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Iterative Multimodal Approach in the Treatment of Abdominal Stromal Tumors

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Abstract

We report two cases of abdominal stromal tumors with prolonged survival after mixed management or multimodal approach combining radical iterative surgery, intraperitoneal chemotherapy and targeted therapy (Imatinib). These two observations illustrate the current possibility of long-term control of abdominal stromal tumors when there are locally advanced and/or metastatic.

Keywords

Abdominal stromal tumors; Immediate intraperitoneal chemotherapy; Targeted therapy; Radical surgery; Multimodal approach; Peritoneal carcinomatosis

Introduction

Abdominal stromal tumors have been individualized using immune staining in the past years. Their treatment is essentially surgical. The placing on the market of targeted therapy (Imatinib) has added another therapeutic possibility in front of these tumors [1]. On the other hand, systemic chemotherapy

has no convincing results with this type of tumor in terms of five year survival [2]. When these diseases are disseminated in the peritoneal cavity and in the image of other histological types, the prognosis remains very reserved. Optimal reduction surgery combined with intraperitoneal chemotherapy associated with targeted therapy is the solution that we have used in two patients whose observations were reported here.

Case 1

This is a 53-year-old patient operated in emergency for a jejunal tumor (second jejunal loop) in occlusion and who benefited from a resection followed by an immediate restoration of the digestive continuity. His postoperative course was unventful. After three months, peritoneal recurrence occured and the patient has been referred to our surgical unit. On admission, the patient was in good general condition, with no palpable mass and with normal rectal examination. The usual biological examinations (blood count, blood sugar, creatinine and urea, prothrombin level, blood ionogram, alkaline phosphatases, transaminases) were also normal. The electrocardiogram and echocardiography were free of abnormalities. Computed tomography showed the existence of tumor masses of 4 to 5cm at the level of the jejunal handles. These last tumors took the contrast agent. The chest x-ray was also without abnormalities. The histological diagnosis of the first intervention was in favor of a leiomyosarcoma. Given the patient's good general condition and the absence of co-morbidities, weopted for an exploratory laparotomy. The intraoperative exploration showed the existence of a peritoneal carcinosis with centimetric lesions at the level of 2 small handles, the descending colon, the high rectum as well as the bladder. The peritoneal carcinomatosis index (PCI) was estimated at 8 points. This observation prompted us to perform the extirpation of all lesions by a colonic resection extended to the jejunum associated with a partial rectal excision and finally a rhombic vesical resection located at the level of the dome. We performed a colo-colic, jejuno-jejunal anastomosis, and rectal and bladder sutures. We ended the operation with the installation of 4 drains for early intraperitoneal postoperative chemotherapy (EPIC). The latter consisted in the creation of a 2-liter ascites mixed with 8mg of Doxorubicin. It was performed from the first to the 5th postoperative day. The operations were simple and the patient was discharged after 15 days. The histological reading of the operating pieces showed positivity on CD 34 and CD 117, there by signifying the stromal nature of the tumor. This patient had completely correct clinical and morphological follow-up (CT scans) up to 114 months. The CT scan reveals the existence of a single supra-vesical tumor without other distant tumor locations. The remote extension report did not show any other location and the decision was made for a new laparotomy. In intraoperative, the exploration finds the described tumor making approximately 4 centimeters and several other millimeter lesions on the level of the small intestine and the stomach. The PCI, was estimated at 8 points and excision possible. The latter is carried out completely (CCO resection) and immediate intraperitoneal chemotherapy based on Adriamycine instituted at the end of the intervention. It lasted 3 days. The operating suites were simple and the patient was discharged after 8 days. He is currently on Imatinib. His general condition is excellent. The overall decline in this patient since the first surgery is 144 months.

Case 2

It is a 63-year-old woman admitted to the department for an exploratory laparotomy for bilateral

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ovarian tumor diagnosed on ultrasound and computed tomography. These examinations were carried out following the appearance of abdominal pain not specific. At the entrance, the physical examination found 2 abdominal masses, firm and painless, without associated ascites. The pelvic feel was normal. The usual biological examinations (blood count, blood sugar, creatinine and urea, prothrombin level, alkaline phosphatases, transaminases) were without significant abnormalities. The electrocardiogram and echocardiography were not specific. Carbohydrate antigen 125 (CA125) was 45IU / ml. Abdominal ultrasound showed the existence of large intraperitoneal masses 6 to 8 cm in diameter, which were confirmed by computed tomography. These masses were tissue-like and took on contrast. The chest x-ray was without features. The patient was operated on with the diagnosis of ovarian cancer and the goal of the intervention was an exploratory intervention with possibly a gesture of excision if it was immediately possible. The intraoperative exploration showed the existence of at least 7 tumor masses sitting on the small intestine and each making at least 5cm. The two ovaries were healthy and so was the rest of the peritoneal cavity. The PCI was estimated at 12 points. An extemporaneous examination was in favor of a sarcomatous tumor. Given the extent of the lesions, we preferred to carry out seven resections-anastomoses with restoration of digestive continuity instead of an extensive resection of the small intestine. EPIC was carried out on the patient after the placement of two liters of SSI associated with 8mg of Doxorubicin, from the first to the 5th postoperative day. The follow-up to the intervention was simple and the patient left the ward on the 14th postoperative day. At twelve months postoperative, the patient presented a palpable tumor recurrence in the firm left sub-costal area that was not painful. It measured at least 10cm in diameter. Computed tomography showed the presence of this tumor next to the stomach and spleen. The rest of the peritoneal cavity was without abnormalities. The diagnosis of tumor recurrence was made and the patient started on targeted therapy (Imatinib) at the rate of 4 tablets per day. After three months, the mass disappeared both clinically and on the CT scan. Imatinib treatment lasted two years and then stopped. At the 60th postoperative month, a new intraperitoneal recurrence was noted clinically and on computed tomography. A new surgery has been decided. The operative exploration found massive peritoneal carcinosis and PCI was estimated at least 22 points. It was decided and performed partial reduction surgery with removal of the uterus, the 2 appendices and several peritoneal nodules. Several very difficult to resect nodules were left in place at the diaphragm. EPIC based on Doxorubicin has been instituted. The aftermath was marked by abdominal pain. The patient is currently on targeted therapy (Imatinib) again. It is alive and asymptomatic at 125 months after the first intervention (Figire1-3).

