The coincidence of testicular and umbilical metastasis of colon cancer: a case report and literature review

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Abstract: The liver and lungs are prone to be the metastatic sites of colorectal cancer. Testicular metastasis is uncommon, as is umbilical metastasis, both of them are associated with advanced disease, when they appear at the same time, it is often associated with multiple metastases and indicates poor prognosis. Here we report a 56-year-old man complained intermittent right testicular mass with scrotal pain initially. In the view of image inspection and pathological examination, he was diagnosed as stage IV transverse colon cancer with widespread metastasis according to the gastrointestinal multidisciplinary team meeting. He had received Oxaliplatin plus Capecitabine for 12 cycles, he failed to use bevacizumab for anti-angiogenesis therapy because of his economic conditions. However, revaluation for the primary and metastatic tumors were partial remission, then he received Capecitabine as maintenance therapy. The coincidence of testicular and umbilical metastasis from colorectal cancer is uncommon, and the prognosis is poor, with appropriate regimen developed by a multidisciplinary medical team used, patients with metastatic colon cancer may achieve significant benefit. We also conduct a review of the literature, the purpose is to summarize the clinical features of colon cancer metastasis to the testis and umbilical area, it is speculate that this case of metastasis may be related to transperitoneal seeding on the basis.

Keywords: Testicular metastasis; umbilical metastasis; colon cancer

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Introduction

The reasons for an upward trend in incidence and mortality of colorectal cancer may be population aging, smoking, drinking, high-calorie diets and lack of physical exercise (1). In China, most patients with colorectal cancer are already in the advanced stage when they seek medical help. Even some of them present at terminal stage with multiple metastasis. Testicular or Umbilical metastasis is mostly associated with advanced metastatic gastrointestinal tumors (2). Metastatic cancer of the testis, was termed as analog Krukenberg tumor in male (3), metastatic cancer of the umbilicus was honored as Sister Mary Joseph's nodule (SMJN) in memory of Sister Mary Joseph (4), both of them indicates poor prognosis. We report a case of stage IV transverse colon carcinoma in a 56-year-old patient, with right testis, umbilicus, liver, lungs and bladder metastasis, for which he has finished 12 cycles of a combined chemotherapy regimen with oxaliplatin plus capecitabine, he is using a single agent of capecitabine as maintenance therapy for the tumors in partial remission. It is uncommon that the coincidence of testicular and umbilical metastasis from colorectal cancer, we try to report this case and review some of the relevant literature. We present the following case in accordance with the CARE reporting checklist (available at http://dx.doi.org/10.21037/dmr-20-102).

Case presentation

A 56-year-old male patient was referred to our department because of right testicular mass, and with complained intermittent scrotal pain without any aggravating or relieving factors, he has no significant urinary symptoms. He also noted a firm and nontender supraumbilical mass during treatment, with frequent loose stools and intermittent melena. Colonoscopy found Colon polyp three years ago, but he did not seek any more medical help at that time. He reported 3 kg of weight loss for last 6 months. He has no past history of hypertension, diabetes, and heart involvement. His mother was died of gastric cancer 19 years ago.

Upon general examination, he had a thin build and pallor, there was a palpable mass in the right abdomen about 6 cm × 3 cm, and there was a supraumbilical nodule measuring 4 cm × 3 cm, which was firm and nontender. A small nodule was found in his right testis measuring 2 cm × 1 cm. Digital rectal examination was unremarkable. Complete blood count confirmed anemia with a hemoglobin of 6 g/dL; carcinoembryonic antigen (CEA) 7.05 ng/mL, carbohydrate antigen 19-9 (CA19-9) 693.55 U/mL, CA125 86.86 U/mL, His other tests such as renal and liver function, testicular tumor markers were within the normal ranges. His chest and abdominal CT scan revealed a tumor in the right colic flexure with ascites (*Figure 1A*), and metastasis to supraumbilical abdominal wall (*Figure 1B*), testis (*Figure 1C*), liver (*Figure 1D*) and lung (*Figure 1E*). CT scan of testis revealed heterogeneously enhancing soft tissue attenuation lesion involving the right testis with hydrocele. Colonoscopy was then performed showing a mass at the hepatic flexure with intestinal stenosis. Biopsy of the lesion revealed a moderately differentiated adenocarcinoma. Ultrasonography of his testes showed a solid nodule appearance of 2.5 cm × 1.8 cm in the right testis, ultrasonography also found a supraumbilical solid nodule measuring 2.2 cm × 1.6 cm, the biopsy of the two nodules were revealed metastatic adenocarcinoma (*Figure 2A*,*B*). Unfortunately, He couldn't undergo genetic testing and use targeted therapy for limited economic condition.

