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Prognostic factors for the recurrence of sporadic desmoid-type fibromatosis after macroscopically complete resection: Analysis of 114 patients at a single institution

X.D. He [a,1], Y.B. Zhang [b,1], L. Wang [c,*], M.L. Tian [d], W. Liu [a], Q. Qu [a], B.L. Li [a], T. Hong [a], N.C. Li [c], Y.Q. Na [c]

[a] *Department of General Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, 100730, China*

[b] *Department of Head and Neck Surgery, Cancer Hospital (Institute), Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, 100021, China*

[c] *Peking University Wu-Jieping Urology Center, Peking University Shougang Hospital, Peking University Health Science Center, Beijing, 100144, China*

[d] *Department of General Surgery, Peking University Third Hospital, Peking University Health Science Center, Beijing, 100191, China*

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Abstract

Aims: Desmoid-type fibromatoses (DFs) are rare soft-tissue neoplasms with frequent local recurrence. We sought to determine the prognostic factors that are predictive of recurrence-free survival (RFS) for these tumors.

Methods: One hundred and fourteen consecutive patients with sporadic DF who received macroscopically complete resection (R0/R1) at a single tertiary hospital between 1985 and 2014 were included. A total of 10 clinical and pathological parameters were analyzed. Histologic slides and the margin status were re-checked; close margins (≤1-mm clearance) were noted separately and were considered together with the R1 margin.

Results: The median follow-up interval was 72.5 months. Thirty-five (30.7%) patients had a local recurrence. The 2-, 5- and 10-year RFSs were 75.2%, 72.1% and 67.0%, respectively. In univariate analysis, age, tumor size, tumor site, margin status and presence of lesions at multiple sites had a significant impact on RFS. In multiple analysis, younger age (age<30 vs. age≥50 years: hazard ratio [HR] = 4.96; 95% confidence interval [95% CI], 1.50–16.4; $p = 0.009$); an extra-abdominal site (extra-abdominal site vs. other sites: HR = 4.08; 95% CI, 1.49–11.2; $p = 0.006$); larger tumor size (≥8 cm vs. <8 cm: HR = 2.43; 95% CI, 1.15–5.13; $p = 0.021$); and close or positive margin status (close margin/R1 vs. R0: HR = 2.64; 95% CI, 1.11–6.25; $p = 0.027$) were independent, unfavorable prognostic factors.

Conclusions: Different prognostic subgroups were identified that allow for the better selection of favorable therapeutic strategies. The role of the margin status should be considered with caution and should be based on a more precise pathological result.

Keywords: Fibromatosis; Surgery; Recurrence-free survival; Risk factors

Abbreviations: DF, desmoid-type fibromatosis; FAP, familial adenomatous polyposis; RFS, recurrence-free survival; HR, hazard ratio; 95% CI, 95% confidence interval; PUMCH, Peking Union Medical College Hospital; AJCC, American Joint Committee on Cancer; WHO, World Health Organization; SPSS, Statistical Package for the Social Science.

* Corresponding author. Address: Peking University Wu-Jieping Urology Center, Peking University Shougang Hospital, 9#Jinyuanzhuang Road, Shijingshan District, Beijing, 100144, China. Tel./fax: +86 10 57830131.

E-mail addresses: surgerypumch@sina.com (X.D. He), yabing_zhang@sina.cn (Y.B. Zhang), wanglei_09243633@163.com (L. Wang), raining2902@163.com (M.L. Tian), liuwei203@126.com (W. Liu), doctorqupumch@126.com (Q. Qu), lisalee@sina.com (B.L. Li), taohong_0423@163.com (T. Hong), ningchenli_puwjpuc@sina.com (N.C. Li), yanqunna69@126.com (Y.Q. Na).

[1] Equal contributors.