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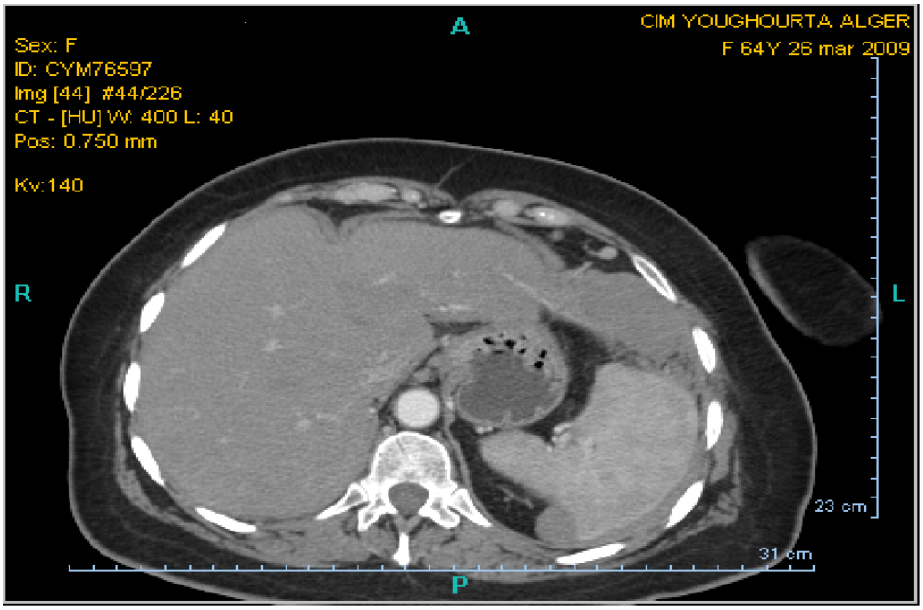

Figure 1: CT SCAN. Left hypochondrium with minimal lesion left in place.Two months postoperative (Case 2).

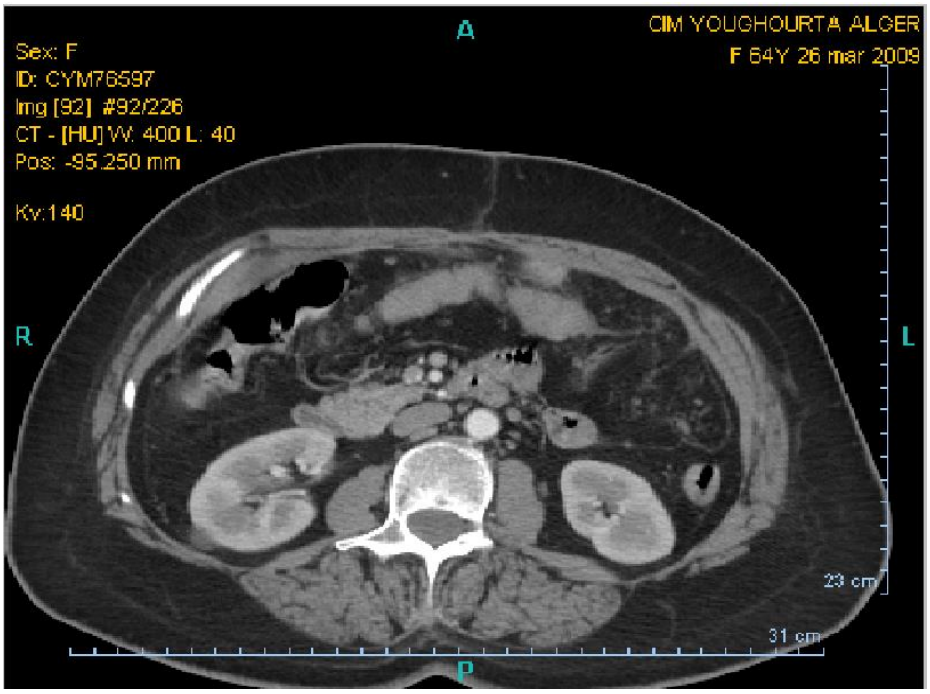

Figure 2: CT SCAN. Sub-mesocolic floor. Absence of lesion at 2 months postoperative (Case 2).

