

## ORAL FIBRO-HISTIOCYTIC LESIONS: IMMUNO-HISTOLOGICAL INVESTIGATION AND REVIEW OF AN UNUSUAL PRESENTATION IN THE TONGUE

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### ABSTRACT

*A right sided mid-tongue growth in a 14-year-old boy diagnosed initially as Pyogenic Granuloma was found subsequently to be a Benign Fibrous Histiocytoma. This lesion had three seeming recurrences with divergent histologic and clinical appearances within a short period of time. Although there was eventual consensus on the morphogenesis and benign histologic nature of the lesion this caused diagnostic and management problems and a potential prognostic dilemma. This report on a unique and aggressive head and neck lesion, possibly the third documented case in the tongue, reviews the bewildering spectrum of clinical and immuno- histologic manifestations of fibrous histiocytic lesions. Wide excision with close follow up is recommended.*

**Key words:** Benign Fibrous Histiocytoma; Inflammatory Pseudotumour; Malignant Fibrous Histiocytoma, Tongue; Pyogenic Granuloma

### INTRODUCTION

Fibrous histiocytoma is a rare head and neck lesion, even rarer in the mouth.<sup>1,2,3</sup> There is a whole spectrum of fibro-histiocytic lesions ranging from benign to malignant. While the malignant fibrous histiocytoma (MFH) is the most common soft tissue sarcoma in adults, benign fibrous histiocytomas (BFH) are relatively uncommon. Pathologic and clinical variants make the diagnosis of these, especially those with clinically aggressive behavior or of an intermediate nature, considerably more complex. This makes management a problem and may affect the eventual prognosis.

A case report of an aggressive, deep benign fibrous histiocytoma (BFH) of the tongue is presented. Different clinical manifestations and three varied histologic diagnostic patterns make this an unusual case. This

would seem to be the third documented case of BFH of the tongue.<sup>4,5</sup> Because of the rarity of both the lesion and, specifically in this location, a literature review was done. This paper examines the bewildering spectrum of histologic variants and clinical manifestations of fibro-histiocytic lesions with emphasis on those in which aggressive and controversial clinical behavior blurs the distinction between benign and malignant.

### CASE REPORT

A healthy 14 year old boy presented to the OMFS clinic on 15 October, 1998, with a 22 month history of a recurrent growth on the right ventrolateral surface of the mid- tongue. Fig 1. The lesion was a sessile, ulcerated, non-tender, 4 x 1 cm spongy growth. It had a reddish brown color and resembled an exophytic response to a laceration. The growth had previously

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been removed when it ulcerated three months earlier. The pathology report (q.v.) was of a pyogenic granuloma.

A routine excision was planned under general anesthesia. In routine tests he had a Hb.12.7G, WBC count of 11,200 with 50% neutrophils, 40% lymphocytes 2% monocytes and eosinophilia of 8%. ESR was 43mm Westergren. Chest x-ray and other tests were normal. We attributed the changes to chronic inflammation and the eosinophilia to intestinal or liver parasites that are quite common here.

At surgery on 31 October the lesion was vascular, fibrous to touch and extended deep into the tongue exhibiting yellow-brown granules. Direct closure was done following the wedge type excision. Our differential diagnosis now included tuberculosis, other chronic infections, and malignancy. A subsequent Mantoux test was negative. The biopsy report (q.v.) was of a deep fibrous histiocytoma.

Three weeks later he returned with two smooth lumps at the same site. Fig 2. A CT, followed by a MRI scan showed a 1.0 x 0.5cm mass involving the postero-dorsal surface of the tongue and abutting the palatoglossus, the tensor palate and the digastric muscles. Fig 3. The mandible and lymph nodes were uninvolved.

A partial right hemi-glossectomy was done on 19 December. This report (q.v.) had no evidence of tumour and essentially, was a foreign body giant cell reaction. In view of the unusual features we sought an opinion from the Armed Forces Institute of Pathology at Washington (q.v.). They concurred with the diagnosis recommending excision and close follow-up as the lesion could potentially recur. The patient was kept under strict follow-up and was free from tumor 2 years later. He has since been lost to review.

