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Short Communication

Aggrandized and Amplified-Gynaecomastia

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Gynecomastia emerges as a benign lesion comprised of enlargement of male breast. Characteristically, a palpable sub-areolar tumefaction is encountered. Notwithstanding, female beast may delineate morphologically identical gynecomastoid hyperplasia of mammary tissue. The benign neoplasm expounds proliferation of ductal epithelial cells and stromal tissue with characteristic occurrence of 'stromal cuffing'. Typically, lesion depicts ducts coated by three layers of epithelial cells. Foci of pseudoangiomatous stromal hyperplasia may concur. Gynecomastia delineates a tri-modal distribution of disease occurrence as ~lesions discerned within infancy or neonatal period ~lesions exemplified within puberty with peak incidence between 13 years to 14 years ~lesions emerging within adult male subjects between 50 years to 80 years, possibly due to quantifiably elevated adipose tissue, decimated serum testosterone levels or ingestion of certain medications. Contingent to precise mode of diagnostic evaluation, estimated disease prevalence appears at ~32% to 65%.

Commonly emerging as bilateral lesions confined to retro-areolar region, gynecomastia may exceptionally appear as a unilateral neoplasm occurring secondary to trauma. Tumefaction may be localized or generalized [1,2]. Although aetiology or pathogenesis may be obscure, neoplasm may be engendered due to an imbalance between oestrogens and androgens on account of various mechanisms. An estimated > 40% lesions are idiopathic. Neonates and infants may delineate lesions arising due to physiological factors as in utero exposure of oestrogens wherein aforesaid lesions may undergo spontaneous resolution. Alternatively, puberty associated hormonal alterations may induce gynecomastia [1,2]. Ingestion of certain drugs as finasteride, anabolic steroids, digitalis, spironolactone or metronidazole may induce the neoplasm. Specific systemic disorders as obesity, hyperthyroidism, hypogonadism, cirrhosis, chronic renal failure or chronic pulmonary disease appear associated with disease emergence. Gynecomastia is concurrent with syndromes as androgen insensitivity, Klinefelter's syndrome, Carney's complex, Peutz-Jeghers syndrome or spinobulbar muscular atrophy. Alternatively, paraneoplastic hormone production as encountered within diverse testicular germ cell tumours, pulmonary neoplasms or adrenocortical tumefaction may engender the condition. Additionally, mechanical trauma occurring due to repetitive impact upon the torso within male rifle shooters may be accompanied by occurrence of unilateral gynecomastia [1,2]. Gynecomastia is a frequently discerned lesion of male breast. Nearly 88% implicated subjects depict mastalgia. Cytological smears depict a biphasic cellular component of epithelial cells with disseminated, singular bipolar nuclei and admixed stromal fragments. Cytological picture may simulate a fibroadenoma. A component of spindle shaped cells, apocrine cells and foamy macrophages may be encountered [2,3]. Grossly, a soft, firm, grey/white tumefaction with rubbery consistency is confined to the sub-areolar region. Alternatively, an inadequately defined induration may be discerned within the sub-areolar region [3,4]. Upon microscopy, tumefaction expounds quantifiably increased ducts. Characteristically, ducts are coated with three layered epithelium as ~luminal epithelial cells immune reactive to CK5/6 and CK14 ~intermediate cuboidal or columnar epithelial cells immune reactive to oestrogen receptors (ER), progesterone receptors(PR) and androgen receptors(AR) ~extraneous layer of myoepithelium immune reactive to CK5/6 and CK14 [5,6]. Irrespective of contributory factors as age of implicated subject or duration of lesion, tumefaction exemplifies definitive patterns of proliferative cellular alterations denominated as ~florid pattern comprised of irregular, branching ducts demonstrating mild to moderate epithelial hyperplasia circumscribed by cellular, myxoid or oedematous stroma with cuffing around ducts. Focal papillary configurations or cribriform architecture may be discerned. Myoepithelial hyperplasia may be encountered ~intermediate pattern delineating an admixture of florid and fibrous patterns ~fibrous pattern exemplifying quiescent epithelial cells and an encompassing hypo-cellular, hyalinised stroma [6,7]. Additionally, morphological alterations as pseudoangiomatous stromal hyperplasia (PASH) or focal apocrine metaplasia or squamous metaplasia may be observed. Up to 5% lesions may demonstrate

concordant foci of atypical ductal hyperplasia (ADH). However, definitive precancerous potential appears absent [6,7].

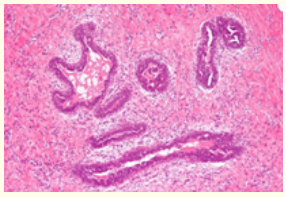

Figure 1: Gynecomastia depicting glandular articulations layered by cuboidal epithelium superimposed upon a distinct myoepithelial cell layer. Surrounding stroma is cellular and fibrotic [9].

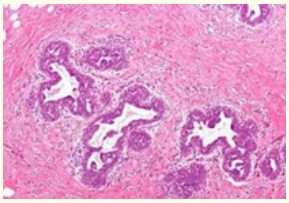

Figure 2: Gynecomastia delineating glandular structures layered by cuboidal epithelium resting upon a distinct myoepithelial cell layer. Circumscribing stroma is cellular and fibrotic [10].

