Case Report

The Counterfeit Canker- Intradermal Nodular Fasciitis

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Preface

Nodular fasciitis is denominated as a benign, proliferative, self- limiting neoplasm of fibroblastic or myofibroblast derivation. Although an exceptional neoplasm of obscure etiology, nodular fasciitis is a frequently delineated pseudo-sarcoma of soft tissues. Nodular fasciitis was initially scripted by Konwaler et al in 1955 and was nomenclated as “subcutaneous pseudo sarcomatous fibromatosis”. Although previously denominated as pseudo sarcomatous fasciitis, nodular fasciitis can additionally be designated as cranial fasciitis (**1**).

On historic analysis, nodular fasciitis was probably contemplated as traumatic in origin. Nevertheless, a sporadic emergence of the neoplasm is currently envisaged (**1**).
On account of rapid neoplastic progression, infiltrative tumor evolution, enhanced cellularity, elevated mitotic activity, or histopathological simulation, nodular fasciitis can be misinterpreted as a malignant neoplasm. As nodular fasciitis is a benign neoplasm, it is essential to circumvent a misinterpretation and initiation of a subsequent, inappropriately aggressive therapeutic intervention (**1**,**2**).

Disease Characteristics

Nodular fasciitis is traditionally described as a benign, self-limiting, fibrous neoplasia delineating a predilection for upper extremities, trunk or head and neck. Like a benign, self-limiting, pseudo sarcomatous neoplasm, nodular fasciitis is comprised of vascular and fibroblastic cellular

proliferation. Traditionally, nodular fasciitis was considered to be a reactive condition instead of a definitive neoplasm. Of obscure pathogenesis, nodular fasciitis can be triggered by a traumatic incident. Nevertheless, the history of preceding trauma is discerned in singularly few instances (**1**,**2**).

Chromosomal rearrangement of ubiquitin-specific protease 6 (USP6) gene emerges as a repetitive and specific feature. Thus, nodular fasciitis can be contemplated to represent a clonal neoplastic proliferation. The majority (100%) of instances of nodular fasciitis delineate the commonly discerned genetic fusion product MYH9-USP6 in addition to the exemplification of chromosomal fusion of USP6 with diverse genetic associates (**2**,**3**).

As a common mesenchymal neoplasm, nodular fasciitis usually occurs in young adults or betwixt third to the sixth decade although the tumor can arise at virtually any age and no age of disease emergence is exempt. A gender predilection is absent and males are incriminated with the equal frequency as the females. Anatomic distribution of nodular fasciitis is comprehensive and the tumefaction can emerge at any site (**2**,**3**).

Nodular fasciitis is a neoplasm that can reoccur. However, tumor relapse is extremely exceptional thus a reoccurring neoplasm, previously diagnosed as nodular fasciitis, can configure as a malignant tumefaction upon a critical reassessment. Nodular fasciitis commonly represents a diagnostic challenge (**2**,**3**).

Clinical Elucidation

Typically, the tumefaction appears as a briskly enhancing, asymptomatic, tender, firm, subcutaneous nodule with a smooth extraneous surface, restricted mobility, tumor magnitude betwixt two to three centimeters and an uninvolved superimposed epidermis. The neoplasm is initially insolent and can rapidly enlarge over weeks or usually within three months.

Generally, lesions of nodular fasciitis are miniature, beneath <3 centimeter magnitude although the tumefaction can be enlarged. The nodule is tender, mildly painful, or asymptomatic wherein a rapid progression of the tumefaction can be indicative of malignant metamorphoses (**3**,**4**). Nodular fasciitis commonly originates within the subcutaneous tissue although the neoplasm can also emerge within the dermis, fascia, or skeletal muscle. A frequent site of tumor implication is the upper extremity, especially forearm, followed by trunk, lower extremity, or head and neck region. Intradermal nodular fasciitis is uncommon within the dermis (**3**,**4**). Additionally, nodular fasciitis can be observed within unusual, divergent locations such as an intravascular, intra-parotid, cranial or placental neoplasm (**4**).

