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Short Communication

The Blubbery Cumulative- Lipoma

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Preface

Lipoma is a frequently discerned, benign, encapsulated, soft tissue neoplasm composed of aggregates of mature adipose tissue cells. As a derivative of mesenchymal connective tissue, lipoma depicts mature, white adipocytes with uniform nuclei, simulating normal adipose tissue. It is the commonest mesenchymal, soft tissue tumefaction, configuring an estimated 16% of mesenchymal neoplasms.

Fletcher., *et al*. in 1996 cited a clinico-pathological concurrence between cytogenetic anomalies and morphological subtypes of lipoma. Aforesaid genomic and morphological concordance is a cogent methodology to diagnose histologically borderline neoplasms [1].

Disease characteristics

Although lipoma is generally discerned within 40 years to 60 years, no age of disease emergence is exempt. However, the neoplasm is infrequent in children [2].

Certain categories of lipomas are frequent within adjunctive age groups. Specifically, hibernoma manifests clinically at roughly 30 years and lipoblastoma or diffuse lipomatosis usually emerges in children exceeding 3 years. An equivalent gender distribution is exemplified.

Of obscure aetiology, an estimated two thirds (66%) of lipomas demonstrate genetic anomalies. A subset of lipomas exhibit an HMGA2 gene situated upon chromosome 12q14.3, a genomic manoeuver incriminated in tumour pathogenesis [2,3].

Structural chromosomal rearrangements denominated in emergence of lipoma are aberration within 12q13-15 region (65%), 13q segmental loss (10%), genomic rearrangements of 6p21-23 region (5%) along with unidentified chromosomal mutations in diverse loci or normal karyotype (15% to 20%). Rearrangement of chromosome 12q13-15 engenders a genetic fusion of extensively mobile group AT-hook 2 (HMGA2) gene to diverse transcription regulatory domains, fusions which promote tumouri-genesis [2,3].

Around 55% to 75% of solitary lipomas with cytogenetic anomalies depict genomic rearrangements of HMGA2 or HMGIC at chromosome 12q13-15. Nevertheless, aforesaid fusion transcripts lack a concurrence of clinical and pathological manifestations. Marker ring or giant chromosomes are extremely exceptional [3].

It is also posited that lipoma is engendered due to trauma at pertinent sites. Emergence of an adipose tissue neoplasm is contingent to a post traumatic event with direct, site-specific impact. Traumatic trigger generating a lipoma is accompanied by necrosis of adipose tissue cells with subsequent, localized inflammation [3,4].

Endocrine, mechanical or inflammatory mechanisms are implicated. Additionally, lipoma can arise due to factors such as obesity, alcohol intake, hepatic disease, hypercholesterolemia, diabetes mellitus or glucose intolerance. Employment of protease inhibitors in subjects with human immune deficiency virus (HIV) infection can initiate configuration of lipoma or lipodystrophy. A pertinent medical and history of previous infections is significant [3,4].

Prevalence of lipoma is documented to be nearly 1% whereas the incidence appears to be 2.1 per 1000 individuals per year [2,4].

Intra-dural lipoma arising within the spinal cord demonstrates a cogent clinico-pathological significance as the neoplasm is commonly observed within thoracic spinal cord and is frequent within males of 20 years to 40 years. Pertinent clinical symptoms are pain, sensory modifications such as paraparesis and urinary incontinence [2,4].

Multiple lipomatosis is discerned in around 5% to 10% subjects wherein an estimated 2% to 3% multiple lipomas are associated with familial form of disease inheritance and diverse genetic disorders. Multiple lipomas usually delineate a normal karyotype and delineate a female preponderance [3,4].

Multiple lipomas may clinically manifest as a component of various syndromic, genetic disorders such as neurofibromatosis, multiple endocrine neoplasia (MEN) syndrome, Gardner's syndrome, Dercum's disease, familial multiple lipomatosis, Proteus syndrome, multiple hereditary lipomatosis, adiposis dolorosa, Madelung disease, Cowden syndrome (mutation of PTEN gene) constituted by multiple lipomas, facial trichilemmomas, oral papillomas, punctate palmoplantar keratosis and diverse malignancies or Bannayan syndrome comprised of macrocephaly, haemangioma and lipoma [3,4].