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Introduction

Desmoid-type fibromatosis (DF), previously known as aggressive fibromatosis, is a rare musculoaponeurotic tumor that has a typical clinical behavior of frequent local recurrences and the absence of distant spread.[1] With a 2- to 3-fold female predominance, it has an estimated annual incidence of 2–4 cases per million people worldwide and can occur in nearly any part of the human body.[2,3] Most cases of the disease are sporadic and are genetically associated with Wnt/β-catenin pathway gene mutations, though a small proportion is associated with *APC* gene mutations and familial adenomatous polyposis (FAP).[4,5] The growth pattern is infiltrative and nonencapsulated, which makes local remission very difficult. Although the survival prognosis of the tumor remains good overall, a reported high recurrence rate of 24–77% and the subsequent treatment sequelae can lead to significant morbidity.[6–8]

The clinical course of DF can be unpredictable and variable. In some cases, the lesion remains stable for long periods and even regresses spontaneously; however, in other cases, the lesion recurs and grows rapidly, even after wide resection.[9,10] Many treatment regimens are available, including surgical excision, radiotherapy, systemic therapy, and a watch-and-wait approach. Surgical resection is considered the first line of treatment, whereas anatomic location can make complete resection impossible or associated with a high morbidity. For operable lesions, wide surgical resection is recommended, but the local recurrence rate remains high.[7,8]

Few studies have rigorously examined the factors associated with DF recurrence. However, the indicated risk factors, including surgical margin, radiation, age and tumor size, are conflicting between different studies.[7–9,11–13] The β-catenin (*CTNNB1*) mutation was also widely studied as a potential risk factor recently, but no consensus was reached.[14,15] These controversial results might be due to the limited sample size or the heterogeneity of the study populations. In addition, the identification of the negative margin status was queried recently, which may shed new light on this issue.[16] We presented a relatively homogeneous cohort of 114 sporadic patients with gross negative margins after surgery, and we adopted the suggestion of JM Cates[16] and considered close margins (≤1-mm clearance) together with the R1 margin both to analyze the prognostic factors that may influence recurrence in operable DF and to best choose additional therapies after surgery.

Patients and methods

Patient cohort

Patients who underwent surgical resection and were pathologically diagnosed with DF between August 1, 1985, and July 31, 2014, were identified and retrospectively reviewed from the institutional sarcoma database at the Peking Union Medical College Hospital (PUMCH) in Beijing, China. Patients undergoing macroscopically complete surgical resection were included in this study. The exclusive criteria were as follows: 1) patients with an incomplete gross resection or an unclear margin status; 2) patients with FAP (Gardner's syndrome) whose prognoses were reported to be significantly different from those with sporadic DF; and 3) patients who were lost to follow-up or who had a very short duration of follow-up <6 months. The study protocol was approved by the Institutional Review Board at PUMCH, and a waiver of informed consent was obtained.

Pathology review

To confirm the histologic diagnosis and document resection margin status, histologic slides of all of the patients entered in this study were re-checked independently by two pathologists at PUMCH. Margin status was classified as macroscopic positive (R2), microscopic positive (R1), or negative (R0) according to the American Joint Committee on Cancer (AJCC) criteria (seventh edition). The number of tissue sections used to evaluate the margin status was based on the tumor dimensions and the number of grossly suspected margins. To decrease the problems caused by false-negative margins, close margins (≤1 mm clearance) were noted separately and were considered together with the R1 margin,[16] and margins >1 mm were considered clear. Histological typing was based on the World Health Organization (WHO) histological typing of soft-tissue tumors.

Clinical data

Data regarding patient characteristics, tumor description, and treatment modalities were obtained from a retrospective review of medical records. The outcome of surgical resection was determined by routine imaging examination after operation and by a comprehensive telephone interview performed on August 2014. The following ten variables were analyzed for their potential prognostic value: gender, age at presentation, admission status, tumor site, tumor size, history of surgery or trauma in the area of the primary tumor, the presence of multiple tumors (more than one lesion at a single site), the presence of lesions at multiple sites (tumors occurring at more than one site at presentation), margin status and the administration of adjuvant radiotherapy. The tumor site was categorized as abdominal wall, intra-abdominal, or extra-abdominal. Lesions at the retroperitoneal site were considered collectively with extra-abdominal lesions. Local recurrence was the main endpoint and was defined as tumor relapse after surgical resection at our institution. The interval between surgical resection at our hospital to local recurrence or the last clinical follow-up was documented.

Statistical methods

The characteristics of the primary and recurrent tumors were compared using chi-squared analysis. Local