

CASE REPORTS

Treatment of rectal liver metastases

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Received: January 1, 2015

Accepted: February 1, 2015

Online Published: June 15, 2015

DOI: 10.14725/dcc.v2n2p29

URL: <http://dx.doi.org/10.14725/dcc.v2n2p29>

Abstract

One case of rectal liver metastases was collected from our hospital, and the results were analyzed according to clinical laboratory examination and auxiliary examination. So this paper aims to enhance the clinicians' awareness of rectal liver metastases through clinical data analysis, and increase early diagnosis rate and resection rate, combined with the application of chemotherapy and interventional treatment to improve prognosis and prolong survival time of the patients.

Key Words: Rectal cancer, Liver metastases, Neoadjuvant therapy, Surgery

1 Medical record

1.1 General information

A 72-year-old female patient was admitted to our hospital due to fatigue and weight loss for two months duration. She suffered from fatigue and weight loss (about 2.5 kg), with occasionally black stool and slight abdominal distension. There was no occurrence of abdominal pain, diarrhea, constipation, nausea, vomiting, fever, jaundice, or cough, expectoration, chest tightness, shortness of breath. Outpatient department receive the patient for weight loss of unknown origin. Since onset of the disease, the patient's mental state is good, with adequate sleep, good eating habit and normal urine volume. Her past medical history includes hypertension for more than 30 years treated with oral antihypertensive drugs with fair effect.

1.2 Physical examination

T 36.8 °C, P 82 beats/min, R 20 times/min, BP 140/95 mmHg. No cutaneous or sclera icterus was included. Conjunctiva was rosy. Double lung breath sounds resonance. Her abdomen is soft but painful(+) to palpation in the upper quadrant. Neither enlargement of liver, spleen and kid-

neys beneath the rib was found nor masses detected in the abdomen. Shifting dullness was positive, bowel sound was normal, without vessel murmur. There was no specialness in anorectal genitalia.

1.3 Auxiliary examination

Blood biochemical test: WBC $4.5 \times 10^9/L$, HGB 128 g/L, PLT $192 \times 10^9/L$. Blood gas analysis: pH 7.37, PCO₂ 24.0 mmHg, PO₂ 42.3 mmHg, HCO₃⁻ 16.3 mmol/L. Four infection index: HBsAg negative, HCV-IgG negative, HIV negative, Anti-TP negative. Liver function test: ALT 35 U/L, AST 78 U/L, TG 3.05 mmol/L; Serum ferritin: 368.5 g/L. Cardiac muscle enzyme: LDH: 308 U/L, CEA: 40 U/L. AFP, CA199, CA50, CA724 are normal. Routine: fecal occult blood positive (++++).

CT and B-ultrasound examination visualized a mass of 5 cm × 5 cm in size on the right lobe of the liver(the fifth segment). Colonoscopy examination revealed a mass of 2 cm in diameter with uneven surface (see Figure 1), covered with filth, soft touch of easily bleeding, and 12 cm away from the anus. Pathological report confirmed rectal differentiation adenocarcinoma (see Figure 2). Liver biopsy showed metastatic carcinoma of the liver (see Figure 3). Bone scan,

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chest X-ray, chest CT were normal.