In the view of these findings, he was diagnosed as a metastatic colon cancer staged cT4bN2M1c according to the gastrointestinal multidisciplinary team, and received CAPEOX regimen for palliative chemotherapy since September 20, 2019, the regimen contains intravenous infusion of oxaliplatin 130 mg/m^2 on day 1, along with oral administration of capecitabine 1,000 mg/m^2 twice daily on days 1–14, the treatment was repeated every 3 weeks, and continued until 28th June 2020. CT scan showed the regression of primary tumor in colon every three cycles (*Figure 3A*,*B*,*C*), similar changes have occurred in umbilical metastases (*Figure 4A*,*B*,*C*), testicular metastases (*Figure 5A*,*B*), Liver metastasis (*Figure 6A*,*B*,*C*) and Lung metastasis (*Figure 7A*,*B*,*C*). Tumor markers were within the normal range (*Figure 8A*,*B*). Reassessment for the tumors were partial remission, then he received Capecitabine as maintenance therapy since 22nd July 2020.

In the beginning of each chemotherapy, apart from physical examination, laboratory such as complete blood count, tumor markers, liver and renal function were done for evaluation. Moreover, CT scan was done every three cycles to assess the size of primary and metastatic tumor, the objective tumor response was evaluated using the Response Evaluation Criteria in Solid Tumors, version 1.1. The toxicity was assessed using the Complete Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). Besides regular follow-up, patient reported certain subjective symptoms to the doctor via WeChat, even during the COVID-19 pandemic. During the treatment, the adverse events such as numbness of hands and feet occurred, using vitamin B and protecting the extremities, the symptoms can be relieved. Therefore, the chemotherapy plan wasn't delayed, and maintenance therapy with capecitabine may be an appropriate option for relief the oxaliplatin-induced neuropathy following CAPEOX. He expected to obtain the best curative effect and minimal side effects through these approaches.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Oral informed consent was obtained from the patient for publication of this study and any accompanying images.

Discussion

Gastrointestinal tumors mainly metastasize to regional lymph nodes through the lymphatic ducts, and then metastasize to the liver, lungs, bones via the hematogenous metastasis, but it is uncommon for colorectal cancers to metastasis to testis (5), so as to umbilicus. The coincidence of testicular and umbilical metastasis from transverse colon adenocarcinoma is a sign of advanced tumor, and it is an uncommon finding. Therefore, we reviewed the relevant literature to understand the clinical features and prognosis of tumor metastasis to the testis and umbilical region.

