Recurrent Unresectable Aggressive Fibromatosis of Neck

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Abstract

Aggressive fibromatosis or desmoid tumors are classified as low grade, locally aggressive sarcomas with high propensity to recur and are lacking a clear census on management of recurrent-surgically in excisable tumors. We report here the case of a 27yrs old male with aggressive fibromatosis that recurred following a surgical excision, and resulted in hampering the quality of life. The disease was managed using cytotoxic chemotherapy with doxorubicin, resulting in significant clinical and radiological response. It was followed by maintenance regimen using a less aggressive approach with non-steroidal anti-inflammatory drugs such as celecoxib that resulted in further clinical response at 2 months follow up. Therefore, the therapy was further continued.

Keywords: *Fibromatosis, recurrent, chemotherapy, nsaids.*

INTRODUCTION

Aggressive fibromatosis, also referred to as desmoid tumors, are mesenchymal neoplasms, frequently considered to be locally malignant but non-metastasizing tumors. The location and presentation of desmoids is variable, from abdominal wall, to intra-abdominal mesenteric masses, and to large extremity masses, which are generally seen in older patients of both genders. Mutations in the CTNNB1 gene encoding the β-catenin pathway have been identified in sporadic desmoid tumors, although the correlation of CTNNB1 mutation status with the clinical outcome remains uncertain [1-5]. The primary treatment for patients with resectable desmoid tumors is surgery [6-10]. With tumor lo-cation, size, patients' age, and margin status been identified as factors associated with recurrence following resection and Extra-abdominal tumors having a higher risk of recurrence than abdominal tumors.

CASE PRESENTATION

27 years old male patient presented in Oncology Outpatient Department with complains of recurrent right neck mass along with numbness and difficulty in griping & holding in right hand over the last 2 months.

On examination there was a firm, non-tender mass just posterior to trachea up to anterior aspect of trapezius and inferiorly it was extending up to supraclavicular fossa on the right side. The ipsilateral winging of scapula and claw hand was appreciable on examination.

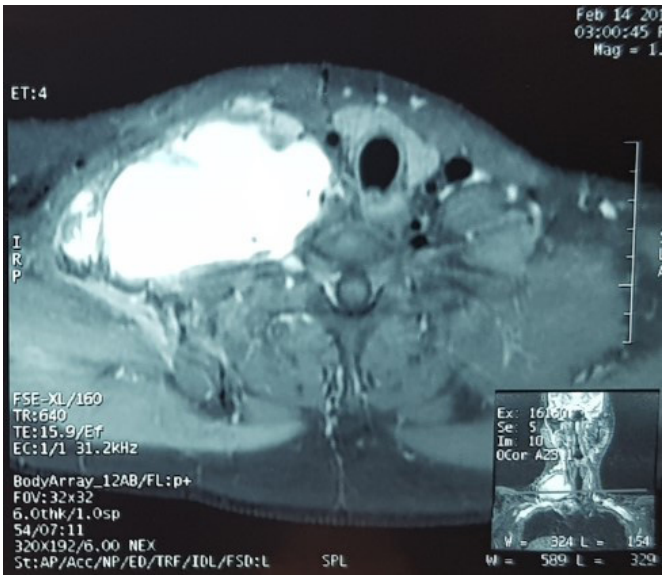
PAST HISTORY

Patient reported history of similar complains at ipsilateral site when he presented at an other health care set up a year ago, where the imaging followed by resection of tumor was done, up to 95% tumor was excised and biopsied, and morphologically composed of spindle shaped cells with immunohistochemistry markers staining with beta-catenin, thus diagnosis of fibromatosis was made and the patient was advised a close follow up and surveillance, due to benign nature of disease.

The patient remained well for about 8 months and then due to recurrence of symptoms, he consulted thoracic surgery department from where the patient was referred in our clinic for opinion.

RADIOLOGICAL DETAILS

On presentation, the patient's MRI neck study with contrast was requested reveling the redemonstrations of abnormal signal intensity mass measuring about 13x6.8x 10cm in the right lower neck with extension into right hemithorax, with lobulated margins (**Figs. 1A&1B**).



