NCCN Guidelines® Insights

Dermatofibrosarcoma Protuberans, Version 1.2014

Featured Updates to the NCCN Guidelines

Abstract

Dermatofibrosarcoma protuberans (DFSP) is an uncommon soft tissue tumor characterized by a relatively high risk of local recurrence and low risk of metastasis. The NCCN Guidelines for DFSP provide multidisciplinary recommendations on the management of patients with this rare disease. These NCCN Guidelines Insights highlight the addition of the Principles of Pathology section, which provides recommendations on the pathologic assessment of DFSP. Because DFSP can mimic other lesions, immunohistochemical studies are often required to establish diagnosis. Cytogenetic testing for the characteristic translocation t(17;22)(q22;q13) can also be valuable in the differential diagnosis of DFSP with other histologically similar tumors. (J Natl Compr Canc Netw 2014;12:863–868)

Please Note

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. The NCCN Guidelines® Insights highlight important changes in the NCCN Guidelines® recommendations from previous versions. Colored markings in the algorithm show changes and the discussion aims to further understanding of these changes by summarizing salient portions of the panel’s discussion, including the literature reviewed.

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Learning Objectives:

Upon completion of this activity, participants will be able to:

• Integrate into professional practice the updates to NCCN Guidelines for Dermatofibrosarcoma Protuberans

• Describe the rationale behind the decision-making process for developing the NCCN Guidelines for Dermatofibrosarcoma Protuberans

Supported by an independent educational grant from Prometheus Laboratories, Inc., and by educational grants from Bayer HealthCare, Onyx Pharmaceuticals, Inc., and Algeta US; Exelixis, Inc.; Genentech; Genomic Health, Inc.; NOVOCURE; and Merck Sharp & Dohme Corp.
Overview

Dermatofibrosarcoma protuberans (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. Because of its slow-growing nature, definitive diagnosis is often delayed and large size at presentation is common. Although metastasis is rare, DFSP can be locally aggressive, resulting in significant morbidity. Local recurrence rates for DFSP in older studies range from 10% to 60%, whereas pooled data from more recent studies using wide surgical margins showed an overall recurrence rate of 7.3%.

NCCN has assembled a multidisciplinary panel of leading experts from NCCN Member Institutions to develop and continually update guidelines for the treatment of nonmelanoma skin cancers. The NCCN Guidelines for DFSP are an extension of these guidelines that provide specific recommendations for DFSP management. The panel
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PRINCIPLES OF PATHOLOGY

• The spindled cells arranged in a storiform or fascicular pattern are typically bland with minimal cytologic atypia.

• Immunohistochemistry for CD34 is mostly positive, and Factor XIIIa negative.

• Fibrosarcomatous transformation (FS-DFSP) is reflected by a higher degree of cellularity, cytologic atypia, mitotic activity (>5/10HPF), and negative CD34 immunostaining.

• Consider additional immunostaining with nestin, apolipoprotein D, and cathepsin K for equivocal lesions, or FISH or PCR for translocation of collagen type I alpha 1 (COL1A1; on 17q22) with platelet-derived growth factor Beta (PDGFβ; on 22q13) to form the oncogenic chimeric fusion gene t(17;22) (q22;q13).

• Margin control during excision may require H&E sections supplemented by CD34 immunohistochemistry.

Also received expert input from the NCCN Guidelines Panel for Soft Tissue Sarcoma during the initial development of this guideline. The latest full guideline, including a complete list of updates, is available on the NCCN Web site at NCCN.org. These NCCN Guidelines Insights highlight the addition of the “Principles of Pathology” section.

Principles of Pathology

Histologically, DFSP typically presents as a storiform or fascicular proliferation of bland spindled cells that extends from the dermis into the subcutis on a routine hematoxylin and eosin (H&E) stain.5,6 DFSP may be difficult to differentiate from other fibrous tumors, especially dermatofibroma; hence, immunohistochemical staining is frequently used to establish a definitive diagnosis. CD34, a glycoprotein expressed by bone marrow stem cells, is expressed in most cases of DFSP.7-10 In contrast, staining for the coagulation factor XIIIa is usually negative in DFSP.7-10 Positive CD34 and factor XIIIa staining is often sufficient for a DFSP diagnosis. Additional markers that are immunoreactive in DFSP include nestin, apolipoprotein D, and cathepsin K,11-13 which may be helpful in difficult cases.

