MRI FEATURES PREDICTIVE OF RESPONSE TO METHOTREXATE AND VINORELBINE IN DESMOID FIBROMATOSIS

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INTRODUCTION

- Desmoid fibromatosis (DF) is a mesenchymal tumor that is locally aggressive and historically treated with surgical resection, with high recurrence rates[1]
- Systemic treatment of progressive DF can be associated with improved progression-free rates; however, the use of medical therapy remains controversial
- Treatment response as defined by RECIST by measuring maximum tumor dimension (D_{max}) may not accurately evaluate response to medical treatment in desmoid patients
- Recent studies suggests alternatives to RECIST criteria[2]
- The current study sought to assess if imaging parameters such as approximate tumor volume (V_{tumor}) and MRI features, specifically T2 signal, were more predictive of response to medical therapy than D_{max}

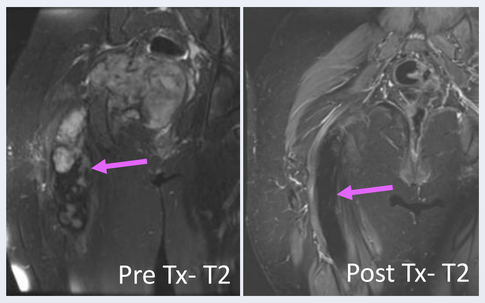

Figure 1: T2-fat-saturated coronal MR images of DF pre- and post- treatment

METHODS

- Using our Sarcoma Database, 22 patients with biopsy proven DF as per WHO Classification[3] who were treated with Methotrexate and Vinorelbine (MTX/VIN) and followed with MRI throughout treatment were identified
- D_{max}, V_{tumor} and quantitative T2 hyperintensity using interquartile range scoring on MRI were compared pre-, mid- (between 3-9 months) and post-treatment
- On T2-weighted or T2-weighted fat-saturated MRI images, tumors were ranked as containing: 0-25%, 25-50%, 50-75% or 75-100% of internal high T2-signal intensity
- V_{tumor} was approximated using an elliptical volume equation ($V=\pi/6*L*W*H$)
- Treatment response was defined as:

Partial Response (PR) - size or T2 quartile score decreased

Stable Disease (SD) - no change in size or T2 quartile

Progression of Disease (PD) - increase in size or T2 quartile

Complete Response (CR) – tumor resolution and/or entire lesion was hypointense on T2-weighted images.

RESULTS

Patient Population

	Number (%)
Gender	
Male	5 (23)
Female	17 (77)
Median Age [range]	31 [14-63]
Presentation	
Primary	18(82)
Recurrent/Residual	4 (18)
Tumor Site	
Extremity	9(41)
Abdominal wall	7(32)
Head and Neck	3(13)
Chest wall/back	2(9)
Mesentery	1(5)

Treatment

	Number (%)
MTX/VIN regimen	
Day 1, 8, q21	2 (9)
Day 1, 8, 15, q28	20 (91)
NSAIDS tried before chemo	
Yes	2 (9)
No	20 (91)
Tamoxifen tried before chemo	
Yes	9 (41)
No	13 (59)
Previous Surgery	
Yes	4(18)
No	18(82)

- Patients were given 25mg/m^2 each of MTX/VIN
- Median months on treatment was 20 (range 9-27)
- Good clinical response (n=13), full therapy of 24 months reached (n=6), and patient preference (n=3) were reasons for stopping therapy

RESULTS

D_{max} and V_{tumor}:

- At end of treatment (median 20 mos (range 9-27)), D_{max} mean decreased by -30% and V_{tumor} decreased by -76%
- 50% of patients (n=11) had SD as per D_{max} but were PR as per V_{tumor} %change (-76%, range -86 to-30)
- In those 11 patients, T2 showed CR in 6 patients and PR in 5 patients.
- In figure 2, pre-tx D_{max} did not show a response to treatment whereas V_{tumor} decreased as did T2 intensity.