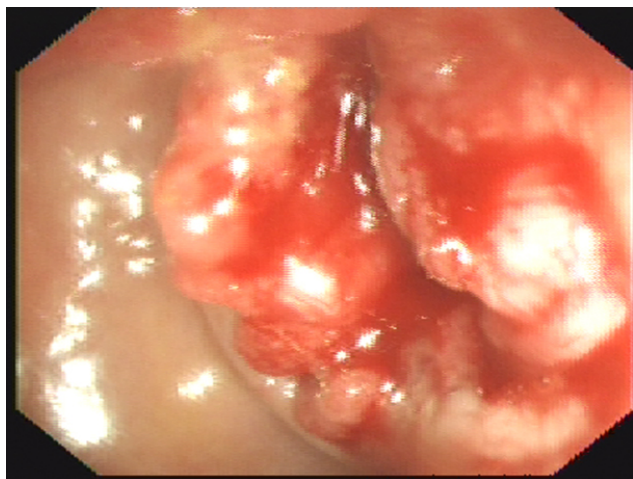


Figure 1: Coloscopy examination

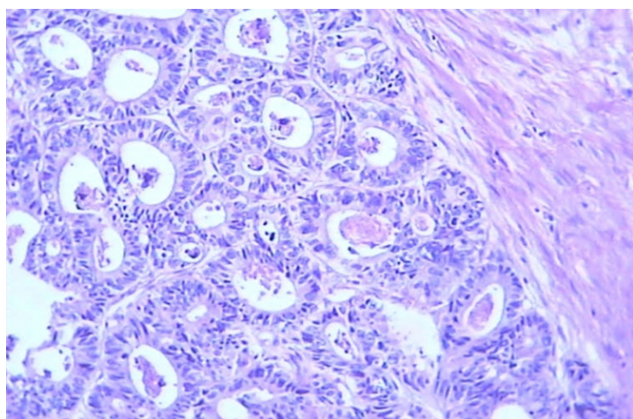


Figure 2: pathological section(×100)

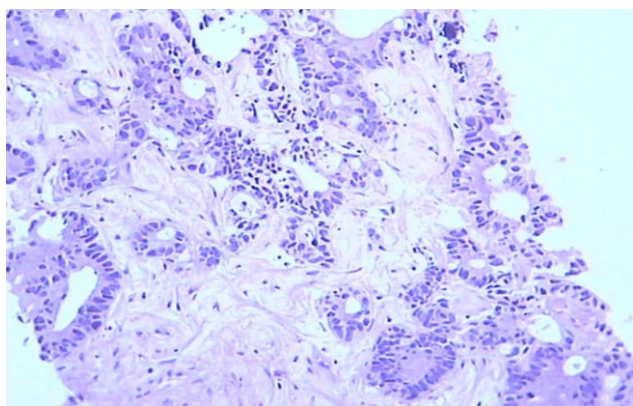


Figure 3: pathological section(×100)

1.4 Primary diagnosis

- (1) Differentiated adenocarcinoma of rectum
- (2) Liver metastatic adenocarcinoma.

1.5 Diagnosis and treatment

Hepatoprotective therapy plus neoadjuvant chemotherapy (FOLFOX regimen) was treated when the diagnosis was established after admission. Further surgical treatment remained to be determined on the basis of comprehensive assessment 3 weeks later.

2 Discussion

2.1 Dr. Shangdong Li

Dr. Shangdong Li is an attending surgeon in the Department of surgical oncology at the Third Affiliated Hospital of Inner Mongolia Medical University, specializing in standardized treatment of colorectal cancer and breast cancer.

Generally, rectal liver metastases refer to liver metastases in patients with rectal cancer, which was confirmed by preoperative imaging and pathological examination. All patients underwent preoperative assessment that included liver function tests, serum CEA, chest X-ray, abdominal ultrasound, endoscopy, endoscopic ultrasonography and CT. Rectal liver metastases (RLM) is one of the most deadly cancers worldwide. Liver, however, is the most common targeted site of metastasis from colorectal cancers. Close to 15%-20% patients have liver metastases either at the time of diagnosis or during the postoperative courses (25%-35%). In most of the patients (80%-90%), the liver metastases could not be radically resected. Liver metastasis is the leading cause of death in rectal cancer.^[1] Liver metastases from colorectal cancer carry a median survival of 6 to 9 months if left untreated and five-year survival rate is close to zero. While the median survival for patients undergoing complete surgical resection is 35 months, five-year survival rate is 30%-50%. How to make an effective treatment plan is directly associated with the prognosis and quality of life of patients. According to National comprehensive cancer network (NCCN), neoadjuvant therapy is advisable prior to the following scheme establishing.