On account of depiction of identical characteristics, it is crucial to segregate the commonly discerned lipoma from malignant liposarcoma [2].

Clinical elucidation

Lipoma is composed of mature adipose tissue and is frequent within the cephalic region, especially fat-rich, subcutaneous tissue of head, neck, upper trunk, shoulders, forearm, proximal extremity and dorsal region. The neoplasm is infrequently delineated within acral sites, hand, foot, face, lower limbs or retroperitoneum [5].

Lipoma is exhibited in diverse cutaneous or non-cutaneous sites, dermal or sub-fascial tissues besides emerging as intermuscular, intramuscular, synovial, bone, nervous system or visceral lipomas. Uncommonly, lipoma is exemplified upon oral cavity, pancreas, breast or gastrointestinal tract [4,5].

The neoplasm manifests as a soft, solitary, mobile, painless, gradually progressive, circumscribed, subcutaneous nodule with an unaltered superimposed epithelial layer. Tumefaction enclosed within thin, fibrous tissue capsule is non adherent to underlying skeletal muscle or superficial fascia. After an initial phase of tumour evolution, the neoplasm is stable or static [4,5].

Encapsulated lipoma appears at varying tissue depths as sessile, pedunculated or submerged neoplasm. Lipoma is usually solitary and appears as miniature, well rounded lesion or enlarged, lobulated, inadequately defined tumefaction [4,5].

Tumour magnitude is typically beneath < 2 inches, generally around 2 centimetres to 3 centimetres although enlarged neoplasms may be discerned. Tumefaction exceeding >10 centimetre magnitude are nomenclated as "giant lipoma" [4].

The tumefaction can be painful and encroach upon joints, nerves or vascular configurations.

Intra-oral lipoma is commonly situated within the buccal mucosa, upper lip, lower lip, palate, tongue, buccal sulcus, floor of mouth or salivary glands. Usually, the colour is yellow although variations exist due to density of superimposed mucosa. Intra-oral lipoma appears as a deep-seated nodule with an unremarkable extraneous surface and an estimated incidence of 1% to 4% [2,4].

Buccal mucosa is a common site for intra-oral lipoma as it depicts an abundance of adipose tissue whereas the tongue or hard palate is infrequently implicated on account of minimal adipose tissue. Intra-oral sites incriminated are buccal mucosa (38.7%), tongue (17.9%), lips (12.6 %), vestibule (7.8%), retro-molar area (4.7%) and associated regions (48.8%) [3,4].

Histological elucidation

On gross examination, superficial lipoma displays a bright yellow, homogenous, fat-laden tumefaction enmeshed within a fine, fibrous tissue capsule and trabeculae traversing the neoplasm. Deep-seated neoplasm may be enlarged. Cut surface is greasy and lipid- rich [5,6].

On microscopy, lipoma demonstrates mature adipocytes imbued with abundant adipose tissue and a miniature, eccentric nucleus. Clusters of adipocytes are intermingled with attenuated fibrous tissue septa with disseminated vascular articulations. Nevertheless, lipoma can be misinterpreted as an accumulation of normal, subcutaneous adipocytes. Lipoma is a lobulated neoplasm

comprised of mature adipose tissue cells with minimal, intervening connective tissue stroma and an attenuated fibrous tissue capsule [5,6].

The neoplasm is composed of mature, white adipose tissue and is devoid of atypia. Tumour cells demonstrate anisocytosis and variation of cellular magnitude exceeds normal white adipose tissue cells by two times to five times. Distinctive, enlarged tumour cells display a diameter of up to 300 microns [5,6].

Uniform cytoplasmic vacuoles are exhibited. Tumour cells may delineate intra-nuclear vacuoles. Tumour parenchyma of neoplasm confined to gluteal region, hand or foot is subdivided by dense, fibrous tissue septa. Foci of fat necrosis with configuration of infarct, infiltration of macrophages and superimposed calcification may ensue. Mitotic figures or cellular and nuclear atypia are absent [5,6].