Histological Elucidation

A cogent tissue specimen demonstrates a spheroidal, greyish- white, un-encapsulated, and well-circumscribed neoplasm. On gross examination, the tumefaction is yellow-white, solid, nodular, rubbery, or lobulated. Macroscopic assessment depicts a solitary nodule typically below < 3-centimeter magnitude which can infrequently enlarge up to 7 centimeters. The neoplasm delineates a white, grey, tan, or light pink nodule with a glistening cut surface, soft to firm consistency besides a tumor periphery which can be circumscribed or infiltrative (**4**,**5**).

Morphological assessment depicts a subcutaneous tumefaction appearing adjacent to sparsely disseminated skeletal muscle fibers. The neoplasm is comprised of cellular proliferation of myofibroblast, spindle-shaped cells with a “tissue –culture” like a pattern of tumor growth. Cellular component demonstrates miniature, distinct nucleoli with a lack of cellular and nuclear

atypia.

Intermingled stroma is myxoid, accompanied by extravasation of red blood cells and minimal quantities of mature lymphocytes (**4**,**5**). On microscopy, nodular fasciitis characteristically displays the proliferation of spindle-shaped cells in a haphazard configuration intermingled within a myxoid stroma. An abundance of mitotic figures is observed, although atypical mitotic forms are absent. An accompanying network of capillaries, miniature blood vessels, and extravasation of erythrocytes is exemplified (**4**,**5**). Nodular fasciitis is variably cellular and encompassing extracellular matrix ranges from myxoid to collagenous. Ancient lesions are comprised of a predominantly collagenous stroma. Areas of cystic degeneration are discerned. Spindle-shaped or stellate cells are configured within a loosely articulated, fascicular to the storiform pattern, thus creating a "tissue- culture" like or a feathery pattern of tumor evolution. Bland, ovoid nuclei, scattered lymphocytes, histiocytes, and osteoclast-like giant cells are often delineated (**5**). The neoplasm is un-encapsulated and well circumscribed. As tumor cellularity is variable, the neoplasm can be hyper-cellular and constituted by bland, uniform, spindle-shaped cells arranged in fascicles or "tissue culture"- like pattern. Stroma is variable, loosely disseminated, myxoid, focally microcystic, or collagenous. Disseminated lymphocytes, plasma cells, and mast cells are frequently discerned (**5**). Nodular fasciitis is sub-classified into three distinct categories contingent to neoplastic occurrence emerging in concurrence with the fascia as subcutaneous, intramuscular, or a fascial neoplasm. A subcutaneous variant of nodular fasciitis is a frequent subtype (**5**).

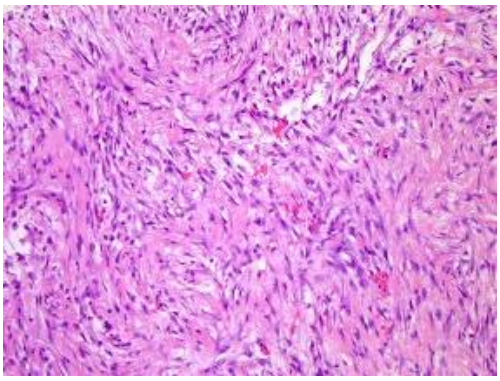

Figure 1: Nodular fasciitis demonstrating bundles and fascicles of spindle-shaped cells, few mitotic figures, minimal cytological atypia and a prominent vascular pattern (**9**).

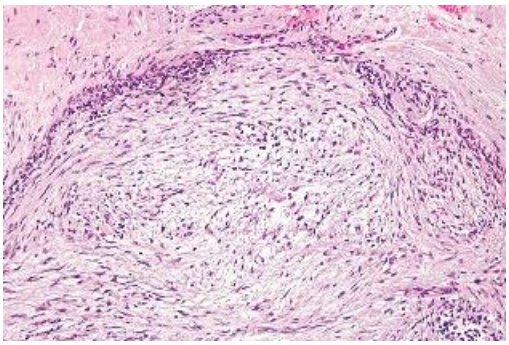

Figure 2: Nodular fasciitis depicting whorls and bundles of spindle-shaped cells with milatypia, prominent vasculature and occasional mitosis (**10**).

