Nodular fasciitis of the head and neck region: a clinicopathologic description in a series of 30 cases

Nodular fasciitis (NF) is a reactive lesion composed of fibroblasts/myofibroblasts and most commonly found in extremities and trunk. NF has been described in the head and neck region (HNR) in 13–20% of cases. It is our impression based on consultation experience that many pathologists do not consider NF in the differential diagnosis of soft tissue masses arising in the HNR. Moreover, it is common for these lesions to be incompletely excised, leading to additional challenges in diagnosis. We describe 30 cases of NF of the HNR in order to focus attention on this frequently overlooked diagnosis. While they had the typical histologic features of NF, the lesions had a tendency for smaller size, increased skeletal muscle involvement (30%) compared to fasciitis elsewhere in the body and diffuse and strong actin expression. Follow up demonstrated one recurrence (7.1%) higher than reported elsewhere in the body. These latter features may add to the challenge in diagnosing NF in these locations.


Introduction
Nodular fasciitis (NF) is a benign reactive lesion composed of fibroblasts and myofibroblasts and most commonly found in the extremities or trunk.1 However, it can be identified in virtually any anatomic region. NF has been described in the head and neck region with percentages ranging from 13 to 20% in previous studies.2,3 Despite the fact that NF represents one of the most common mass forming soft tissue lesions, it is our impression based on consultation experience that many pathologists do not consider NF in their differential diagnosis when it arises in the head and neck region, leading to the potential for serious diagnostic confusion. Moreover, it is not uncommon for these lesions to be biopsied or incompletely excised in head and neck sites, leading to additional challenges in diagnosis. In this study, we describe the features of 30 cases of NF of the head and neck in order to focus attention on this frequently problematic diagnosis.

Methods
Cases were retrieved from the University of Washington Medical Center (UWMC) (Seattle, Washington), Cleveland Clinic Foundation (CCF) (Cleveland, Ohio) and University Health Network (UHN) (Toronto, Ontario, Canada) computer archives using the key words “NF.” Only cases located in the head and neck were included in this study. Twenty-one cases were from patients of the UWMC, four additional cases were obtained from CCF and another five cases were from UHN. Of the cases that were seen in consultation, diagnoses offered by the referring pathologists included spindle cell neoplasm (two), atypical spindle cell lesion favor
benign/NF (two), NF (four), fibromatosis (two), dermatofibrosarcoma protuberans (DFSP) (three), deep benign fibrous histiocytoma (BFH) (one), leiomyosarcoma (one), atypical fibroxanthoma (one), and sarcoma NOS (one).

Routine hematoxylin and eosin slides were available in all cases. Immunohistochemical studies were performed from a representative paraffin block or unstained slides when available. Immunohistochemistry was performed by the avidin–biotin–peroxidase complex technique using commercially available antibodies to the following antigens: desmin (clone D33; [dilution] 1 : 1000; DAKO, Carpinteria, CA), alpha-SMA (IA4; 1 : 4000; Coulter Immunotech, Westbrook, ME), CD34 (QBEnd 10; 1 : 100; DAKO), CD68 (KP-1; 1 : 16000; DAKO), S-100 (polyclonal; 1 : 8000; DAKO) and Factor XIIIa (polyclonal, 1 : 1000; Calbiochem, La Jolla, CA). Antigen retrieval consisted of 15 min of microwave pretreatment in citrate buffer prior to the application of all primary antibodies when appropriate. Appropriate positive and negative controls were performed throughout. The cases were scored as: no staining; focal positivity (0–50% of cells staining) or diffuse positivity (50–100% of cells staining).

Results

Clinical findings

There were 18 males (60%) and 12 females (40%). The median age was 36.9 years with a range of 3–71 years. Five patients were younger than age 18 and 25 patients were 18 years or older at the time of diagnosis. Sizes ranged from 0.1 to 3.0 cm in greatest dimension with a median of 1.2 cm. The lesions were reported to arise in the neck (five), forehead (six), cheek (four), periorbital (one), scalp (two), lip (three), mouth (two), submental (one), jaw (one), ear canal (one) and nose (one). Antecedent trauma was not a known feature in any of the cases. The duration of symptoms was not known for most cases. For the cases where duration was provided, it ranged from 3 months to 2 years (mean 8.4 months). Most lesions represented incomplete excisions or biopsies. Follow-up was available in 14 cases and ranged from 1 month to 48 months with an average of 16.8 months. One recurrence occurred at 6 months for a recurrence rate of 7.1% and appeared identical to the original lesion. Examination of the initial specimen in this case revealed an incomplete excision for this case. No additional masses in the rest of the body were reported in any case.

