NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™)

Dermatofibrosarcoma Protuberans

Version 1.2012

NCCN.org
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Updates in Version 1.2012 of the NCCN Guidelines from Version 2.2011 include:

**DFSP-2**
- After Excision; Negative margins pathway: The option to “Consider adjuvant RT” was removed.
- Recurrence pathway: The third option for treatment changed to “Imatinib mesylate in cases where disease is unresectable, or unacceptable functional or cosmetic outcomes will occur”.

**DFSP-A---Principles of Excision**
- Goal:
  - The following statement was added, “Some form of complete histologic surgical margin examination is recommended, whenever possible.
- Reconstruction:
  - The statement “Immediate reconstruction in most cases” was removed.
  - The following statement “It is preferable to delay reconstruction involving extensive undermining or flaps until negative surgical margins are assessed and certified pathologically clear” was revised as follows, “It is recommended that any reconstruction involving extensive undermining or tissue movement be delayed until negative histological margins are verified.
  - Last bullet changed to, “If there is concern that the surgical margins are not completely clear, consider split thickness skin grafting (STSG) to monitor for recurrence.”
- Footnote 2 regarding CCPDMA that states, “Usually performed as a meticulous, comprehensive en face permanent section examination of all surgical margins,” is new to the algorithm.
Suspicous lesion
• H&P
• Complete skin exam

Biopsy^a
• H&E
• Immunopanel (eg, CD34, factor XIIIa)
• Note and report evidence of fibrosarcoma change

CLINICAL PRESENTATION

WORKUP

CLINICAL FINDINGS

^aThis tumor is frequently misdiagnosed, even with multiple preliminary biopsies.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
# Dermatofibrosarcoma Protuberans

## TREATMENT

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### ADJUVANT TREATMENT

- Consider radiation therapy or Imatinib mesylate

### FOLLOW-UP

- Observe
- • Check primary site every 6-12 months
- • Patient education about regular self-exam

### THERAPY FOR RECURRENCE/METASTASIS

- Re-resection as feasible or Consider RT if not given previously or Imatinib mesylate d in cases where disease is unresectable, or unacceptable functional or cosmetic outcomes will occur
- Consider clinical trial, Imatinib mesylate d, chemotherapy, RT or resection as feasible, given the specific clinical circumstances

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*b* The surgical approach to DFSP must be meticulously planned. Size and location of the tumor and cosmetic issues will dictate the most appropriate surgical procedure. [See Excision (DFSP-A)].

c5,000-6,000 cGy for close-to-positive or positive margins (200 cGy fractions per day). Fields to extend widely beyond surgical margin (eg, 3-5 cm), when clinically feasible.

dTumors lacking the t(17;22) translocation may not respond to imatinib. Molecular analysis of a tumor using cytogenetics may be useful prior to the institution of imatinib therapy.
Goal:
- Every effort should be made to achieve clear surgical margins. Some form of complete histologic surgical margin examination is recommended, whenever possible. Tumor characteristics include long, irregular, subclinical extensions.

Varied Approaches:
- Mohs technique
- Modified Mohs = Mohs technique with additional final margin for permanent section assessment.
- CCPDMA= Complete circumferential and peripheral deep-margin assessment.
- 2-4 cm margins to investing fascia of muscle or pericranium with clear pathologic margins, when clinically feasible.

Reconstruction:
- It is recommended that any reconstruction involving extensive undermining or tissue movement be delayed until negative histological margins are verified.
- If there is concern that the surgical margins are not completely clear, consider split thickness skin grafting (STSG) to monitor for recurrence.

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1Mohs technique is used primarily in DFSP to insure complete removal and clear margins, and secondarily for its tissue sparing capabilities.
2Usually performed as a meticulous, comprehensive en face permanent section examination of all surgical margins.
Discussion

NCCN Categories of Evidence and Consensus

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

Overview

The NCCN Non-Melanoma Skin Cancer Panel has developed these guidelines outlining the treatment of dermatofibrosarcoma protuberans (DFSP) to supplement their other guidelines (NCCN Basal Cell and Squamous Cell Skin Cancers Guidelines and NCCN Merkel Cell Carcinoma Guidelines). The NCCN Soft Tissue Sarcoma Panel provided expert input in the development of DFSP guidelines. DFSP is an uncommon, low-grade sarcoma of fibroblast origin with an incidence rate of 4.2 to 4.5 cases per million persons per year in the United States. It rarely metastasizes. However, initial misdiagnosis, prolonged time to accurate diagnosis, and large tumor size at the time of diagnosis is common. Three-dimensional reconstruction of DFSP has revealed tumors with highly irregular shapes and frequent finger-like extensions. As a result, incomplete removal and subsequent recurrence are common. The local recurrence rate for DFSP in studies ranges from 0-60%, whereas the rate of development of regional or distant metastatic disease is only 1% and 4-5%, respectively.