In general, 1-year and 5-year survival rate of neoadjuvant chemotherapy are higher than those treated with surgery alone so that an obvious survival advantage and increased potential for radical resection of the treatment are noted. In addition, the application of new drugs may enhance the clinical efficacy of neoadjuvant chemotherapy for liver metastases from rectal cancer. Recent data have suggested^[2] that new molecular targeted agents and cytotoxic drugs in conjunction allowed long-term survival. The combination of VEGF inhibitor bevacizumab scheme can improve the objective response rate and prolong survival in the treatment of first and second-line therapies. Clinical trials of OPUS showed that the combined use of^[3] Cetuximab and FOLFOX4 could significantly improve the objective response

rate and resection rate. It has also been confirmed that Cetuximab has effect of increasing treatment efficiency and removal rate on colorectal liver metastases when combined with FOLFIRI chemotherapy, AIO/ irinotecan and topotecan and FOLFOX. The FIRST BEAT of ASCO meeting report and N016966 clinical trial data suggest that.^[4] Bevacizumab and chemotherapy in combination with first-line treatment of metastasis of colorectal cancer, and subsequent radical surgery can effectively reduce the occurrence of wound-healing complications with an interval of 28 days or more. The clinical application mode of neoadjuvant chemotherapy not only creates higher quality of surgical conditions but also lays a solid foundation for the long-term effect of adjuvant therapy. The second-line chemotherapy is required if patients resistant to chemotherapy, such as tumor markers are elevated and new lesions are suspected by MRI examination. Surgical resection, as the center of the comprehensive treatment, is the main method for the treatment of colorectal liver metastases. A reasonable treatment plan relies heavily on the actual situation of patients in order to improve his survival time.

2.2 Dr. Yong Zhang

Dr. Yong Zhang is the Associate Chief Physician in the Department of surgical oncology at the Third Affiliated Hospital of Inner Mongolia Medical University, specializing in diagnosis and treatment of elderly patients with low rectal cancer.

Rectal cancer is the third or fourth cancer worldwide with the incidence rising yearly. Liver metastasis is the major factor influencing the prognosis of the disease. Patients with liver metastasis usually have shorter survival time and poorer prognosis. If colorectal cancer is accompanied by isolated liver metastases, there is still a large chance of surgery. According to previous studies,^[5] experience with complete liver resection is associated with a 25% to 40% 5-year survival. Therefore, radical resection and postoperative adjuvant chemotherapy may potentially achieve a higher curative rate for the treatment of isolated liver metastases of rectal cancer as long as the conditions permit. Liver metastasis from rectal cancer does not mean curative opportunity loss. Currently, with the advances in diagnostic methods and new therapies, resectability rate and survival rate have increased obviously, and operative mortality rate decreased distinctly. Surgical resection of liver metastases is considered the most curative management. Nowadays, the widely accepted surgical indications for rectal liver metastases^[6] include: (1) complete resection of primary lesions; (2) the amount of liver remnant after resection should not be less than 30% (metachronous liver metastases) or 50% (synchronous resection of primary tumor of rectal carcinoma with simultaneous liver metastasis) of the total liver volume; (3) cardiac and pulmonary function and other general con-

ditions of the candidates enable the feasible treatment. No unresectable extrahepatic lesions were found. Relative contraindications include: an inadequate volume of liver remnant, incomplete resection of primary lesions, cardiac and pulmonary function and other general conditions of the candidates is inadmissible, the presence of extrahepatic metastases. Neoadjuvant chemotherapy is recommended prior to the operation in the light of the patient's advanced ages, physical condition and poor tolerance. Rectal cancer tumor lesions resection was carried out in the first place to expose the root of the inferior mesenteric artery or vein of the rectum, and cleaned the surrounding lymph nodes and ligation of the corresponding blood vessels. Dixon surgery or Miles surgery will be performed according to the specific circumstances.

Patients who had been primarily diagnosed eligible for surgical resection of liver metastases are treated with systemic chemotherapy or hepatic artery interventional therapy, among which oxaliplatin with 5-fluorouracil and CF are the foundations of the theory. The use of hepatic artery perfusion may exert a downsizing effect on the metastatic tumors, prolong the survival time of patients with liver metastasis, and improve the survival rate.