## **PATHOLOGIC FINDINGS**

Two pieces, 1.3x 0.5cm and 0.7x 0.4cm were removed on 26.7.1998. Histopathologic examination revealed: "a lesion comprising of numerous vascular channels interspersed within inflamed stroma. Features were consistent with pyogenic granuloma."

Two pieces, 3x 2x 1.5cm and 2x 1x 0.5cm were removed in our excision on 31.10.1998. Histopathologic report stated: "Ulcerated squamous epithelium with

underlying tissue showing areas mimicking granuloma pyogenicum. Deeper areas however exhibited a spindle cell lesion with cells arranged in a storiform pattern and showing a few normal mitotic figures. A number of giant cells and foamy histiocytes were also present along with inflammatory cells. The lesion was poorly circumscribed. No evidence of nuclear atypia, necrosis or abnormal mitoses was seen. Features were consistent with deep fibrous histiocytoma. Initial diagnosis of pyogenic granuloma was probably made on the biopsy material taken from the superficial portions of the lesion that showed numerous vascular channels". Fig 4 (a, b).

One large piece, 5x 4x 2.7cm was removed in our second, wide excision, procedure on 19.12.1998. Histopathologic report stated: "hyperplastic squamous epithelium with marked underlying fibrosis and chronic inflammation with multiple foci of foreign body giant cell reaction. Only focally spindle cell proliferation of fibroblasts seen. However, no convincing evidence of residual tumor was identified"

On submission of 4 micro-slides and 1 tissue block to the AFIP Washington their report of 21.12.1998 concurred. "The ulcerated lobulated 1.8 cm capillary-rich lingual nodule demonstrates sheets of 'histiocytic' to plump fusiform cells (focally forming storiform interlacing fascicles) and a diffuse moderate infiltrate of inflammatory cells (including lymphocytes, macrophages [some representing lipid laden xanthoma cells] plasma cells, granulocytes, and infrequent multinucleated giant cells). The cells exhibit focal nuclear atypia, and focal evidence of an elevated mitotic index is seen. The section immunostained for CD34 [QBEND] displays numerous evenly dispersed capillaries, but "histiocytic" or fusiform stromal cells lack CD34 immunoreactivity. Predominantly perivascular myoid / pericytic cells are immunoreactive for smooth muscle actin [IA4], but plump lesional stromal cells are smooth muscle actin immunonegative [a significant myofibroblastic component is not appreciated]. The scattered multinucleated giant cells display the greatest immunoreactivity for the lysosomal marker CD68 [KPI]. Lesional stromal cells lack immunoreactivity for cytokeratin [AE1/AE3 and CKI cocktail], S100 protein, muscle specific actin [HHF 35] and desmin [De-R-II]. We interpret these histologic features and immunohistochemical findings to be most suggestive of an in-

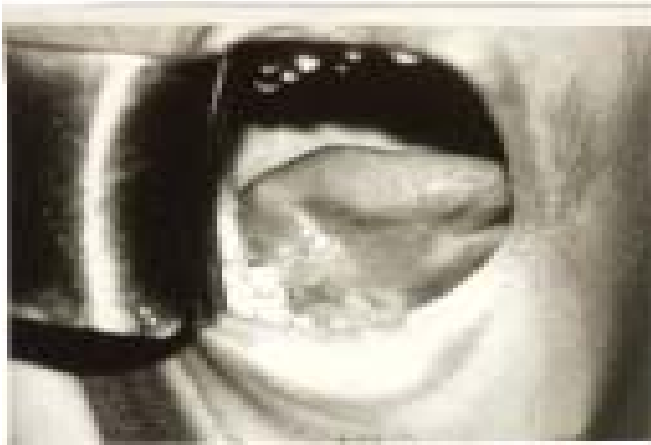


Fig 1: Ulcerated growth on the right ventrolateral side of the tongue on initial presentation



Fig 2: Tongue showing twin lumps (large arrows) three weeks after initial resection. The thin arrow marks the site of previous surgery



Fig 3: Magnetic Resonance image (MRI) T2 weighted coronal scan showing mass (arrowed) in the right postero dorsal aspect of the tongue.

