News Release

Title

The outcome of active surveillance for extra-abdominal desmoid-type fibromatosis: The first report with a large cohort from Asia

Key Points

- This is the first report in Japan on the results of active surveillance for DF.
- The 5-year active treatment free survival of extra-abdominal DF was 54.8%.
- Neck location and CTNNB1 S45F mutation were significantly associated with the transition to active treatment.

Summary

Tomohisa Sakai, assistant professor of Rare Cancer Center, Nagoya University Hospital, and Yoshihiro Nishida, professor of Department of Rehabilitation Medicine, reported the treatment outcomes of active surveillance for 168 extra-abdominal desmoid-type fibromatosis, and the risk factors for transition to active treatment.

Desmoid-type fibromatosis (DF) is a (myo-) fibroblastic soft tissue tumor that is classified as an intermediate malignancy according to the World Health Organization classification. DF is highly locally invasive and has a high postoperative recurrence rate. It does not cause distant metastasis like soft tissue sarcomas. Occasionally, it may spontaneously regress or disappear without any treatment in some patients, so careful follow-up (active surveillance: AS) has been conducted on patients with DF with slight or moderate symptoms.

Several studies have reported clinical outcomes for AS in western countries; however, few have reported the significant factors associated with the transition from AS to active treatment (AT). Moreover, the clinical outcome of AS for DF with sufficient patient's number has not been reported yet in Asian countries, including Japan.

Of the 168 DF lesions, 94 (56%) were able to continue AS, with a 5-year AT-free survival of 54.8%. Of the 68 lesions with progressive disease, 21 (30.9%) lesions were able to continue AS. Neck location ($p = 0.043$) and CTNNB1 S45F mutation ($p = 0.003$) were significantly associated with the transition to AT, and S45F mutation was a significant factor associated with the transition to AT by multivariate analysis [hazard ratio: 1.96, $p = 0.048$)]. Clinical outcomes of AT after AS were evaluable in 65 lesions and 49 (75%) lesions did not require a transition to a second AT.

Research Background

Desmoid-type fibromatosis (DF) is a (myo-) fibroblastic soft tissue tumor that is classified as an intermediate malignancy according to the World Health Organization classification. DF is highly locally invasive and has a high postoperative recurrence rate. It does not cause distant metastasis like soft tissue sarcomas. Occasionally, it may spontaneously regress or disappear without any treatment in some patients, thus it has been named “enigmatic” lesion. DF is a rare tumor that occurs in less than four people per million people annually.

The standard of treatment modality for DF had been surgical resection, generally with a wide surgical margin, similar to those for soft tissue sarcomas. However, even after extensive resection with significant loss of function, a high recurrence rate of 20%–40% has been reported. Systemic therapy, including chemotherapy, has been reported as a possible treatment alternative other than surgical resection; however, the activities of daily living (ADL) disturbance due to adverse events by the treatment is a considerable problem. Considering the surgical and systemic treatment results, in addition to the occasional spontaneous regression and inability of distant metastasis in DF, careful follow-up (active surveillance: AS) has been conducted on patients with DF with slight or moderate symptoms. Active treatment (AT), including surgery and/or systemic treatments, will be considered in cases of tumor growth that causes severe pain, functional impairment, and life-threatening situations after the treatment modality of AS. Several studies have reported clinical outcomes for AS in western countries; however, few have reported the significant factors associated with the transition from AS to AT. Moreover, the clinical outcome of AS for DF with large number of patients has not been reported yet in Asian countries, including Japan.

This study aimed to clarify the clinical outcomes of AS for patients with DF and identify the risk factors of AT after AS at our institution. Additionally, AT methods and their outcomes after AS modality was also investigated.

Research Results

Of the 168 DF lesions, 94 (56%) were able to continue AS modality, with a 5-year treatment free survival. of 54.8%. A transition from AS to AT was required in 74 (44%) lesions, with an average time to the intervention of 15.1 months (1–90 months). Of the 94 lesions for which AS could be continued, response to AS could be evaluated in 89 lesions by RECIST, and the outcomes were CR in 7, PR in 17, SD in 44, and PD in 21. Of the 74 lesions that required AT, 67 cases could be evaluated by RECIST, and the outcomes were SD in 20 and PD in 47. PD status by RECIST showed a significant association with the transition to AT ($p < 0.0001$, chi-square test). Age, gender, tumor diameter at the first visit, tumor location, recurrent lesions, CTNNB1 S45F mutation, and history of drug administration did not show any significant association with PD. The reasons for the transition to AT in patients with SD ($n = 20$) were to prevent the occurrence of functional impairment in 9 cases, to reduce pain in 6 cases, to regulate tumor growth (evaluation: SD) in 4 cases, and patient wishes in 1 case.

Neck location (p = 0.042) and CTNNB1 S45F mutation (p = 0.003) were significantly associated with poor treatment free survival. Contrarily, age (p = 0.27), gender (p = 0.29), tumor diameter at first visit (p = 0.50), limb development (p = 0.38), recurrent lesions (p = 0.93), and drug administration history (p = 0.33) did not show any significant association with treatment free survival. The COX-hazard multivariate analysis revealed significant relationship between CTNNB1 S45F mutation and poor treatment free survival (hazard ratio: 1.96, 95% confidence interval: 1.01–3.80, p = 0.048).

Research Summary and Future Perspective

AS might be a useful treatment approach for DF patients, particularly having risk factors for recurrence after surgery, such as younger patients, limb location, and recurrent disease. Not a few facilities still perform surgery as the first line of the treatment without considering AS. It is necessary to publicize the results of treatment for AS and spread awareness that it is an appropriate treatment. Surgical treatment is currently the first choice in many Asian countries yet, so it is necessary to disseminate the importance of AS through EAMOG (East Asia Musculoskeletal Oncology Group). In addition, we believe that the significance of AS, including the best timing of active treatment intervention, will be clarified by evaluating the clinical outcome of AS using patient-reported outcomes through a multicenter prospective study.

Publication

Clinical results of active surveillance for extra-abdominal desmoid-type fibromatosis

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