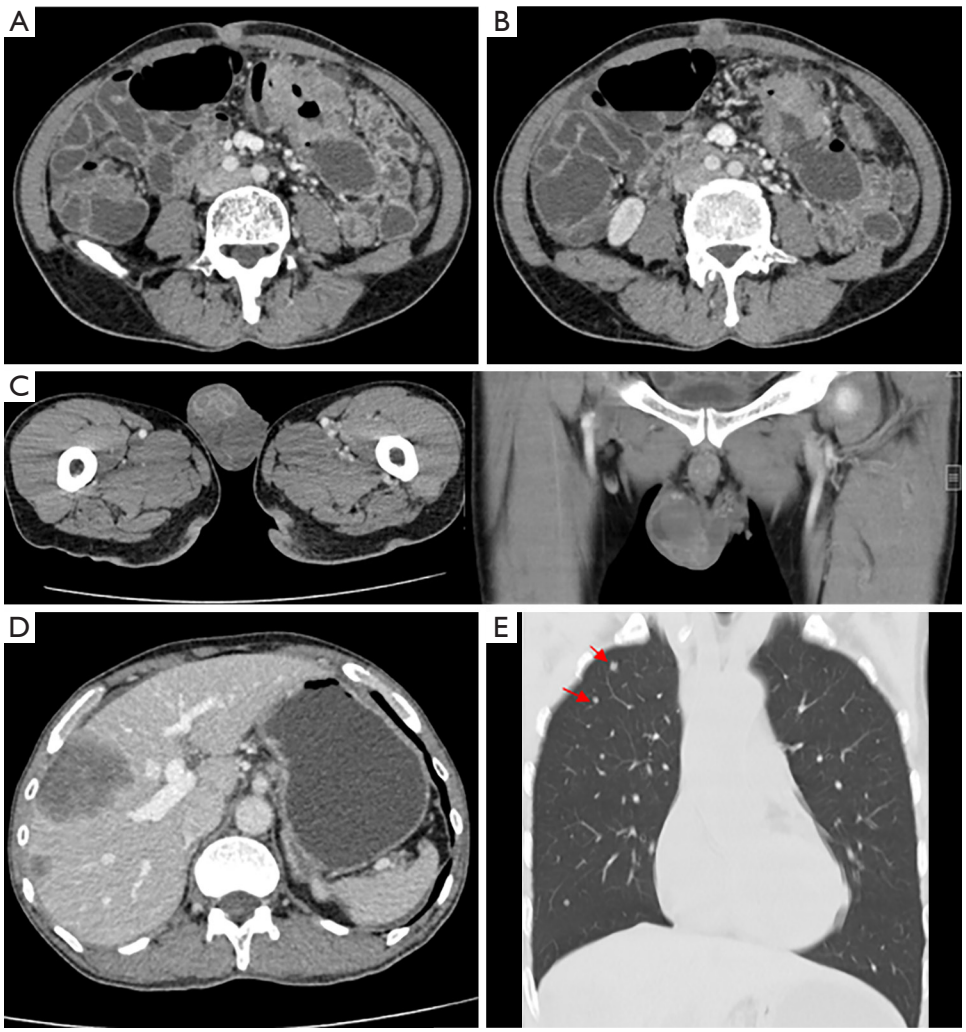

Figure 1 CT scan on September 10, 2019 (before treatment) demonstrated that unevenly enhanced segment of mid transverse colon can be seen, thickest wall with locally constricted lumen and blurry surrounding lipoid space, periumbilical abdominal wall nodule can be seen, an irregular nodule can be seen below the right testicle with bilateral hydrocele, metastatic nodes can be seen in liver segments S4-8, Multiple metastatic nodules can be seen in the lung (red arrows).

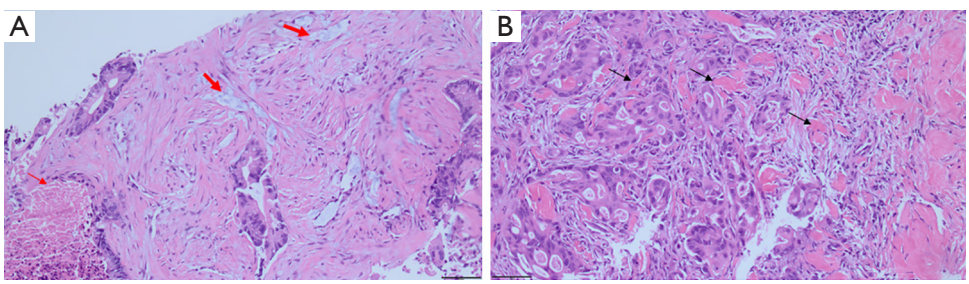

Figure 2 (A) Histology showed adenocarcinoma infiltrates in fibrous tissue with hyperplasia and hyalinization, necrotic tissue (red arrows) and extracellular mucus (broad arrows) can be seen locally in the right testicular sample. (Hematoxylin and eosin, ×100). (B) Histology revealed adenocarcinoma infiltrates in hyperplastic fibers and atrophic striated muscle tissue in the umbilical sample (black arrow, ×100).