Histologic findings

Histologically, the lesions varied in cellularity, ranging from relatively hypocellular and myxoid to those that were densely cellular with varying amounts of collagenous stroma. The lesions were composed of short fascicles of spindle shaped to stellate cells (Fig. 1a) with a moderate amount of pale eosinophilic cytoplasm, often arranged in a storiform pattern focally. The nuclei were oval and without irregularities and contained pale chromatin and small, inconspicuous nucleoli. Many cases showed a zonated architectural pattern (Fig. 1b), containing a centrally located myxoid and/or hyalinized (often keloidal) area with a more cellular periphery. Keloidal hyalinization was seen in 13 cases (43%) (Fig. 1c). The stroma was at least focally myxoid in all cases and there were frequent cystic spaces in these myxoid areas (Fig. 1d). Numerous fine capillaries lined by plump endothelial cells could be seen in the lesions and were highlighted by staining with CD34. None of the cases demonstrated staghorn vascularity, palisading of cells, duct formation or chondroid stroma. Virtually all cases had extravasated erythrocytes and inflammatory cells within the lesion (Fig. 1a). Isolated mitotic figures were noted in the majority of cases. Cases with more than rare mitotic figures showed counts ranging from 2 to 5/10 hpfs. The mitotic figures were scattered throughout these lesions and no abnormal/atypical mitoses were present. Ten cases (30%) involved the surrounding skeletal muscle focally and superficially (Fig. 1e). No cases showed deep skeletal muscle involvement or intramuscular location. Two cases (6.7%) were entirely intravascular with a third case suspicious for intravascular origin (Fig. 1f–g). Two cases (6.7%) were adjacent to a salivary gland (one parotid and one minor salivary gland) and one of these showed lesional cells interspersed with atrophic minor salivary gland tissue. The lesion in question appeared to entrap the salivary glands rather than arise from them. Osteoclast-type giant cells and/or ganglion-like cells were present in the majority of cases and prominent in two cases (6.7%) (Fig. 1h). There was no evidence for osteoid/ossification.

Immunohistochemical findings

Immunohistochemical studies were performed in 24 cases. All of the lesions tested (24/24) were positive for smooth muscle actin and most of these (19/24) showed diffuse and strong reactivity in a classic “tram track” pattern (Fig. 2). The other five cases showed focal positivity with a similar pattern. The lesional fibroblastic/myofibroblastic cells were negative for S-100 (0/22), desmin (0/19), CD34 (0/19), CD68 (0/15) and Factor XIIIa (0/15). One case contained a number of cells that were positive for Factor XIIIa; however, these cells contained elongated processes and were inflammatory/dendritic cells that were

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Fig. 1. (a) A typical example of nodular fasciitis composed of a spindle cell proliferation with intralesional erythrocytes and admixed chronic inflammatory cells. (b) Many tumors demonstrate zonation with a myxoid central region abutting a more fibrocellular peripheral region. (c) Keloid-like collagen was present in almost half of the cases and was occasionally very prominent. (d) Microcytic spaces in the myxoid regions are a common feature of nodular fasciitis. (e) Approximately 30% of nodular fasciitis of the head and neck show superficial skeletal muscle infiltration and entrapment of individual muscle fibers. (f) Two cases were entirely intravascular. These lesions showed circumscription by a vascular wall with cleft-like endothelial-lined spaces at the periphery. (g) High power of the same region as in Fig. f; this case of intravascular fasciitis showed extension into smaller neighboring vessels. (h) Most cases contained numerous osteoclast-like giant cells and in two cases this finding was prominent.
Fig. 2. Actin was expressed by all cases of nodular fasciitis of the head and neck, the majority of which showed strong and diffuse staining. Admixed within the lesional tissue, CD68 was positive only in the osteoclast-like giant cells.

Discussion

NF is a distinctive soft tissue lesion composed of fibroblasts and myofibroblasts in a variably myxoid and inflammatory stroma. The vast majority of cases present as superficial soft tissue masses in the extremities or trunk.2 Although NF also occurs in the head and neck region, most of the focused reports in the literature have been case studies and the head and neck region has not been extensively studied. There have been two previous series of NF in the head and neck region; one which was specifically focused on the ear and external auditory canal.7 NF has also been reported to occur in the skin, parotid gland, neck, cheek and oral cavity.4–6, 8–10 Recurrence of NF in general, and of the head and neck specifically, has been reported to be rare1,6,7 and metastases do not occur. The importance of this diagnosis is primarily in its recognition, separation from a wide differential diagnosis and avoidance of unnecessary additional surgery.

