into an undifferentiated carcinoma in which the tumor cells had cytologic features somewhat similar to those of cytotrophoblasts (figure 2). There was lymph node and liver involvement (pT3N1M1). The metastatic foci in the liver were composed exclusively of choriocarcinoma. Adjacent colonic mucosa showed signs of UC with areas of high grade dysplasia (figures 3).

Identification as choriocarcinoma was made on the basis of typical histological appearance, immunohistochemical demonstration of human chorionic gonadotropin (hCG) in the tumor cells (figure 4) and the high serum hCG level (8235,48 mUI/ml), unrelated to trophoblastic disease (exploration of the genital tract was negative). The postoperative course was eventful and the patient died one month after surgery.

Figure 1 : The tumour was composed of adenocarcinoma and choriocarcinoma (HE x 100).

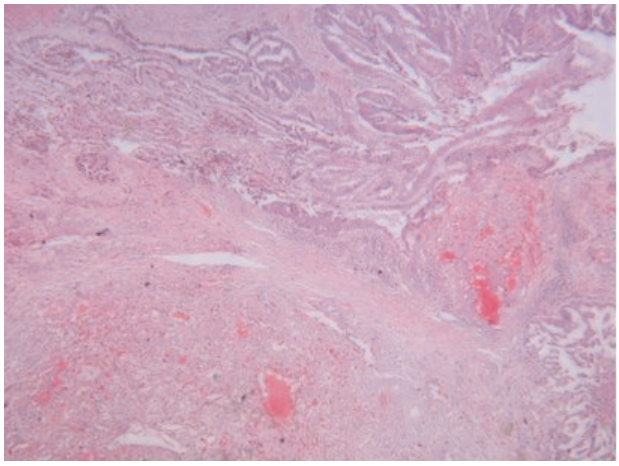


Figure 2 : Transition of adenocarcinomatous elements into choriocarcinomatous elements (HE x 250).

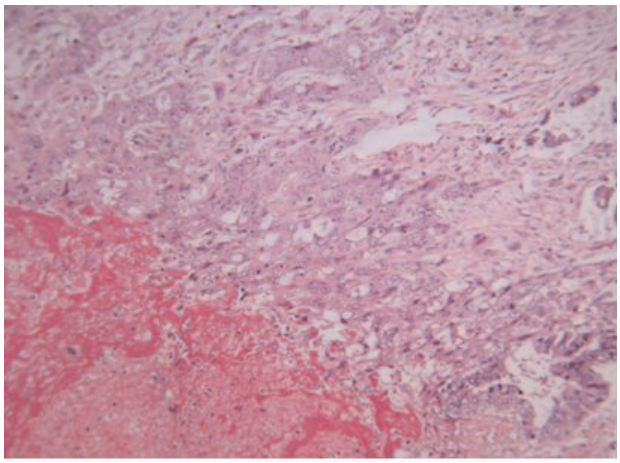


Figure 3 : Dysplasia/cancer sequence (HE x 100).

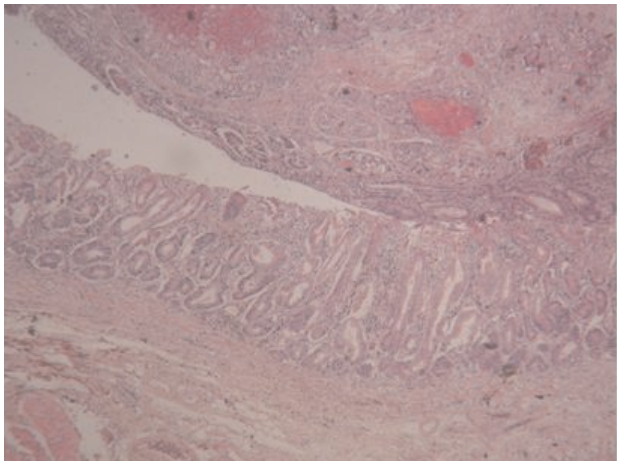
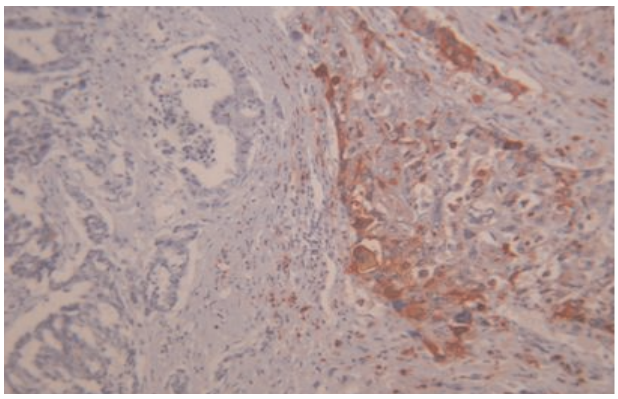