A

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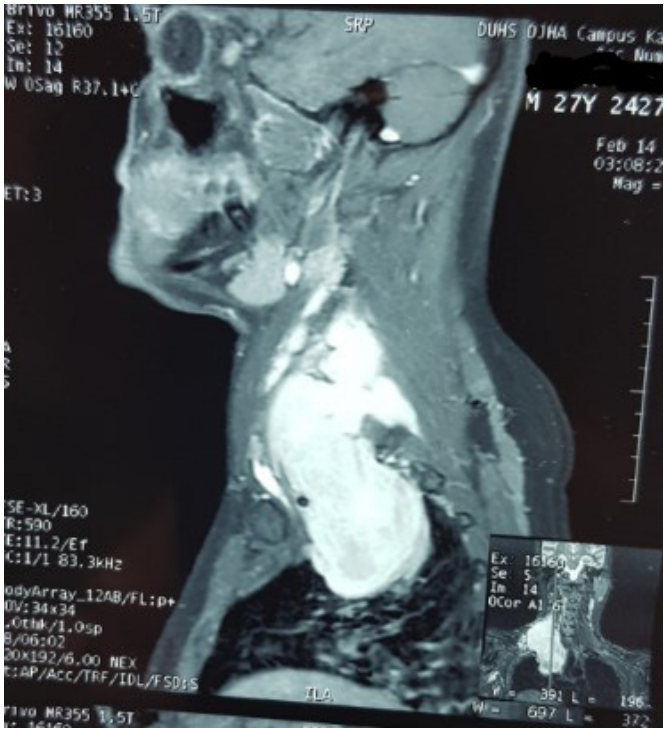

B

Fig. (1): (A) Axial & **(B)** sagittal images of MRI showing tumor at the time of relapse after surgery. Abnormal signal intensity mass in the right side of neck, extending into right hemithorax.

The imaging showed marked disease progression as compared to previous (Post excision) imaging.

HISTOPATHOLOGY

Since complete surgical resection was not possible therefore, a repeat image guided biopsy of neck mass was done.

Morphologically the sections showed linear core of spindle cell lesion composed of large sweeping (A) of bland spindle shaped cells against collagenous background stroma. The cells contained indistinct cellular outlines, moderate eosinophilic cytoplasm. There was no convincing evidence of malignancy.

Immunohistochemical stains were performed and stained positive for Desmin, & Beta Catenin, thus concurring with the diagnosis of fibromatosis.

TREATMENT COURSE

Due to aggressive and unresectable nature of disease and symptoms impacting the quality of life, the decision of starting chemotherapy was made by the multidisciplinary tumor board.

The chemotherapy with liposomal doxorubicin was initiated at dose of 50mg/m2 every 28 days and continued for 4 cycles followed by a repeat scan that showed significant disease reduction. However, the mass was still abutting the carotid vessels and surgical excision was not possible. Therefore, the decision to continue chemotherapy was made.

Thus, the patient received 6 cycles of chemotherapy (total cumulative doxorubicin dose 300mg/m2). The follow up scan was done and showed further disease reduction (**Fig. 2**). There was also significant subjective as well as clinical improvement in motor strength and hand gripping. However, a surgery with R0 resection margin was still not achievable from surgeon's perspective. The case was therefore taken to a multidisciplinary meeting for discussion.

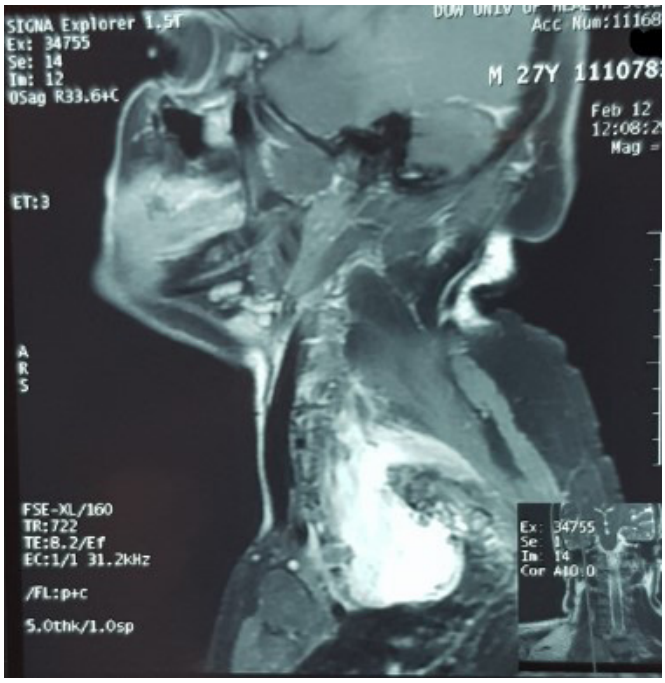

Fig. (2): MRI sagittal image of the patient after chemotherapy showing abnormal signal enhancing mass at right thoracic inlet traversing through root of neck, with radiological evidence of disease reduction, now measuring 8.4 cm in craniocaudal extent (previously: 14.7cm, refer **Fig. (1A&1B)**.