Most of the cases in our series arose in the neck, forehead/scalp and cheek area, while a small number of cases arose in the lip, oral cavity and nose. The vast majority were purely soft tissue tumors with only one case isolated to the dermis of the skin (scalp). Two cases were intravascular (lip and scalp). The mean size of the tumors was 1.2 cm, most of which were under 1.0 cm and smaller than previously cited instances of NF elsewhere.2 This is likely due to the lack of abundant subcutaneous fat in the head and neck, early local symptoms/interruption of body functions (e.g., chewing) and early cosmetic effects leading to expedited patient referral. Histologically, the cases described in the current series were similar to NF elsewhere.

Skeletal muscle was involved in 30% of the cases described herein, more than in other areas of the body in our experience. This may have a worrisome appearance histologically, because entrapment of the muscle cells at the periphery of the lesion often results in muscle cell atrophy and atypical appearing multinucleated cells. Desmin is helpful in confirming that these cells are atrophic skeletal muscle cells; however, the limited and superficial involvement of the muscle remains the best clue in separating NF from sarcomas. The frequent finding of skeletal muscle involvement by NF in the head and neck region is due to the superficial nature of the skeletal muscle in this location and lack of well-defined fascial planes that typically separate skeletal muscle from subcutaneous tissues. Despite this potentially worrisome finding, follow-up in this series has revealed that NF has a low rate of local recurrence (7%), similar to the recurrence rate in the ear region7 and somewhat higher than the recurrence rate at other sites.1 Local recurrence in the single case in this series was related to the presence of incomplete excision; however, even incomplete excisions typically do not result in recurrence and never result in aggressive/destructive behavior.

Another distinctive feature of NF of the head and neck in this series is the diffuse and strong nature of actin expression by the myofibroblasts in the lesion. Most cases of NF in trunk and extremities show focal or patchy positivity for actins and when diffuse often show weak expression in our experience. The higher rate of actin expression may reflect a referral bias, as these lesions may pose greater difficulty for pathologists. The authors cannot offer a biologic explanation as to why location should have any effect on diffuseness of actin expression. The strong expression of actin in this series may evoke the differential diagnoses of leiomyosarcoma and myofibroblastic sarcoma. The absence of abundant eosinophilic cytoplasm, perinuclear halos or cigar-shaped nuclei and invariable desmin negativity coupled with typical myxoid/keloidal areas in all cases at least focally, should make distinction with leiomyosarcoma easy in most cases. A more difficult distinction is the cellular examples of NF from low-grade myofibroblastic sarcoma, which while rare, have a predilection for the head and neck region.1 These tumors are generally larger at presentation, have an infiltrative appearance and often have a “destructive growth pattern” radiologically.1 In addition, they typically have at least focal, if not obvious cytologic atypia (a feature lacking in all cases of NF).
One case in our series involved minor salivary gland tissue. This is a common finding in a variety of benign tumors at head and neck mucosal sites and is not a sign of aggressive behavior by NF. More importantly, it raises the differential diagnosis of a primary spindled salivary gland tumor. Myoepitheliomas and mixed tumors (pleomorphic adenoma) typically and consistently show a spindle cell population in a myxoid stroma with strong actin positivity. These tumors should be considered especially in incomplete excisions or biopsies, as the morphology of myoepithelioma/mixed tumor is heterogeneous and chondroid matrix or ducts may be left unsampled. The complete absence of keratin staining in NF coupled with features such as zonation, osteoclast-like giant cells and inflammation help distinguish these lesions. This is an important distinction, as NF usually requires no further therapy, while salivary gland tumors carry a small but significant risk of recurrence and malignant transformation.

Another salivary gland lesion worthy of discussion is chronic sclerosing sialadenitis (CSS), which is a tumor-like condition associated with other systemic sclerosing lesions. Unlike NF, CSS is a lesion that is intrinsic to the salivary tissues with remnant salivary ducts often showing hyperplasia. NF tends to form a mass lesion without intrinsic salivary elements or at most peripheral salivary entrapment. In addition, CSS does not show microcystic changes and is characterized by a plasmacytic infiltrate with IgG4 positivity. Plasma cells are not a predominant feature of NF and IgG4 has not been associated with NF to our knowledge.