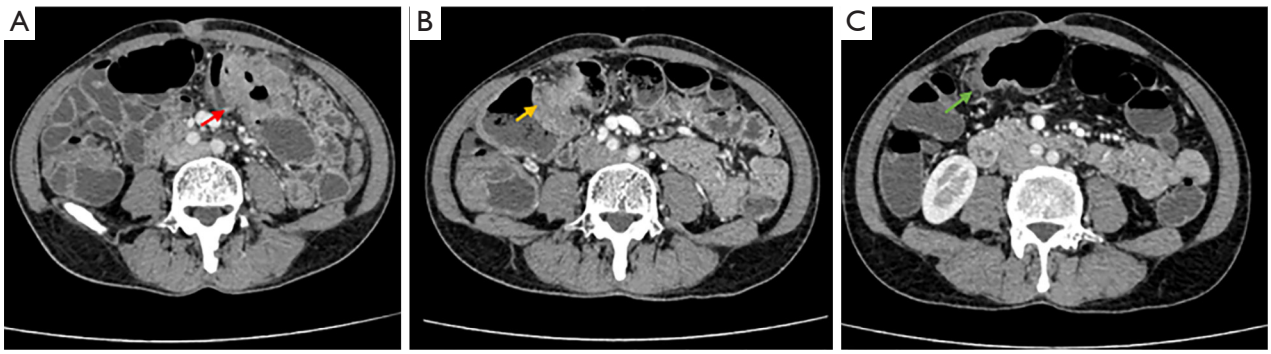

Figure 3 CT scan demonstrated that the primary tumor before treatment (A), the regression of tumor after third treatment cycle (B), and after ninth treatment cycle (C).

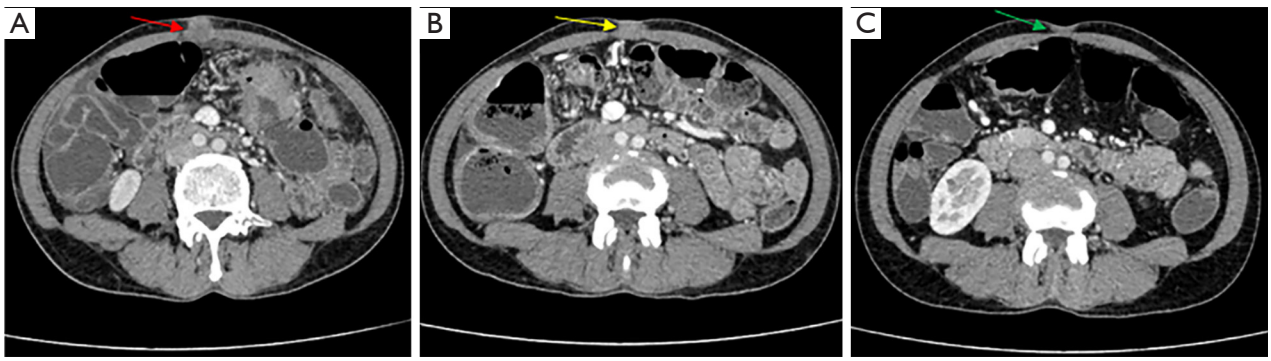

Figure 4 CT scan revealed the umbilical metastasis before treatment (A), the shrink of tumor after third treatment cycle (B), and after ninth treatment cycle (C).

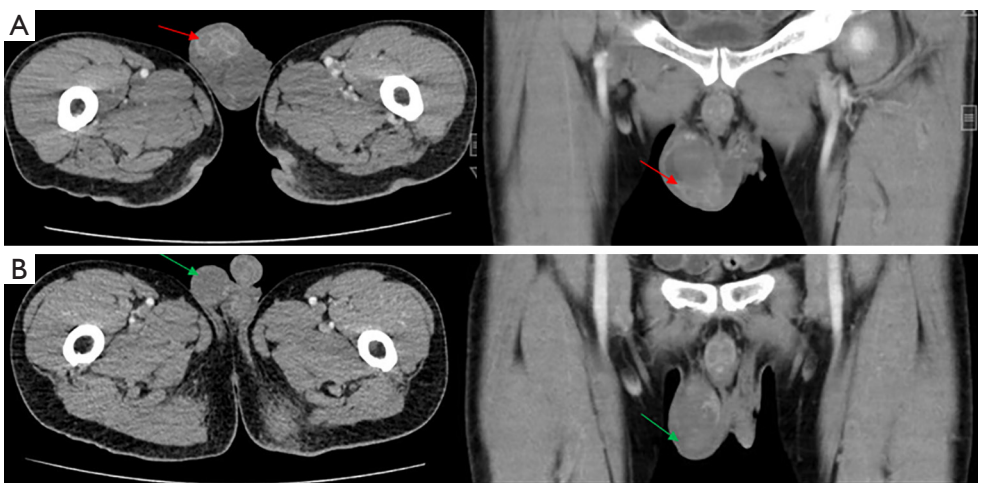

Figure 5 CT scan demonstrated that the right testicular metastasis before treatment (A), and the regression of tumor after ninth treatment cycle (B).