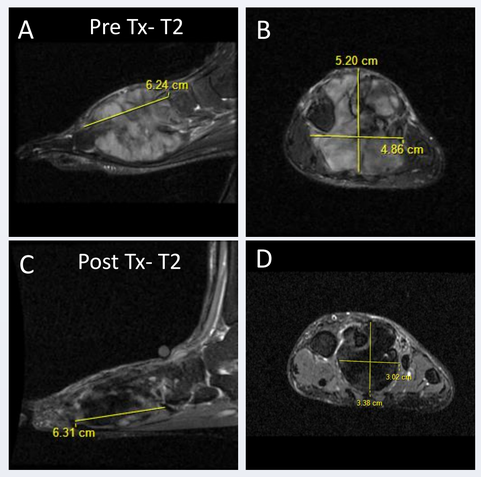

Figure 2: T2-fat-saturated sagittal and coronal MRI images of DF in L foot pre- and post MTX/VIN.

T2 Response:

- On T2-weighted imaging, CR was observed in 13 and PR in 5 patients
- Mid-treatment, 2 had PD and 7 patients had SD as per D_{max} and V_{tumor} with T2 change indicative of PR in all cases
- Both patients with PD continued therapy and had CR at end of treatment
- Four patients progressed post-treatment, median Progression Free Survival (PFS) was 31 months (95% CI: 14.9-137), and all had complete response (CR) at the end of MTX/VIN treatment on T2 imaging

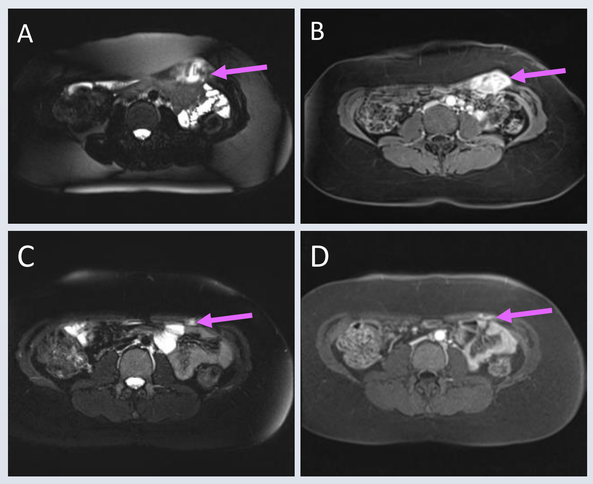

Figure 3: T2-fat-saturated (A) and T1-post-contrast (B) axial MR images of abdominal wall DF pre-treatment demonstrates high T2 signal and avid enhancement. Post treatment T2-fat-saturated and T1-post-contrast (C and D) showed decreased size and enhancement of DF.

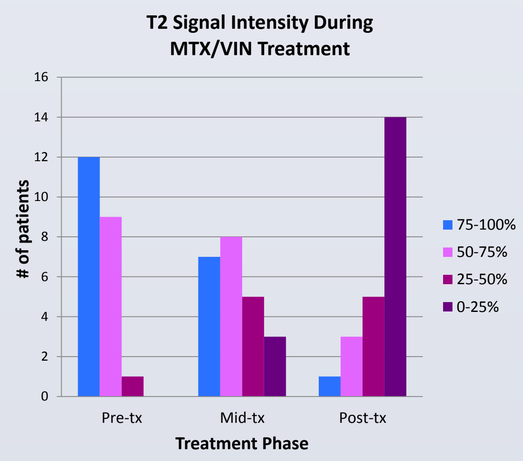

Figure 4: T2 signal intensity pre-, mid- and post- MTX/VIN treatment

DISCUSSION

- Assessment of response to MTX/VIN with D_{max} in patients with DF is problematic as longest axis of tumor may not change
- Estimated volume of tumor shows greater response to therapy than D_{max} for half of the patients in the study
- T2 signal intensity assessment mid-treatment may be more indicative of response than RECIST, resulting in continued therapy for patients who may benefit

CONCLUSION

- Evaluation of treatment response for DF utilizing an estimated volume of tumor and monitoring the degree of T2-weighted signal intensity change within the tumor may be better predictors of response to medical therapy than maximum tumor dimension
- Findings from this study warrant prospective multi-institutional validation

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