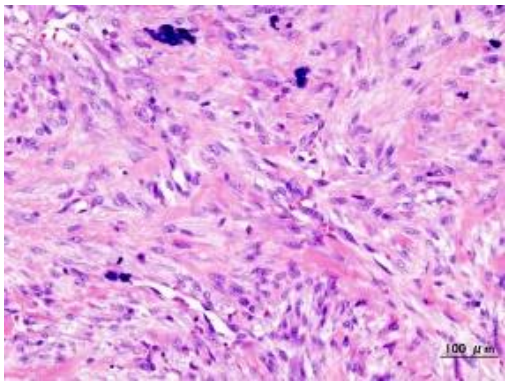

Figure 2: Nodular fasciitis delineating a plump, spindle cell configuration, few mitotic figures, a fascicular architecture and preponderant capillaries (**11**).

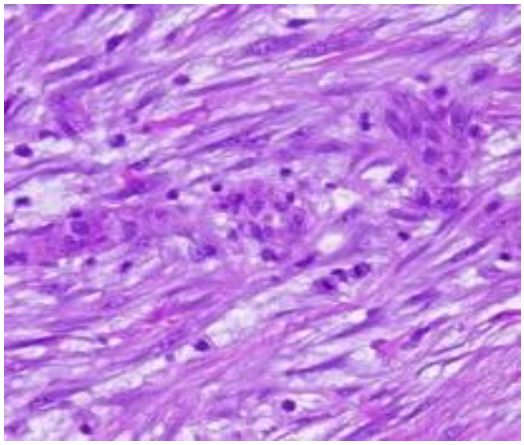

Figure 3: Nodular fasciitis exemplifying fascicles and bundles of spindle-shaped cells, mild atypia, occasional mitotic figures and red cell extravasation (**12**).

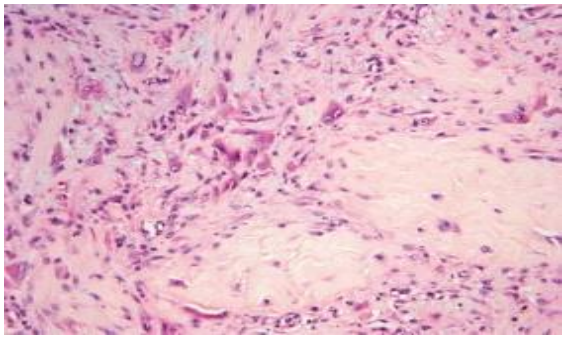

Figure 4: Nodular fasciitis with fascicles of spindly cells with uniform, wavy nuclei, foci of fibrous tissue aggregates and prominent vascularity with red cell extravasation (**13**).

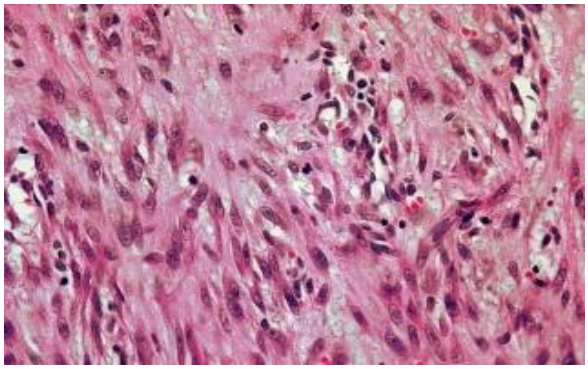

Figure 5: Nodular fasciitis with fascicles of plump spindle-shaped cells, patent capillaries, red cell extravasation, aggregates of fibrous tissue and occasional mitotic figure (**14**)