Additional lesions in the differential diagnosis of NF of the head and neck include BFH (cutaneous or deep), benign nerve sheath tumors, DFSP, desmoid fibromatosis, inflammatory myofibroblastic tumors (IMTs), tumefactive fibroinflammatory lesions (TFLs) and myofibroma. BFH is a proliferation of fibroblastic spindled and stellate cells with overlying epidermal hyperplasia and lateral entrapment of collagen fibers. Immunohistochemical studies typically reveal only focal immunoreactivity for actin and variable numbers of Factor XIIIa-positive dendritic cells. Compared to NF, BFH contains a more organized arrangement of cells rather than a “tissue-culture” appearance and rarely has subcutaneous infiltration, with only superficial involvement when present. On the other hand, deep BFH is characteristically situated in soft tissue and may enter the differential diagnosis with NF, especially in cellular examples. Deep BFH often shows osteoclast-like giant cells, intratumoral inflammation and stromal hyalinization, similar to many cases of NF; however, they are also generally well circumscribed, have storiform architecture, and up to 40% have CD34 positivity and a staghorn vascular pattern with usual actin negativity. These latter features are generally lacking in NF.

Schwannomas may show myxoid degeneration and variable cellularity and mimic NF but are encapsulated, have hyalinized vessels and contain S-100 positive Schwann cells. DFSP is extremely infiltrative and contains a monomorphous proliferation of CD34 positive fibroblasts arranged in a characteristic storiform growth pattern. Desmoid fibromatosis consists of long and sweeping fascicles of benign appearing fibroblasts/myofibroblasts set in a collagenous, sometimes keloid-like background. In contrast to NF, it is extremely infiltrative, has a variably prominent thin-walled vascular pattern and has a tendency for locally aggressive behavior. In addition, it rarely shows more than focal actin staining and typically does not contain myxoid change outside of mesenteric examples.

Two tumors, which enter the differential diagnosis of NF on the basis of prominent inflammation, include IMT and TFL. TFLs are related to retroperitoneal fibrosis, Reidel’s thyroiditis and sclerosing mediastinitis. They are composed of a fibroblastic proliferation with dense sclerosis and prominent inflammation. They differ from typical NF in being less cellular, more sclerosing and containing more prominent chronic inflammation and admixed neutrophils. They also have a greater capacity for recurrence than NF. IMTs may have areas with an “NF-like” appearance. However, the inflammation in IMT is more heterogeneous with lymphocytes, neutrophils, eosinophils and conspicuous plasma cells. IMTs are also generally larger than NF with an average size of >6.0 cm. Careful examination of large lesions should make an easy distinction from NF possible in most cases. A portion of IMTs are associated with anaplastic lymphoma kinase-1 (ALK-1) positivity with some showing rearrangement of the gene by fluorescence in situ hybridization (FISH) or other techniques. This would be most important to exclude in younger patients with NF, as most ALK-1 positive IMTs occur in young patients, although only rarely in head and neck locations. Immunohistochemistry can be used in this regard; however, a negative finding does not exclude IMT completely rendering this of little value in the majority of cases.

Intravascular examples of fasciitis [intravascular fascitis (IVF)] may enter the differential diagnosis with myofibroma, which is a relatively common lesion in the head and neck region, particularly the oral cavity. Myofibroma may show spindle cell areas with a collagenous background, show striking actin positivity and extend into vessels at the periphery of the lesion, similar to IVF. In contrast to IVF, however, myofibroma often contains areas with small

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round cells and a staghorn vascular pattern and has a chondroid-like appearance to the stroma as opposed to the myxoid and cystic appearance of the stroma of fasciitis. In addition, myofibroma does not contain osteoclast-like giant cells.

In summary, we have described the clinicopathologic features of 30 cases of NF of the head and neck. While these cases have the typical histologic features of NF identified at other anatomic sites, the lesions have a tendency to have a smaller size, an increased frequency of skeletal muscle involvement compared to fasciitis elsewhere in the body and diffuse and strong actin expression. The differential diagnosis of NF of the head and neck is broad. Therefore, awareness by general and head and neck pathologists that NF can arise in this region is helpful in accurately diagnosing this sometimes problematic diagnosis and avoiding unnecessary additional treatments after simple/incomplete excisions.

References

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