Ultrastructural examination depicts univacuolar, mature adipocytes with compressed, peripheral nuclei and pinocytotic vesicles. Singular cell is enveloped by an extraneous lamina [5,6].

Atypical histological variants of lipoma are denominated by angiolipoma, chondroid lipoma, lipoblastoma, myolipoma, angiomyolipoma, myeloplipoma, fibrolipoma, ossifying lipoma, neural fibrolipoma pleomorphic lipoma/spindle cell lipoma, lipomatosis of nerve, lipoma arborescens, multiple symmetric lipomatosis, diffuse lipomatosis, adiposis dolorosa, hibernoma, intramuscular and intermuscular lipoma or lipoma of tendon sheath and joint [5,6].

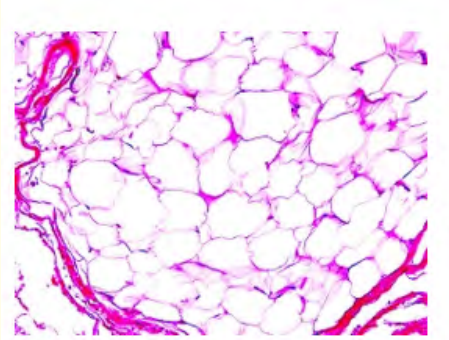

Figure 1: Lipoma manifesting aggregates of mature adipose tissue cells subdivided into lobules by fibrous tissue septa [10].

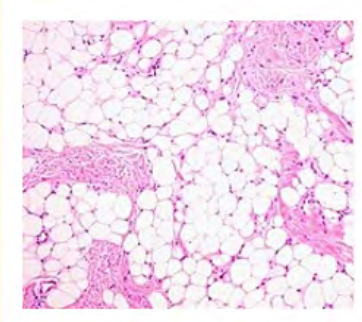

Figure 2: Lipoma delineating accumulation of mature adipose tissue cells intermingled with foci of chronic inflammatory cells and fibrous tissue septa [11].

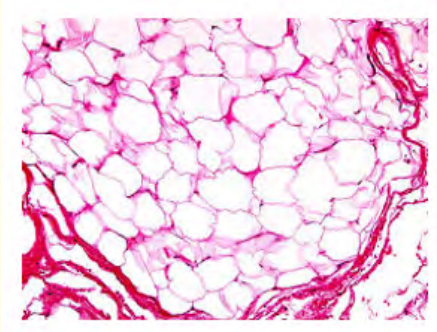

Figure 3: Lipoma enunciating collection of mature adipose tissue cells with peripheral, compressed nuclei and traversing fibrous tissue septa [12].

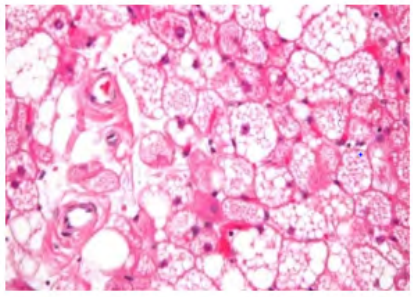

Figure 4: Lipoma exemplifying cells imbued with neutral fats, uniform nuclei and a lobulated architecture with fibrous septa [13].

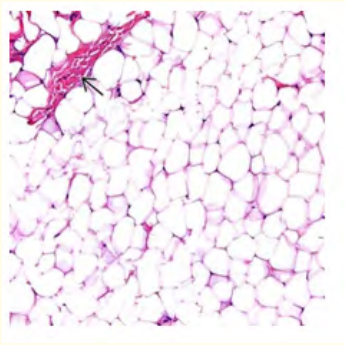

Figure 5: Lipoma exhibiting nests of mature adipose tissue with intracytoplasmic impaction of adult fat and fibrous tissue septa [14].