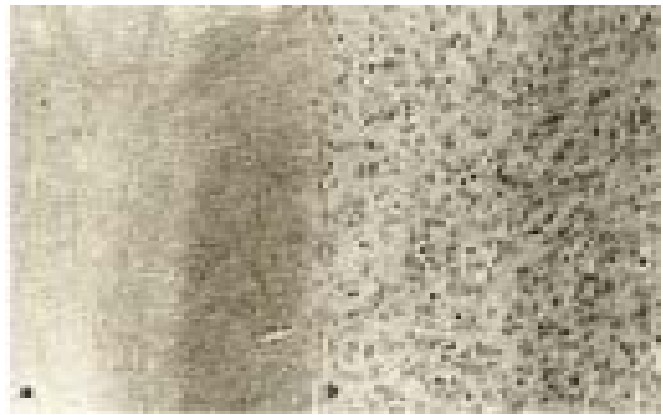


Fig 4: Deep fibrous histiocytoma pattern seen following our initial excision. **a.** (H&E, original magnification x10). **b.** (H&E, original magnification x40). See text for details.

flamed fibro-histiocytic proliferation or a benign cellular fibrous histiocytoma. Conservative but complete excision and / or close follow up might be considered (this lesion could potentially recur / persist). Features permitting a malignant interpretation are not observed”.

## DISCUSSION

Pyogenic granuloma is a common growth thought to be an exuberant tissue response to local irritation, trauma and non-specific infection occurring in a wide age range and with no gender preference.<sup>2</sup> There is an overzealous proliferation of a vascular type of connective tissue which may become progressively more fibrous in older lesions.<sup>6</sup> The tongue is one of the common sites and the clinical appearance can mimic more aggressive lesions. Pyogenic granulomas often recur especially following conservative but inadequate removal. The initial appearance resembled a pyogenic granuloma and, in conjunction with the histologic picture, provided no cause for concern. The mildly elevated white blood cell count was attributed to chronic infection and possible parasites or allergy. Our first excision was conservative but probably adequate. The presence of yellowish brown “granules” and the excessive fibrous feel to the lesion was unusual and raised the possibility of other etiology. A raised ESR even in the absence of other significant pathology may be associated with tuberculous infection.<sup>7,8</sup> Oral manifestations of tuberculosis,<sup>9</sup> often as the primary presentation and in young persons, are increasingly being seen.<sup>10</sup> The tongue may be involved in nearly 20% of

oral presentations as a nodular, granular or ulcerated area.<sup>11</sup> Our differential diagnosis reflected this. However, both chest X-ray and the Mantoux test, a simple screen, even if of questionable value, were negative.<sup>12,13</sup> Positivity runs as high as 80% in developing countries.<sup>11</sup>

Fibrohistiocytic tumors form a large and divergent group of cutaneous and soft tissue neoplasms with a wide spectrum of clinical and histopathologic characteristics that range from the benign to the frankly malignant.<sup>1,14</sup> Much material is available on the malignant neoplasms but surprisingly little on the benign or intermediate. This is where the diagnostic and management problems arise.