TUMOR BOARD DISCUSSION

In the multidisciplinary meeting, involving departments of General, Thoracic and Plastic surgery, Diagnostic and interventional radiology, Medical as well as Radiation Oncology, discussion was held on this case and due to marked improvement in quality of life, it was planned to consider maintenance treatment using non-cytotoxic agents while keeping options such as radiation as well as chemotherapy saved for progressive disease. In this regard several therapeutic options were considered, treatment recommendations reviewed, and the decision to initiate treatment, using COX 2 inhibitor, was made. The patient was kept on tab. Celecoxib at 200mg divided into twice daily dose after explaining the possible benefit and potential side effects for 3 months followed by reevaluation.

Upon follow up consultation *via* telemedicine service, beyond 2 months therapy, the patient reported remarkable clinical response, had resumed his job, and there was near complete restoration of his baseline pre disease life activities. Thus, the patient was advised to continue the treatment further and visit clinic in 1 month.

ONCOLOGIST'S PERSPECTIVE

Desmoid tumors or aggressive fibromatosis often present difficult challenge for patients because of the extent of surgery required for optimal control, their high recurrence rate, and their long natural history. Although they do not exhibit the histopathologic features to classify them as sarcomas, desmoid tumors are often categorized as low-grade sarcomas because of their high tendency to recur locally after excision. The primary treatment for patients with resectable desmoid tumors is surgery [6-10]. The extremity tumors, as we report, have relatively lower response and disease-free survival when compared to patients with abdominal wall tumors, with 10-year DFS rates 88% *vs* 62%, respectively (P < .01) [11, 12]. The impact on local control and risk of recurrence, due to positive resection, remains controversial [13]. Recent meta-analysis including data from 1295 patients, from 16 studies, found that R1 resections were associated with an almost 2-fold higher risk of recurrence [14].

Treatment choices for symptomatic patients with large tumors that cause morbidity, pain, or functional limitation, should be based on the location of the tumor and potential morbidity of the treatment. Options include surgery and/or RT and/or systemic therapy. The consensus upon optimal chemotherapy regimen for such low-grade tumors has not yet been clearly defined. However, in patients with definitely progressing tumors, the decision about systemic treatment should be individualized in a multidisciplinary setting. The options for systemic therapy such as cytotoxic chemotherapy drugs, hormonal or biological agents, or non-steroidal anti-inflammatory drugs (NSAIDs), have shown promising results in patients with desmoid tumors [15, 16]. Doxorubicin-based chemotherapy has been effective in patients with recurrent or unresectable tumors [17-19]. The combination regimens of methotrexate with either vinorelbine or vinblastine has also been shown to be associated with prolonged stable disease in case of unresectable or recurrent tumors [20, 21].

The current guidelines have included NSAIDs (sulindac or celecoxib) as systemic therapy options for patients with advanced or unresectable desmoid tumors. Other NSAIDS such as meloxicam has also been tried and demonstrated efficacy [22]. The effectiveness of celecoxib has been proven in cases involving the use of genetic testing [23]. As well as in intra-abdominal desmoid tumors where the disease response using celecoxib after surgical resection, was demonstrable up till 2-year follow up period [24].

Considering the young age and active life style of the patient, the rationale behind using an approach of maintenance treatment was to provide maximum possible response while keeping treatment related toxicities to a minimum, and saving more invasive options such as further cytotoxic chemotherapy or radiation for future, until maximum response is achieved and clear guidelines or a more novel approach becomes available and well suited.

SURGEON'S PERSPECTIVE

Surgery can offer complete cure from localized disease. Surgery with tumor free margin (approx. 3cm) is required.

Therefore, in large fibrous tumor excision, this may result in loss of limbs and / or debilitating post-surgical deformity. All of this is tolerable if we can reasonably assure eradication of localized disease.

Frequently surgery is performed, as in this case with inadequate resection margins resulting in local recurrence of tumor. After incomplete resection and subsequent recurrence of tumor, it is rarely possible to do a Redo surgery with adequate resection margins.

However, in this case, though the disease was advanced, there was a chance to get a complete resection but this would have involved loss of upper limb. This was not acceptable to the patient; therefore, surgery was declined by the patient [25].

In such cases, if Oncology achieves regression of tumor then we can reassess for surgical resection.

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