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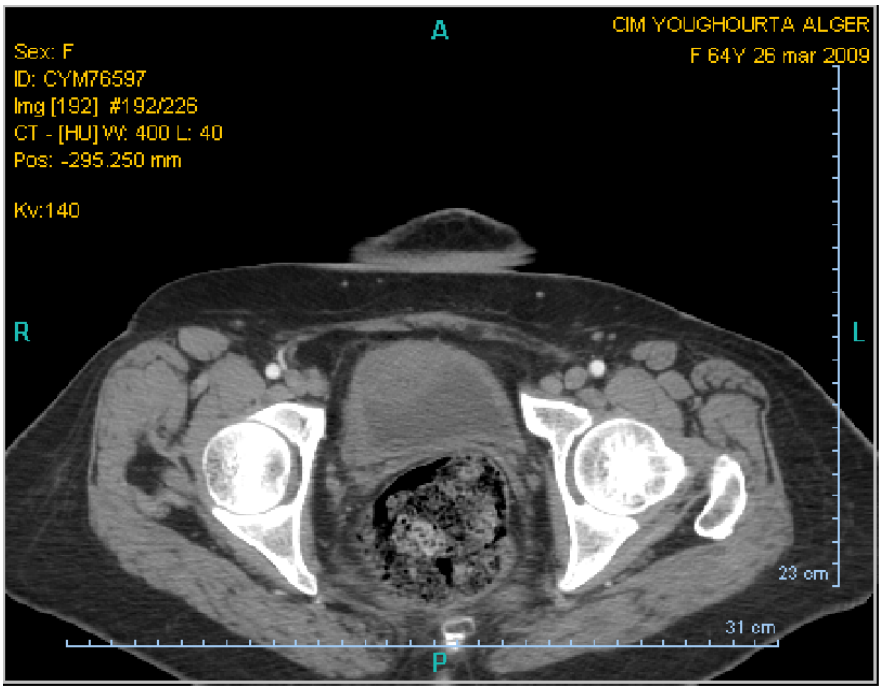

Figure 3: CT SCAN: Pelvic computed tomography. Absence of lesions at 2 months postoperative (Case 2).

Comments

Locally advanced and/or metastatic abdominal stromal tumors are classically non-chemo sensitive and not surgically curable. But, since the advent of targeted therapy (Imatinib) it's management has been transformed [1,2]. Our two cases probably illustrate another therapeutic possibility for advanced forms. We think that the peritoneal localization of the abdominal stromal tumors in the form of diffuse carcinomatos is can be taken care of like the other histological types namely a surgery of maximum eradication associated with an intraperitoneal chemotherapy as hyperthermic intraperioneal chemotherapy (HIPEC) or EPIC. This latter form of therapy has been shown to be effective in the management of pseudomyxoma [3], mesothelioma [4] and colorectal carcinomatos is [5,6]. Baratti et al [7] reported a series of 37 patients with tumors of various origin (retroperitoneal sarcoma, uterine sarcoma and other sarcomas) including 8 stromal tumors, treated by cytoreduction surgery associated with intraperitoneal chemo-hyperthermia (Adriamycin, Cisplatin and mitomycin). The authors considered the results interesting only for uterine sarcomas while the other etiologies and in particular tumors stromal, the survival results were considered disappointing. For our two observations, we thinck that the association of therapeutic arms have a great importance for the disease control than surgery or intraperitoneal chemotherapy or targeter therapy used alone. That was, what happened with the patient of case 1 in whom the surgery was unable to control a pathology in recurrence 6 months after the first intervention carried out in emergency. For the second observation, the control of peritoneal disease was controled with association of surgery and EPIC for two years. Putting the patient on targeted therapy (Imatinib) was able to control the peritoneal recurrence for more than 3 years. For this patient, it is this argument of long-term control (chronicity) by mixed therapy that prompted us to re-intervene in the 68th month postoperative on recurrence. The second reintervention in the first patient

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for a second recurrence with complete resection associated with EPIC and his entry into targeted therapy (Imatinib) as an adjuvant, is part of the same reasoning for multimodal management. It seems to us that mixed management of this type of tumor is a real possibility that must be exploited in the future. It is perfectly conceivable that intraperitoneal chemotherapy is effective in the face of peritoneal dissemination of this disease.

Conclusion

Our two observations probably illustrate the possibility of mixed management or multimodal therapy of locally advanced and/or metastatic abdominal stromal tumors especially peritoneal carcinomatosis. However, that remains insufficient to be able to draw solid scientific conclusions. Longer follow-up and other similar cases will provide arguments for this approach which associates iterative surgery and medical therapies in neo adjuvant or adjuvant way and by intraperitonal or systemic road.

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