Kaufmann and Stout<sup>15</sup> first established the Fibrous Histiocytoma as a distinct clinico-pathologic entity in 1961. It is a mesenchymal tumor where the histiocyte, under appropriate conditions, could assume the function of facultative fibroblasts capable of differentiating both into histiocytes and fibroblasts and thus accounting for the dual cell population commonly seen in this tumor.<sup>16</sup> An alternative view favors an undifferentiated mesenchymal cell or the fibroblast as the progenitor cell which give rise to both fibroblast and histiocyte like cells.<sup>16</sup> Even the phenotypic markers based on tissue cultures and immunochemical analysis have not fully resolved the question of histiogenesis, which still remains uncertain.<sup>2,17</sup>

Benign Fibrous Histiocytomas (BFH) are uncommon in adults but are the most common fibrohistiocytic tumors in children and adolescents.<sup>1</sup> Regional anatomic distribution favors the head, neck and trunk but it is rare in the oral and perioral region where it tends to occur in middle aged and older adults.<sup>2,3</sup> The tumor usually presents as a firm, nodular, well circumscribed, un-encapsulated, non-tender lump and is often richly vascularized. It is an uncommon benign lesion with aggressive behavior. The differential diagnosis includes a variety of relatively common and innocuous lesions including fibromatosis, foreign body reaction, scar tissue or keloid, granulation tissues, neurofibroma and nevus.<sup>1</sup> Lesions that have pleomorphic histologic features tend to involve bone more frequently and are more likely to be aggressive or malignant than pure soft tissue lesions. In this situation this may be of prognostic importance regardless of the histologic appearance.<sup>18</sup> However, the recurrence rate of these

lesions is stated to be low, especially in the head and neck area.<sup>3</sup>

Dermatofibroma (DF) is a superficial, cutaneous, form of BFH. It is one of the most common cutaneous neoplasms, occurring at any age, with increased frequency in mid- adult life.<sup>2</sup> Histologically, DF is composed of a mixture of fibroblastic and histiocytic cells.<sup>19</sup> The fibroblastic cells are often arranged in a storiform or cartwheel pattern accompanied by variable amounts of collagen and inflammatory cells in the stroma. In children and young adults these may be the dermatologic counterparts of superficial mucosal lesions and may be proliferative, reactive, lesions. Systemic, visceral or deep-seated lesions in the lower extremities appear to be true neoplasms.<sup>20</sup> 10%- 25% of storiform fibrous histiocytomas (dermatofibrosarcoma protuberans) occur in the first two decades of life and may show an intermediate biologic behavior. It has a high recurrence rate and requires wide excision.<sup>21</sup>

Deep Fibrous Histiocytomas may have a more atypical morphological appearance and may invade locally into the surrounding tissues. Non cutaneous soft tissue lesions may be larger and better circumscribed than their cutaneous counterparts and tend to be more monomorphic and have a more consistent storiform pattern.<sup>22</sup> A pericytoma like vascular pattern, xanthoma cells and giant cells may be prominent features: rarely small foci of necrosis and intravascular growth may be seen. The giant cells may be so numerous as to cause difficulties with differentiation from giant cell tumor.<sup>3</sup> Cellular atypia, mitotic activity and necrosis indicate malignant potential.<sup>1</sup> Even in the absence of obvious anaplasia a rapidly growing deep BFH tends to be larger, may achieve a size of 6cm and recur after simple excision.<sup>2</sup> Metastases are rarely seen. In a review of laryngeal BFH<sup>16</sup> it is suggested that histologic features play a disappointingly small role in predicting the biological and clinical behavior of these neoplasms, therefore, the diagnosis of malignancy must frequently be correlated with the clinical course. The fact that such a tumor has negative margins and does not recur some years after wide local excision is consistent with a benign histological diagnosis.

Another paper discusses an Inflammatory Pseudotumor (IP) in the Submandibular gland.<sup>23</sup> This shows rapid growth, local invasiveness and recurrence



and the ultrasound, CT and MRI aspects are confusing and can mimic both benign and malignant neoplasms, therefore the histopathologic diagnosis may be a challenge. Histopathology of IP covers a spectrum of appearances according to the cellularity and degree of fibrosis. It shows a variable mixture of three main cell types: histiocytes or macrophages, myofibroblasts or fibroblasts and abundant plasma cells with low mitotic activity and absence of cytological abnormalities in an ill-circumscribed and rather fibrous lesion. Immunohistochemistry is of value in identification. These are rare oral lesions, more common in the lung where they may be low-grade mesenchymal neoplasms with a secondary inflammatory component, capable of aggressive and unpredictable biologic behavior.<sup>14</sup> Again, our case bears a resemblance to some of these features.