2.3 Dr. Zhichun Song

Dr. Zhichun Song is the Chief Physician in the Department of surgical oncology at the Third Affiliated Hospital of Inner Mongolia Medical University, specializing in diagnosis and surgical treatment of gastrointestinal tumor and liver tumor, especially the minimally invasive surgery for gastrointestinal cancer.

Surgical timing, modalities together with treatment methods are much related to the prognosis of patients with rectal liver metastases. We should correctly assess the patient's general state, choose the best timing of surgery and treatment options in order to improve the long-term survival rate of patients. Consensus has not been reached as to the timing of surgical resection of the hepatic secondaries and the primary colorectal tumor. Traditionally, these patients were managed by a second laparotomy 3-4 months after the resection of the primary tumors.^[7] Most researchers today support simultaneous resection in view of tumor diffusion and ineffective metastases. Namely, tumor cells from liver metastasis to other organs rarely grow so that simultaneous surgery is feasible during the time window to achieve the best outcome. In addition, simultaneous resections are referred when the amount of metastases is less than 3, metastatic lesions are confined to liver, and hepatic pedicle lymph nodes metastases are not involved. Negative margin, however, is an important means to increase the survival rate. Chemotherapy is not the curative therapy for colorectal liver metastases, and its curative functions are not comparable to liver metastases resection. So we should actively seek appropriate indi-

vidualized chemotherapy regimen, and strive to extend the survival period for unresectable patients.

We proposed to perform neoadjuvant chemotherapy prior to surgery resection in consideration of the patient's physical status in our case. Simultaneous resection was not recommended seeing that the patient would not tolerate the two-stage resections at the same time. The patient was firstly treated with resection of rectal lesions, and resection of metastatic lesion was then followed after 3-4 months. He received chemotherapy treatment during perioperative period, including hepatic artery ligation plus absolute ethanol injection or hepatic artery ligation plus chemical drug treatment and pump infusion chemotherapy to improve the patient's physical condition, to increase the success rate of the two phase of resection at the same time.

2.4 Dr. Liang Xi

Dr. Liang Xi is the Associate Chief Physician in the Department of surgical oncology at the Third Affiliated Hospital of Inner Mongolia Medical University, specializing in minimally invasive treatment of gastrointestinal tumors, diagnosis and treatment of thyroid, breast and pancreatic tumors.

There is a variety of treatment methods for rectal liver metastases management, including surgical treatment, interventional therapy (hepatic artery infusion chemotherapy, embolization, percutaneous ethanol injection, etc.), chemotherapy and so on. Among those, surgical treatment currently carries the best clinical effect.^[8] The 5-year survival rate for patients undergoing hepatic metastasis resection is 30%-50%.^[9] In fact, the use of embolization will be employed to downstage the tumor of larger volume, render a previously unresectable tumor resectable so as to make the second hepatectomy feasible. Repeat resection is acceptable when the patient's physical conditions are contented. The results of repeat curative resection are comparable to the first one.

In the 1990s, the standard treatment for colorectal liver metastases, both at home and abroad, is resection of primary colorectal lesions firstly, followed by the second-stage hepatectomy after chemotherapy for 3-4 months' duration. It is generally believed that the first-stage hepatectomy drags on time of operation so that extension of the incision or two incisions may be required.^[10] Intestinal surgery would potentially result in the increased risk of abdominal contamination and difficulties of postoperative recovery. In recent years, with the gradual improvement in perioperative management and surgical technique, most studies demonstrate that there is no significant difference between the first-stage surgery and the second-stage surgery regarding the issue of security. The surgical indications of the first-stage surgery include: resectable primary colorectal tumor lesions; small size, located in the peripheral or limited to half liver;^[11]