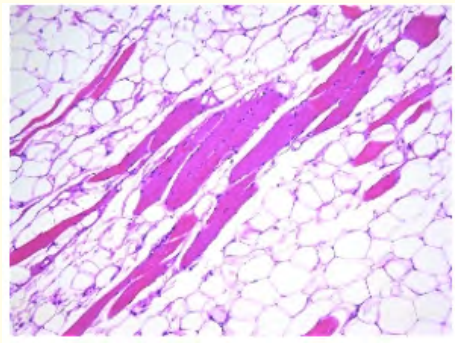

Figure 6: Lipoma depicting clusters of mature adipose tissue cells with compressed, uniform nuclei and intermingled skeletal muscle fibres [15].

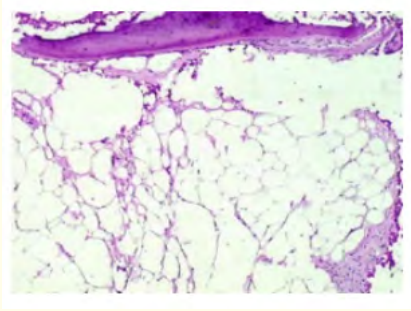

Figure 7: Lipoma delineating accumulation of mature adipose tissue cells with intervening and circumscribing fibrous septa [16].

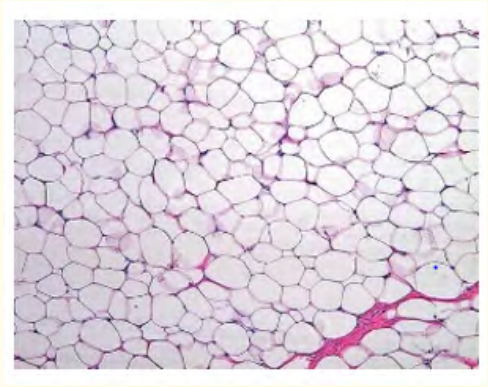

Figure 8: Lipoma demonstrating aggregates of mature adipose tissue cells divided into lobules with fibrous tissue septa [16].

Immune histochemical elucidation

Lipoma is immune reactive to vimentin and S100 protein. The slender, spindle-shaped cells are immune reactive to CD34. Staining with leptin and periodic acid Schiff's (PAS) stain demonstrates capillaries and vascular articulations. Reticulin fibres circumscribe individual adipocytes [2,4].

Differential diagnosis

- Lipoma mandates a segregation from benign and malignant neoplasia such as epidermoid cyst, hibernoma, angiolipoma, angiomyolipoma, and liposarcoma [7].
- Epidermoid cyst typically delineates a superficial punctum. However, epidermoid cyst devoid of a punctum can be indistinguishable from lipoma.
- Hibernoma is an exceptional, benign, gradually progressive neoplasm composed of brown fat. The tumefaction typically arises in adults and is discerned within the mediastinum, inter-scapular or dorsal region. Tumour magnitude varies from 3 centimetres to 12 centimetres.
- Angiolipoma is frequently painful. The neoplasm is typically situated upon acral sites or forearm of teenagers or young adult males. The well circumscribed tumefaction is usually beneath< 2 centimetres in magnitude [7,8].
- Lipoma and common variants necessitate a distinction from liposarcoma which is a malignant, dedifferentiated lipomatous neoplasm constituted of lipoblasts characteristically

incorporated with coarse, lipid vacuoles and singular or multiple, scalloped, hyperchromatic nuclei.

- Liposarcoma commonly represents as a deep-seated neoplasm restricted to the retroperitoneum or classically emerges upon the thigh.
- Normal adipose tissue is non-circumscribed and un-encapsulated. Distinct tumour nodule is absent [7,8].
- Pneumatosis cystoides intestinalis appearing within the small intestine is not configured by aggregation of adipocytes.
- Mesenchymal cells generating acid muco-polysaccharides are denominated by fluid-filled vacuoles. Cellular outlines are indistinct and nuclei are not compressed or contorted [7,8].
- Haematoma delineates a cystic cavity incorporated with necrotic debris, coagulation products and fibrin fragments. Cyst wall demonstrates hyalinised fibrous tissue, chronic inflammatory cells and granulation tissue [7,8].
- Panniculitis is associated with lobular neutrophilic infiltration and focal fat necrosis.
- Intra-oral lipoma requires a distinction from salivary gland or associated benign mesenchymal neoplasms.
- Adjunctive adipocytic tumours exemplify pertinent morphological features contingent to specific mesenchymal constituents of the neoplasm such as cartilage, bone, blood vessels or fibrous tissue [7,8].