A recent paper reports the first case of an epithelioid cell histiocytoma presenting on the ventral mucosal tongue surface of an 84 year old woman.<sup>24</sup> Although this lesion has three distinct cell populations, ie, epithelioid histiocytes, dermal dendrocytes and mast cells, which are contained in a richly vascularized connective tissue and may be further identified through a battery of immunohistochemical tests this benign dermal dendrocytic tumor is often histologically confused with both the pyogenic granuloma and the BFH which it is considered by some to be a variant of.<sup>24</sup> In the review of the literature and on both clinical and histologic grounds this lesion bears the closest resemblance to our rapidly growing exophytic lesion.

Malignant Fibrous Histiocytoma (MFH) is the most common soft tissue sarcoma in adults and most commonly occurring in the extremities and retroperitoneum.<sup>2,17,25</sup> Males are more affected with maximal incidence in the fourth and fifth decades of life.<sup>26</sup> Less than 10% of all MFH occurs in the head and neck region with about 100 cases reported.<sup>27</sup> To date there have been only three cases reported in the tongue.<sup>28</sup> It is uncommon in children and adolescents<sup>29</sup> with less than 6% cases reported in children where 30- 45% occur in the head and neck.<sup>1</sup> Prognosis is complicated by variability in histologic and pathologic patterns and an extensive differential diagnosis. Apart from size and grading a positive surgical margin is the single most important factor leading to local failure. Barnes and Kanbour<sup>26</sup> suggest that MFH involving the head and neck is a more aggressive neoplasm than that in other

sites. MFH of jawbones<sup>30</sup> and oral soft tissues are stated to be more fatal than those in other head and neck sites.<sup>2</sup>

Although intermediate to borderline FH shows some features of IP it can also demonstrate atypical histologic features which can cause diagnostic and management dilemmas. IP usually remains stable or can even reduce in size with complete resolution. Still, up to 10% of IP's grow slowly or quite rapidly. Some cases of IP may be true neoplasms capable of malignant evolution that may prove fatal.<sup>14</sup>

The wide spectrum of fibrohistiocytic lesions thus includes at the one end those with a benign appearance and clinical course such as BFH or IP. At the other end are lesions with obvious malignant features represented by MFH. However, at times, it may be morphologically difficult to distinguish BFH from MFH. Gal *et al*,<sup>14</sup> have suggested histologic identification criteria. Borderline cases have histologic features overlapping between IP and MFH. They are usually morphologically similar to BFH in addition to showing 3 of the following 5 criteria: increased cellularity, focal cytologic pleomorphism, a high mitotic count (3/50 hpf), a possible focus of vascular invasion or focal necrosis.<sup>14,31</sup>

This unusual tongue lesion showed aggressive behavior and histologic features representing the complex spectrum of fibrohistiocytic lesions ranging from BFH to IP. There were also aspects that mimicked borderline fibrohistiocytic lesions. While the absolute criteria for malignancies are well established these features blur the distinction between totally benign and locally aggressive lesions. The application of specific clinical, gross and microscopic pathological criteria and immunohistochemical features,<sup>3,19</sup> helps in the diagnosis provided that, in addition to the histological /morphological features, biological behavior is considered. Immunohistochemical analysis eventually confirmed the benign nature. Diagnosis of benign but locally aggressive lesions must often be corroborated with the clinical course.<sup>16</sup> Wide excision of such lesions is recommended and close follow-up is mandatory. The former may be mutilating; the latter is easier said than done, especially in developing countries where patient follow up is limited and with supposedly benign lesions.

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