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Case Report

Anthracycline-Based Combination Chemotherapy (Doxorubicin and Dacarbazine) For the Desmoid Tumor in a Neoadjuvant Setting. Report of a Case

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Summary

We report a case of a 41-year-old female with a sporadic abdominal wall desmoid tumor. After a period of 12-month observation, chemotherapy was given with Doxorubicin and Dacarbazine to facilitate minimal surgery. The patient received 4 cycles of chemotherapy. Treatment was well tolerated and resulted in a significant reduction of the tumor size from 48mm to 25mm, 48% reduction. The tumor was surgically resected, and the histopathology from the resected specimen revealed a partial pathological response. At 6 months post-surgery, there is no recurrence or surgical complications.

Background

Desmoid tumors are rare and benign. They are locally aggressive, and even after complete resection, the recurrence rate is high. Surgical resections often lead to morbidity and cosmetic complications. The non-surgical or minimally invasive approach is more attractive to patients, mainly due to the high recurrence rate. Data for neoadjuvant treatment for desmoid tumors is limited (Desmoid tumor, a novel approach for local control, journal of surgical oncology 2002). We used Anthracycline based combination chemotherapy to downsize the tumor for minimal surgical procedure.

Case Presentation

A 41-year-old female felt a lump on the left side of the abdomen without local or systemic symptoms. It was a sporadic presentation with no family history of Familial adenomatous polyposis (FAP) or other malignancy. She did not have any significant past medical history and was breastfeeding her 1-year-old son at the time of diagnosis.

Examination revealed a 3cm discrete soft mass in the periumbilical area, adherent to the underlying structure. It was non-mobile and non-tender. Initial blood work was within normal limits. Ultrasound of the abdomen showed 26mmx16mmx13mm mass in rectus abdominis muscle. MRI revealed well-defined heterogeneous enhancing ellipsoid mass within the rectus abdominis muscle measuring 39mmx18mmx11mm. Fibromuscular soft tissue with a spindle cell lesion revealed on the core biopsy. Immunohistochemistry was positive for beta-catenin (predominantly nuclear). Desmin, Bcl2, and actin showed nonspecific weak positivity. Overall features were compatible with desmoid fibromatosis.

After confirmation of diagnosis, first-line treatment, i.e., surgical resection, was discussed, but she opted for a wait and watched approach as she was breastfeeding. We continued to observe until it increased to size 48mmx40mmx14mm at 12 months after the initial diagnosis. The patient wanted to have non-surgical treatment due to the notorious potential of recurrence and stress of relatively more extensive surgery. We chose chemotherapy to reduce or potentially treat the tumor and facilitate a relatively minor surgical procedure. We used Doxorubicin 60mg/m2 and Dacarbazine 1000mg/m2 and gave four treatment cycles.

Treatment was well-tolerated, and the patient did not report any significant side effects. MRI post-treatment showed a significant tumor size reduction to 25mmx40mm (initial size of 48mm, 48% reduction). The patient underwent surgical resection of the tumor after four weeks of chemotherapy. Histopathology of the resected specimen revealed a similar morphological appearance; however, the size was significantly reduced to 18mm.

Outcome and Follow-up

After 6 months of surgery, she remains asymptomatic with no signs of recurrence or surgical complications.

Discussion

Desmoid tumors can have unpredictable clinical courses. Observation or Local therapy with surgery/radiotherapy is the preferred treatment for localized asymptomatic tumors, especially those who are not intra-abdominal or associated with FAP. Systemic therapy is generally considered for patients with unresectable tumors, large symptomatic tumors, or rapidly progressively desmoid tumors. Given toxicity profile, it is not recommended as first line therapy. The concept of Neoadjuvant chemotherapy to reduce tumor bulk before an attempt at surgical resection is relatively new, and minimal data available for this approach. The multimodality treatment approach to avoid surgical morbidity is getting the attention of oncologists worldwide, mainly because of the demonstration that several chemotherapy regimens are active in the setting of advanced or unresectable disease.

There are no evidence-based or consensus-based guidelines regarding the appropriate choice of agent for systemic therapy, and there are few randomized trials to aid in the decision-making process. Systemic therapy options are limited and include cytotoxic chemotherapy and non-cytotoxic therapies such as tyrosine kinase inhibitors (TKI), hormonal treatment (Tamoxifen), and non-steroidal anti-inflammatories (NSAIDs). No Randomized trial for Tamoxifen and NSAIDs to establish their efficacy in treating the desmoid tumor. TKIs (Sunitinib and Pazopanib) has efficacy in the unresectable progressive or symptomatic desmoid tumor [1,2].

There is no standard chemotherapy for systemic treatment. Patel *et al*. reported 2 complete responses (CR), 4 partial responses (PR) & 2 Stable disease (SD) with 60-90mg/m2 Doxorubicin and 750-1000 mg/m2 Dacarbazine with a median follow up 28-235 months in a study of 12 patients [3]. Similarly, Gega *et al*. showed 3 CR & 4 PR in a study involving 7 patients with fractionated Doxorubicin 20 mg/m2 D1-D4 & dacarbazine 150 mg D1-D4 every 28 days [4]. Cytotoxic chemotherapy is associated with good response rates in various studies [Table 1]. Non-Doxorubicin-containing chemotherapy regimens include Methotrexate with Vinblastine [5] or Methotrexate with Vinorelbine [6]. Anthracycline monotherapy with Doxorubicin and pegylated liposomal Doxorubicin are other options. Doxorubicin-containing chemotherapy combinations have a higher response rate than non-anthracycline-based chemotherapy against desmoid tumors. The other regimens did not have any complete response or long-term follow-up data. Hence this regimen was chosen.

Table 1

Regimen	Number of patients	Duration of therapy (cycles)	Response	Duration of response	Author; year
Doxorubicin plus Dacarbazine	11	2 to 10 (median 5)	2 CR 4 PR 1 MR 2 SD	29 to 235 months	Patel; 1993
Doxorubicin plus Dacarbazine	5	4 to 6 (Median 5)	2 pCR 3 PR	21 to 72 months	Geopfert; 1982
Doxorubicin plus Dacarbazine plus Meloxicam	7	4 to 5 (median 5)	3 CR 4 PR	32.5 to 107.5 (median 74)	Gega; 2006
Doxorubicin plus Dacarbazine (7 cycles followed by Carboplatin and Dacarbazine	5	6 to 19	1 CR 3 PR 1 SD	10 to 30 months	Schnitzler; 1997

CR=Complete response, PR=Partial response, pCR=Pathological complete response, SD=Stable disease, MR=Minor response

We used chemotherapy as a neoadjuvant approach to downsize tumor for minimally invasive surgery. Partial response was observed significant enough for surgical resection with minimal post-surgical sequelae.

Conclusions

Desmoid tumors are rare and have a high recurrence rate. The multimodality treatment approach can minimize the surgical requirement with a better and prolonged response. Neoadjuvant chemotherapy is a suitable option for resectable desmoid tumors. Doxorubicin and dacarbazine combination is effective in this setting with minimal side effects. Prospective randomized controlled studies are required in this area to establish efficacy.

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