Investigative assay

Lipoma can be adequately diagnosed by a competent physical examination. Differentiation of superficial, subcutaneous lipoma, deep-seated lipoma articulated beneath an enclosing fascia and the infrequent intermuscular or intramuscular lipoma can be achieved. Cogent tissue sampling and subsequent analysis is not routinely required as clinical determination of the benign neoplasm is satisfactory. Besides, histological differentiation of lipoma from adjunctive, normal mature adipose tissue can be challenging [9].

However, specimens received following surgical excision are subjected to appropriate histological evaluation [8,9].

Radiographic imaging prior to surgical extermination is recommended in pertinent instances such as giant lipoma exceeding 10 centimetre magnitude, rapidly enhancing lipoma, occurrence of pain, adherence to underlying soft tissue and deep-seated lipoma as discerned within thigh or retroperitoneal space [8,9].

Ultrasonography of the tumefaction demonstrates a lipoma or adipose tissue aggregation which is deep-seated or disparate from circumscribing mature adipose tissue [8,9].

Diverse adipocytic neoplasia can be segregated with cogent gene sequencing on account of demonstrable genetic anomalies [9].

Therapeutic options

Lipoma is an innocuous neoplasm mandating therapy or surgical excision on account of pain, inappropriate tumour sites, inferior cosmetic outcomes with subcutaneous localization or a detrimental visceral function. Treatment is usually unnecessary unless the benign neoplasm is rapidly progressive or appears upon inconvenient sites such as joints [8,9].

Lesions are stable and spontaneous involution of lipoma is undocumented. Lipoma can be highlighted or made prominent with significant weight loss. Adopted therapeutic strategies are contingent to factors such as tumour magnitude, anatomic location, cogent clinical symptoms as pain and associated comorbid conditions [8,9].

Surgical extermination with eradication of tumour capsule is a desirable and commonly adopted treatment option. Enlarged lipoma can be eradicated with liposuction. Administration of steroids is beneficial.

As liposuction or surgical eradication of the neoplasm is efficaciously employed, surgical extermination can circumvent tumour reoccurrence, although comprehensive and competent eradication of tumour capsule is mandated to decimate proportionate tumour relapse [8,9].

Surgical eradication of lipoma is preferably adopted for miniature neoplasms as enlarged tumours can impinge upon joints, nerves or vascular articulations and surgical resection can be challenging and infiltrative [9].

An aggressive surgical excision can penetrate tumour capsulate and engender spillage of tumour cells which may generate tumour

reoccurrence. Thus, a firm, non- aggressive surgical resection with competent peripheral dissection of circumscribing soft tissue is recommended [9].

Additional, applicable therapeutic techniques are intra-lesional, transcutaneous sodium deoxy-cholate in combination with or absence of injectable phosphatidylcholine, intra-lesional steroids in conjunction with injectable isoproterenol (beta-2 adrenergic agonist) [8,9].

Surgical extermination of benign lipoma is accompanied by superior prognostic outcomes. Tumours excised for cosmetic concerns are often devoid of tumour reoccurrence. An estimated 1% to 4% of lipomas are associated with tumour reoccurrence [8,9].

As lipoma is a benign tumefaction, additional radiotherapy or chemotherapy is unnecessary [9].

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10. Image 1 Courtesy: Pathology outlines.
11. Image 2 Courtesy: Wikiepedia.com.
12. Image 3 Courtesy: Nikon microscopyu.com.
13. Image 4 Courtesy: Orthobullets.com.
14. Image 5 Courtesy: Basic Medical Key.
15. Image 6 Courtesy: Twitter.
16. Image 7 and 8 Courtesy: Springer link.