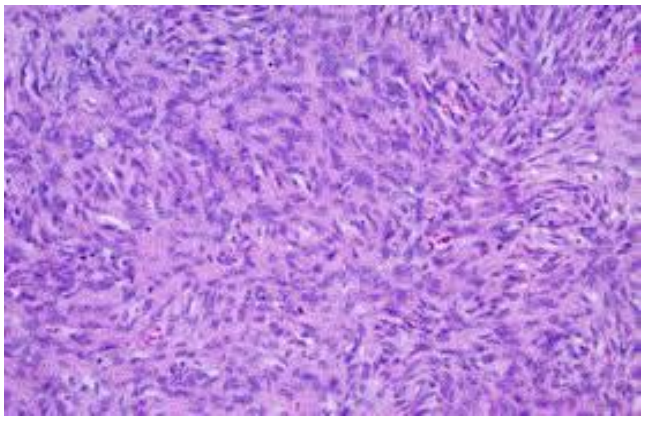

Figure 6: Nodular fasciitis with whorls, fascicles and articulations of plump, spindle-shaped cells, entangled fibrous tissue fragments and occasional mitosis (**15**).

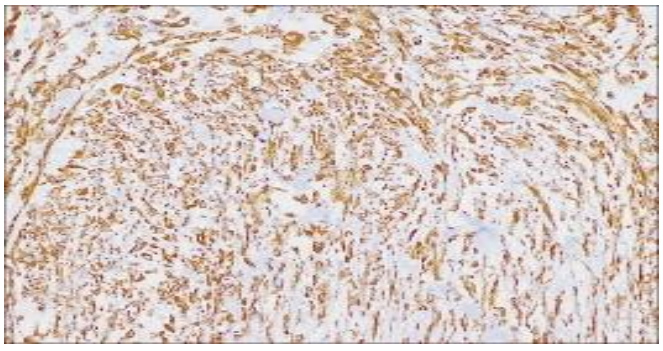

Figure 7: Nodular fasciitis enunciating immune reactivity to vimentin (**16**).

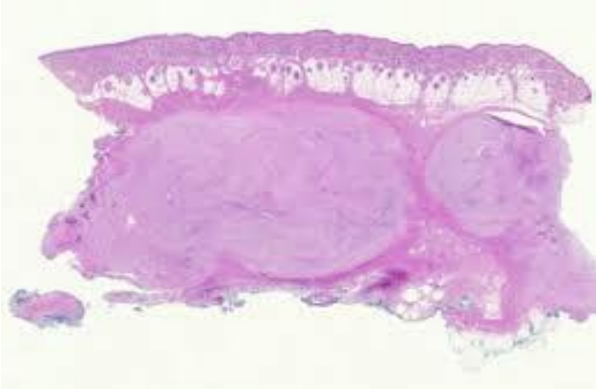

Figure 8: Nodular fasciitis enunciating distinct nodules composed of spindle-shaped cells articulating fascicles, a circumscription with fibrous tissue and a hyperplastic superimposed epithelium (**17**).

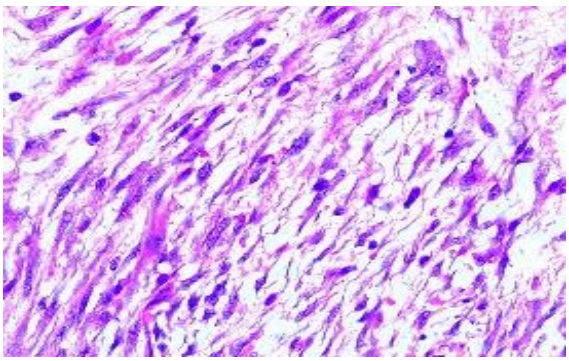

Figure 9: Nodular fasciitis with distinct bundles and fascicles of plump, spindles-shaped cells, lymphocytes, giant cells, few mitotic figures and fragments of fibrous tissue (**18**).

Immune Histochemical Elucidation

Cogent immune reactivity is beneficial in accurately interpreting the neoplasm. Characteristically, the neoplasm is immune reactive to smooth muscle actin (SMA) and vimentin. The neoplasm is immune nonreactive to S100 protein, cytokeratin AE1/AE3, epithelial membrane antigen (EMA), or CD34.