Figure 4 : HCG immunoreactivity of the choriocarcinomatous elements (IHC x 400).



Transplant patients are predisposed to develop cancer due to immunosuppression. This high incidence of cancer may be related to impaired immunosurveillance, direct neoplastic action of immunosuppressive agents, oncogenic viruses such as Epstein-Bar virus or cytomegalovirus, chronic antigenic stimulation, uremia, or genetic predisposition [2]. Cancers occurring in transplanted patients are generally de novo and they are fundamentally diagnosed after the third year, increasing after the tenth year [3]. Although the risk of haematological malignancies and skin cancer are clearly increased in this setting, the association with colorectal cancer is controversial. The mean time of appearance for colorectal malignancies in some series was 10,4 years [2]. In our case, the elapsed time from renal transplantation to development of colon carcinoma was 10 years. New onset inflammatory bowel disease (IBD) cases after transplantation and in particular after liver transplantation have been reported by some authors [4]. It seems that new onset IBD may have an aggressive course after organ transplantation. The course of de novo ulcerative colitis after organ transplantation has been reported as variable, but there have been reports of an increased risk of early colorectal cancer [5]. Our patient developed colonic cancer with liver metastasis 2 years after the diagnosis of UC was made. To date there is no hypothesis to explain the course of de novo UC after organ transplantation and its relation to immunosuppression. Inappropriate drugs or inadequate posology may be responsible for UC cases presenting with aggressive disease after renal transplantation despite immunosuppression. The current case is characterized by coexistence of well differentiated adenocarcinoma and choriocarcinoma. There can be several possibilities accounting for this unique lesion [6]; these elements are: the result of dual differentiation of an immature malignant cell, incidental coexistence of two different malignancies, transformation of colonic carcinoma into choriocarcinoma, or transformation of choriocarcinoma into colonic carcinoma. We favour the third possibility since morphologic observation suggested that the choriocarcinomatous element derived from the colonic carcinoma: focally, the tumor cells became clearer and, in accordance with the loss of the polarity, produced thick cellular trabeculae or small solid cell nests and simultaneously, their nuclei became rounded, gradually converting into cytotrophoblasts. It is unknown whether immunosuppressed subjects follow dysplasia/cancer sequence as in immunocompetent population. In our case, the pathological examination showed low-grade and high-grade mucosal dysplasia adjacent to areas of adenocarcinoma and this supports the hypothesis of dysplasia/cancer sequence (figure 3). The adenomatous polyposis coli (APC) gene is mutated in most sporadic colonic cancers and is thought to be an early event in the carcinogenesis pathway [7]. It is unknown whether the same molecular mechanisms are applicable in immunosuppressed patients. Several recent studies suggest that the APC gene is less significant in the dysplasia-carcinoma sequence of UC when compared to sporadic colorectal carcinomas [8]. The p53 gene is also one of the tumor suppressor genes in which either loss or mutation is the most frequently observed genetic change in human cancers. It is possible that changes in p53 expression are important in the development of cancer in UC. In fact, some authors detected the overexpression of p53 in UC associated neoplasms and suggested that alteration of the p53 locus might be important in the progression from the non malignant phenotype to carcinoma [9]. In a study [3], alterations of the p53 gene were observed in colorectal adenocarcinomas occurring after renal transplantation.

In conclusion, the issue of de novo UC after organ transplantation is still a matter of debate. Further investigations are necessary to understand the tumorogenesis of colorectal cancer in de novo UC after renal transplantation, and to provide new insight into the cause and pathogenicity of malignancies in organ transplant patients. Moreover, further study of colorectal adenocarcinoma with choriocarcinoma differentiation may allow more precise classification, prognostication and treatment planning.

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