Diagnosis

As with all solid tumors, clinical suspicion is confirmed by biopsy. In most cases, examination of hematoxylin and eosin-stained specimens by light microscopy results in an unequivocal diagnosis. However, differentiation of DFSP from dermatofibroma can be difficult, at times. In such instances, immunostaining with CD34, factor XIIIa, metallothioneins, tenascin, and/or stromelysin-3 may be useful. Therefore, the panel recommends that appropriate and confirmatory immunostaining be performed in all cases of suspected DFSP. Finally, it is unclear whether the histologic features of a high mitotic rate or evidence of fibrosarcomatous change (typically in more than 5% of the surgical specimen) have prognostic significance in DFSP. Studies in the biomedical literature both support and refute this notion. Thus, the panel requested that these two features be noted in all pathology reports assessing this tumor.

When the clinician’s suspicion for DFSP is high, but the initial biopsy does not support the diagnosis, re-biopsy is recommended and may reveal tumor presence. Multiple non-supportive or equivocal biopsies over time, before definitive diagnosis, are common in the clinical history for this tumor; thus, DFSP is frequently misdiagnosed. Because metastatic disease is rare, an extensive workup is not routinely indicated unless suggestive aspects in the history and physical examination (H&P) or adverse prognostic histologic features are present. Stage I is local disease, stage II is regional disease, and stage III is distant disease.
Treatment

Initial treatment of DFSP is surgical. Because of its proclivity for irregular and frequently deep subclinical extensions, every effort should be made to completely remove this tumor at the time of initial therapy. If initial surgery yields positive margins, re-resection is recommended whenever possible, with the goal of achieving clear margins. The surgical approach to DFSP must be meticulously planned. Size and location of the tumor as well as cosmetic issues will dictate the most appropriate surgical procedure. As noted in the algorithm, some form of complete histologic assessment of all surgical margins before reconstruction is preferred. See NCCN Soft Tissue Sarcoma Guidelines for principles of sarcoma surgery. Mohs or modified Mohs surgery, and traditional wide excision, typically with 2 to 4 cm margins to investing fascia that are subsequently verified to be clear by traditional pathologic examination, are all methods to achieve complete histologic assessment. In a recent series of 244 DFSP patients, tumor depth is the only factor associated with disease-free survival in the primary setting, underscoring the importance to excise the deep fascia to remove any infiltrating tumor cells. In another retrospective review of 48 patients, positive margins were more frequent with wide excision than with Mohs, but the local recurrence rates were statistically similar (3.6% vs 0%, respectively, P = 1.0). Confirmation of negative margins should precede any reconstruction that requires extensive undermining or tissue movement. If there is concern that the surgical margins are not completely clear, tissue rearrangement should be avoided, and split thickness skin grafting (STSG) should be considered to monitor for recurrence.

DFSP is characterized by a translocation between chromosomes 17 and 22 [t(17:22)] resulting in the over expression of platelet-derived growth factor receptor β (PDGFRB). These findings suggest that targeting PDGF receptors may lead to the development of new therapeutic options for DFSP. In recently published results, imatinib mesylate, a protein tyrosine kinase inhibitor, has shown clinical activity against localized and metastatic DFSP tumors containing t(17:22). Imatinib mesylate has recently been approved by the FDA for the treatment of unresectable, recurrent and/or metastatic DFSP in adult patients. Because tumors lacking the t(17;22) translocation may not respond to imatinib molecular analysis of a tumor using cytogenetics may be useful prior to the institution of imatinib therapy.

Radiation has occasionally been used as a primary therapeutic modality for DFSP, but it is more commonly used as adjuvant therapy after surgery. Postoperative radiation therapy or imatinib mesylate should be considered for positive surgical margins if further resection is not feasible (unresectable disease). If a negative margin is achieved, no adjuvant treatment is necessary.

Recurrent tumors, whenever possible, should be resected. Radiation therapy, if not given previously, or imatinib mesylate should be considered if this is not possible, or if additional resection would lead to unacceptable functional or cosmetic outcomes. Clinical trials, imatinib mesylate, chemotherapy, radiation therapy or re-resection as feasible under specific clinical circumstances should all be considered in the rare event of metastatic disease.

Several clinical trials are underway for the treatment of DFSP with imatinib. To access current clinical trials, go to www.clinicaltrials.gov.

Follow-up

Finally, given the historically high local recurrence rates for DFSP, ongoing clinical follow-up of the primary site every 6-12 months is indicated, with re-biopsy of any suspicious regions. Although metastatic
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disease is rare, a guided H&P should be performed as well, with additional imaging studies as indicated.
References