DFSP is characterized by a t(17;22)(q22;q13) translocation or a supernumerary ring chromosome that results in the fusion of the platelet-derived growth factor B gene (PDGFB) on chromosome 22 to various exons of the collagen type I alpha 1 (COL1A1) gene on chromosome 17.14 Found in more than 90% of DFSP tumors, this translocation upregulates PDGFB, a tyrosine kinase and key growth factor for connective tissue cells.15 Imatinib mesylate, a tyrosine kinase inhibitor, has shown clinical activity against localized and metastatic DFSP tumors containing the translocation.16-20 This agent has been approved by the FDA for the treatment of unresectable, recurrent, and/or metastatic DFSP in adult patients.
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Whether high mitotic rate or evidence of fibrosarcomatous change (typically in >5% of the surgical specimen) has prognostic significance in DFSP remains unclear. Studies in the literature both support and refute this notion.

**NCCN Recommendations**

The NCCN Guidelines outline the initial workup for DFSP in the algorithm (see DFSP-1, page 865). Because metastatic disease is rare, an extensive workup is not routinely indicated unless suggestive aspects in the history and physical examination or adverse prognostic histologic features are present. Because misdiagnosis is common, the panel strongly recommends clinicians obtain sufficient tissue from a deep subcutaneous punch biopsy or incisional biopsy for accurate pathologic assessment. When the clinician’s suspicion for DFSP is high but the initial biopsy does not support the diagnosis, rebiopsy is recommended and may reveal tumor presence. Wide undermining of the skin is discouraged because it may potentially result in tumor seeding. It can also interfere with the pathologic examination of re-excisions.

The “Principles of Pathology” section is a new section providing additional guidance on the analysis, interpretation, and reporting of pathologic results (see DFSP-A, page 866). Currently, no synoptic reporting is recommended. In most cases, examination of H&E stains using light microscopy results in an unequivocal diagnosis. However, differentiation of DFSP from dermatofibroma and other fibrous tumors can be difficult at times. In these instances, immunostaining with CD34 and factor XIIIa can be valuable. Other tests that can be useful include nestin, apolipoprotein D, cathepsin K, and fluorescence in situ hybridization or polymerase chain reaction analysis for t(17;22)(q22;q13). The panel recommends that appropriate and confirmatory immunostaining be performed in all cases of suspected DFSP.

Fibrosarcomatous change and malignant transformations should be noted, because these are high-risk features that should prompt multidisciplinary consultation to optimize clinical and reconstructive outcomes. Clinicians should consult the NCCN Guidelines for Soft Tissue Sarcoma when fibrosarcomatous transformations are present (to view the most recent version of these guidelines, visit NCCN.org).

**Conclusions**

These NCCN Guidelines Insights highlight the addition of a “Principles of Pathology” section to the NCCN Guidelines for DFSP. The NCCN Guidelines are updated at least annually, and more often when new high-quality clinical data become available in the interim. The most up-to-date version of these continuously evolving guidelines is available online at NCCN.org. The recommendations in the NCCN Guidelines are based on evidence from clinical trials where available, combined with expert consensus of the panel. Independent medical judgment is required to apply these guidelines individually to provide optimal care. The physician and the patient have the responsibility to jointly explore and select the most appropriate option from among the available alternatives. When possible, consistent with NCCN philosophy, the NCCN panel strongly encourages participation in prospective clinical trials.

**References**


Instructions for Completion
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Posttest Questions
1. Which of the following is a characteristic translocation found in DFSP?
   a. t(9;22)(q34;q11)
   b. t(15;17)(q22;q21)
   c. t(8;14)(q24;q32)
   d. t(17;22)(q22;q13)
2. DFSP is associated with a good prognosis due to frequent early diagnosis in patients.
   a. True
   b. False
3. Which of the following represents a typical immunohistochemical stain of DFSP?
   a. CD34 positive, factor XIIa negative
   b. CD34 negative, factor XIIa positive
   c. CD34 positive, factor XIIa positive
   d. CD34 negative, factor XIIa negative