Nodular fasciitis is immune reactive to muscle-specific actin (MSA) and Calponin. The neoplasm is immune nonreactive to desmin, h-caldesmon, Sry-related HMG –box gene 10 (SOX10), and ETS related gene (ERG)(6,7). On ultrastructural examination, typical manifestations of fibroblasts are discerned in addition to peripheral or longitudinal myofilaments and hemidesmosome- like structures. Genomic rearrangement of the MYH9-USP6 fusion gene is discerned comprehensively within the tumefaction (**6**).

Differential Diagnosis

Nodular fasciitis requires clinical segregation from diverse neoplasia such as lipoma, fibromatosis, dermatofibroma, neuroma, neurofibroma, myxoma, benign cyst, benign and malignant fibrous histiocytoma, dermatofibrosarcoma protuberans, fibrosarcoma, leiomyosarcoma, spindle cell carcinoma, and malignant melanoma. Nodular fasciitis requires a distinction from

dermatofibrosarcoma protuberans which predominantly depicts a storiform pattern and is diffusely immune reactive to CD34(6,7). A desmoid subtype of fibromatosis preponderantly delineates a fascicular configuration besides the enunciation of beta-catenin.

Intradermal nodular fasciitis requires segregation from fibrous histiocytoma and spindle cell sarcomas. A fibrous histiocytoma is comprised of spindle-shaped cells admixed with histiocytic cells, entrapped bundles of collagen, and hyaline substance appearing at the tumor perimeter. Superimposed epidermis demonstrates acanthosis. Fibrous histiocytoma essentially exhibits a mixed cellular population with innumerable foamy macrophages, peripheral entrapment of collagen fibers along with a variable immune reactivity to Factor XIIIa (**6**,**7**).

Nodular fasciitis can be misinterpreted as a sarcoma especially in tissue specimens demonstrating enhanced cellularity and frequent mitotic activity. Nevertheless, in contrast to spindle cell soft tissue sarcomas, nodular fasciitis is a miniature neoplasm that progresses rapidly in addition to a discernible lack of nuclear hyperchromasia, pleomorphism, and atypical mitoses (**7**).

Investigative Assay

Nodular fasciitis is a morphologically distinctive neoplasm and can be adequately classified on a paraffin-embedded, hematoxylin and eosin-stained section. As the tumefaction depicts fibroblastic or my fibroblastic immune phenotype, a cogent immune histochemical reactivity is minimally beneficial for the ascertainment of the neoplasm. Genomic rearrangements of the USP6 gene can be confirmed by fluorescent in situ hybridization (FISH), polymerase chain reaction (PCR), ribonucleic acid (RNA) sequencing, or next-generation sequencing (NGS) (**7**,**8**).

Cogent radiographic imaging and magnetic resonance imaging (MRI) is comprised of nonspecific features and the distinction of nodular fasciitis from a definitive sarcoma can be challenging (**8**).

Computerized tomography (CT) demonstrates a well-defined, nodular, soft tissue neoplasm with the absence of concomitant, encompassing bone destruction. As nodular fasciitis is considered a benign neoplasm a superior prognosis is encountered (**8**).

Therapeutic Options

A comprehensive, localized surgical extermination of the neoplasm is recommended. However, the tumefaction often retrogresses spontaneously and neoplastic reoccurrence is extremely exceptional (**8**). Localized surgical extermination of the tumor is a therapeutic preference although partial surgical eradication can be satisfactory as a residual mass of nodular fasciitis can subsequently retrogress or undergo scarring. Conservative treatment with appropriate monitoring can be adopted as a satisfactory treatment option as nodular fasciitis can spontaneously regress (**7**,**8**). Thus, simple surgical extermination of the neoplasm is generally curative. Spontaneous retrogression of nodular fasciitis can be suitably determined with a competently obtained tissue specimen. Inadequate surgical excision is infrequently accompanied by tumor relapse (**7**,**8**).

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