Figure 6 CT scan revealed the hepatic metastases before treatment (A), the recession of tumor after third treatment cycle (B), and after ninth treatment cycle (C).

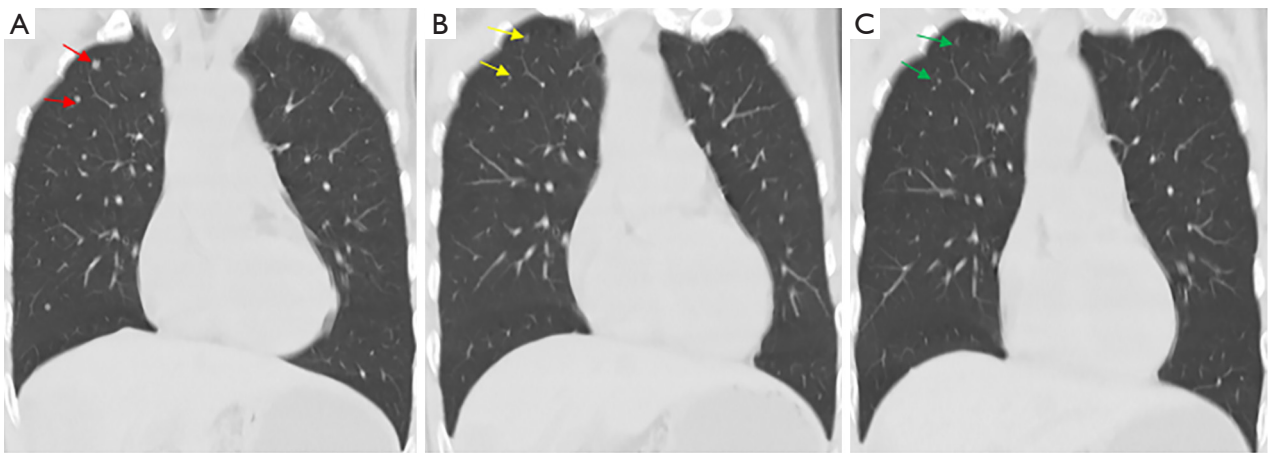

Figure 7 CT scan revealed the pulmonary metastases before treatment (A), the change of tumor after third treatment cycle (B), and after ninth treatment cycle (C).

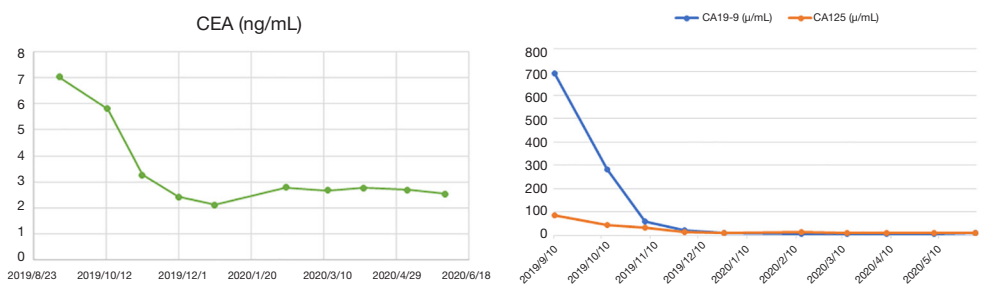

Figure 8 Fluctuations of CEA (normal values: 0–5 ng/L), CA19-9 and CA125 (normal values: 0–35 μ/mL) levels in the blood.

Hatoum *et al*. had reviewed 33 cases of testicular metastasis from colorectal cancer, showed that the metastasis usually found at the ages of 52. Most of them present as testicular mass, swelling, tenderness, hydrocele and necrotic scrotal ulcer, may mimick primary neoplasms of the testis (6), it should be noted that testicular metastasis could be the first sign of widespread disease (2). Colon cancer was the most common gastrointestinal tumor metastasized to the

testis or peri-testis, and the sigmoid colon cancer was the most frequent colorectal cancer metastasized to the testis, followed by the cecal cancer, rectal cancer, and other colonic cancer (6).