without the presence of liver hilar lymph nodes, abdominal or distant metastasis; physical tolerance to the surgery; technically proficient in liver resection. The patient is eligible to the first-stage surgery only if the following requirements are met: the radical resection can be guaranteed, the resection margin is negative, the enough residual liver to compensate, and the extrahepatic metastases can be removed simultaneously. The second-stage surgery is feasible when the patient could not tolerate the first-stage surgery and the primary lesions could not be eradicated completely. Surgical resection of the primary tumor and metastases could be carried out simultaneously only if the following requirements are met: liver metastatic lesions are solitary or confined without the occurrence of extrahepatic metastasis, or no metastases are found in diaphragm or portal vein adjacent organs, hepatic resection volume is less than 50%, and the patient has good tolerance. For patients who do not meet the above requirements, the first resection of primary lesion of rectal cancer is required, followed by the removal of metastatic lesions after a few months. Chemotherapy, including the use of hepatic artery ligation plus absolute ethanol injection or hepatic artery ligation plus chemotherapy, should be given during the operation.

Systemic chemotherapy is a palliative treatment method of metastatic liver tumors, aiming to control tumor growth, prolong survival time and alleviate the symptoms of patients. In systemic chemotherapy for rectal cancer, 5-FU remains the top choice and its efficiency is 30% when combined with CF. In the past, it was usually combined with other chemotherapeutic agents,^[12] but no better outcome was achieved. In recent years, along with the development of chemotherapeutic agents, and the enhanced effect of intravenous chemotherapy on hepatic metastatic lesions, oxaliplatin combined with fluorouracil and leucovorin has been gradually regarded as the first choice drug of liver metastasis from rectal cancer. Liver metastasis from rectal cancer, the main challenging during clinical treatment, is an important factor that affects the survival of patients with rectal cancer. Non-surgical treatment (including interventional therapy and systemic chemotherapy) alone doesn't impose any great effect on reducing recurrence and metastases in other parts and prolonging the survival time for patients. In addition, the high recurrence rate of liver metastasis after surgery restricts the long-term curative effect of colorectal cancer. In addition to incomplete resection of primary tumor lesions that contributes to recurrence, the presence of micro metastasis caused by a variety of reasons could not be denied. Though surgery is the main treatment method, postoperative comprehensive treatment measures are still essential. On the one hand, raise the accuracy of preoperative diagnosis and resection rate. On the other hand, comprehensive treatment of surgery should be combined with chemotherapy and intervention in order to improve the prognosis and prolong the survival time of patients.

In view of the advanced age and general condition of the

patient in our case, the second-stage surgery was recommended. However, the second-stage surgery not only increases hospitalization expenses and patient's psychological pressure but also lengthens the cumulative duration of hospitalization due to the increased difficulties of second laparotomy. According to the location, size, number and distribution of metastasis, liver metastasis resection was performed in patients through irregular/regular liver lobectomy or segmentectomy. Irregular liver segmentectomy may leave more liver parenchyma, while it enhances the possibilities of postoperative bleeding and effusion. Regular resection ensures the complete removal of the lesions with clear margin. However, the incidence of postoperative liver failure is higher if more liver parenchyma^[13] is resected so that less surgical opportunity is left for patients with reoccurrence of liver metastasis.^[14] In that case, regular liver segmentectomy is recommended if the patient's physical condition permits. During the surgery, low dose of 5-FU continuous infusion by portal vein intubation into the liver will eradicate the tumor cells with lower systemic side effects, improving the safety of medication.

3 Conclusions

In conclusion, liver metastases are the main cause of death for patients with rectal cancer. Usually, the occurrence of liver metastases leads to poor prognosis so that an effective treatment for liver metastasis of rectal cancer is particularly important. Comprehensive treatment, mainly on the basis of surgery, is a more effective method for treatment of the disease. First neoadjuvant chemotherapy is recommended prior to rectal cancer resection of the primary tumors for patients with poor tolerance.^[15] Whether to combine organ resection or the resection of primary tumor plus metastatic lesions depends on the specific conditions of the patients. Appropriate treatment not only prolongs the survival rate but also improves the quality of life of patients.

Conflicts of Interest Disclosure

The authors have no conflict of interest related to this article.

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