Pathological examination of testicular tissue can help distinguish whether testicular tumors are primary or secondary, it was a sign of metastasis that the presence of massive lymphatic and vascular infiltration accompanied with interstitial lesions while the seminiferous tubules are undamaged via microscopic examination (7,8). It is said that CDX2, CK20, epithelial membrane antigen (EMA) and beta-catenin can help distinguish tumors or benign tissues. It also could be conducive to distinguish whether the tumor is primary or metastatic (9,10). Regrettably, it couldn't help distinguish whether testicular tumors were primary or metastatic for Alpha-feto Protein (AFP) and human chorionic gonadotropin (hCG) were not derived from testicular tumor tissue (7).

The exact mechanism of spread is unknown, it had confirmed that there were various possible modes of spread such as direct diffusion, retrograde venous embolization, arterial embolism, retrograde lymphatic invasion from the lymph nodes around the aorta, and peritoneal seeding (6,11). Tumor cells might also disseminate from the peritoneal cavity to the testes pass through a patent processes vaginalis. It was most likely transperitoneal seeding in our case for there were evidences of transverse colon cancer and extensive spread in the abdominal wall and cavity, and he also presented with testicular nodule accompany hydrocele. It is possible to infer that there may be microscopic channels between the peritoneum and testes. Another reason why the rarity of testicular metastasis is the temperature of the scrotum is lower than that of the abdominal cavity, resulting in an unfavorable condition for the secondary tumor growth (12), maybe it's the other reason that the testicular metastasis was sensitive to chemotherapy in our case. According to the reports, Therapeutic strategies used for testicular metastases include palliative chemotherapy, radiation and surgery (11). The prognosis of testicular metastases is not optimistic. A review had shown that the patients of colon cancer who had metastasized to the testicles survive an average of 6–12 months after diagnosis (6).

SMJN is another rare manifestation represents advanced stage of internal malignancy with grim prognosis, it is the eponym to describe this umbilical metastatic nodule that used by Sir Hamilton Bailey, in honor of Sister Mary Joseph (13), who initially observed that the umbilical nodule was often founded in patients with gastric cancer, and these patients died earlier than who did not have umbilical nodules. And it was confirmed later that patients with umbilical metastases had poorer outcome generally, about 1–3% of the abdominal and pelvic tumors metastasize to the umbilicus (4). Like testicular metastasis, SMJN may be the first or the only performance of an intra-abdominal neoplasm under certain conditions. Patients with SMJN often present with a painful nodule, usually ranges from 0.5–2 cm, with irregular margins and hard consistency. The surface of the nodule may be ulcerated or necrotic, with bloody, serous, purulent, or mucous secretions. SMJN has different primary lesions in different genders, the most common primary malignancies of SMJN in male patients is the gastric cancer, followed by the colonic and pancreatic carcinomas, while in female patients, the most common Primary tumor is the ovarian cancer, followed by the gastric, colonic and pancreatic carcinomas (14,15). The fine needle aspiration cytology (FNAC) was a straightforward, economical and dependable method in making the diagnosis of umbilical nodules (16). Umbilical metastases are mostly derived from adenocarcinoma, followed by squamous cell carcinoma and undifferentiated malignant tumor (17).

The primary tumor metastasis to umbilical area involves several ways, such as adjacent tumor invasion, hematogenous and lymphatic spread. It also diffused along the vestigial remnants of embryonal ligaments, such as the round ligament, urachus, the vitello intestinal duct remnant, and the obliterated vitelline artery (4,18,19). Moreover, direct implantation following surgery was another condition that may cause tumor metastasis to the umbilical area, as Otsuka I etc. reported (20).

SMJN is a sign of advanced malignant disease, it indicates a poor prognosis, researchers have advocated some palliative therapy strategies such as chemotherapy, radiotherapy, and surgery with adjuvant therapy. The survival of these patients was range from 2 to 11 months after diagnosis according to reports (4,18,19).

Conclusions

In conclusion, the coincidence of testicular and umbilical metastasis from transverse colon adenocarcinoma is an uncommon finding. Whether testicular or umbilical metastasis is associated with diffuse systemic disease and poor prognosis. These cases can receive only limited treatment, including palliative surgery, mild chemotherapy, or best supportive care.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Oral informed consent was obtained from the patient for publication of this study and any accompanying images.

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