Simon's classification system is expounded as ~grade I wherein lesion depicts miniature enlargement in the absence of cutaneous excess ~grade IIa wherein lesion delineates moderate enlargement in the absence of cutaneous excess ~grade IIb wherein lesion displays moderate enlargement with minor cutaneous excess ~grade III wherein lesion enunciates marked enlargement with cutaneous excess and simulation of female breast ptosis [4].

Rohrich's classification system is exemplified as ~grade I comprised of lesions with minimal hypertrophy and weight <250 grams in the absence of ptosis ~grade II comprised of lesions with moderate hypertrophy and weight between 250 grams to 500 grams in the absence of ptosis ~grade III comprised of lesions with severe hypertrophy and weight >500 grams with grade I ptosis ~grade IV comprised of lesions with severe hypertrophy and grade II or III ptosis [5].

Intermediate epithelial cells appear immune reactive to oestrogen receptors(ER), progesterone receptors(PR), androgen receptors(PR), BCL2 or cyclin D1. Luminal epithelial cells and myoepithelial cells appear immune reactive to CK5 and CK14. Myoepithelial cells are immune reactive to p63(5,6). Gynecomastia

Grade	Description	Infiltration volume+ treatment
Ia	Puffy nipple	50 ml + excision in LA from infra-areolar incision
Ib	Minor breast enlargement. Limited fat, 250ml, increased fibro-glandular tissue	200 ml + suction and gland excision in LA from infra-areolar incision and stab in inframammary area
IIa	Moderate breast enlargement. Fat component between 250g and 500g. No ptosis	500 ml + suction and stab incision in the axillary area and gland excision in GA from infra-areolar incision
IIb	Moderate breast enlargement with ptosis. Fat component between 250g and 500g	500 ml + suction from stab incision in the axillary area and gland excision + U skin lift from the supra-areolar approach in GA
IIIa	Chest enlargement with side rolls without ptosis. Fat component is 500g to 750 g. Fat in breast rolls.	1000 ml (each side and axilla) + suction from stab incision in the axillary area and gland excision in GA
IIIb	Chest enlargement with side rolls and expected ptosis. Fat component and axilla rolls	1000 ml (each side and axilla) + suction from stab incision in the axillary area and gland excision + U skin lift from supra-areolar approach in GA
IVa	Severe chest enlargement without significant ptosis. Fat component >750 g and axilla rolls	1500 ml (each side and axilla) + suction from stab incision in axillary area and gland excision in GA
IVb	Severe chest enlargement with significant ptosis and large breast rolls	Same stage axillary role excision or second stage for excess skin. 1500 ml (each side and axilla) + suction from stab incision in axillary area and gland excision + U skin lift from supra-areolar approach in GA. Second stage O lift & circumferential skin mastopexy may be required

Table 1: Contemporary Proposed Classification of Gynecomastia [6].

LA: Local Anaesthesia, GA: General Anaesthesia

requires segregation from neoplasms as carcinoma male breast, atypical ductal hyperplasia, myofibroblastoma, mammary gland hamartoma, fibroadenoma, lymphoma or dermoid cyst [5,6]. Biochemical assay with values of oestrogen to testosterone ratio (E2/TTE), serum follicle stimulating hormone (FSH), serum luteinizing hormone (LH), serum prolactin, serum thyroid stimulating hormone (TSH), serum β-hCG, serum α-fetoprotein (AFP), serum dehydro-epiandrosterone (DHEA) and serum cortisol appear advantageous in ascertaining cogent contributory factors of disease occurrence. Besides, karyotyping may be beneficially employed [6,7]. Mammography depicts a distinct pattern denominated as ~nodular pattern encountered in ~72% individuals. Lesion is concordant with 'florid' histological phase wherein tumour cells expound a 'fan' shape with radiation from nipple into encompassing adipose tissue ~dendritic pattern constituting ~18% lesions. Tumefaction concurs with 'fibrous' histological phase wherein tumour cells configure a 'flame' shaped opacity comprised of radiating projections which penetrate circumscribing adipose tissue or upper outer quadrant of breast ~diffuse pattern constituting ~10% of lesions. Typically, tumefaction is confined to transgender female subjects subjected to gender affirming hormonal therapy. Neoplasm is heterogeneous, devoid of Cooper's ligaments and appears reminiscent of dense female breast. Additionally, cogent imaging techniques may be beneficially adopted to exclude conditions as pseudo-gynecomastia or carcinoma of male breast [6,7]. Gynecomastia may be appropriately discerned with morphological assessment of surgical tissue samples. Exclusion of malignant metamorphosis appears pre-eminent [6,7]. Certain lesions may under spontaneous retrogression, especially within 2 years and may not necessitate therapeutic intervention. Emergence of sudden or symptomatic gynecomastia may be appropriately alleviated by medical manoeuvers as administration of aromatase inhibitors, anti-oestrogen agents or androgen therapy with drugs as tamoxifen or danazol. Additionally, recognition and alleviation of concurrent conditions or contributory factors is necessitated [7,8]. Surgical extermination of the lesion is advantageous and recommended in lesions occurring within adult subjects in order to exclude malignant metamorphosis and for superior cosmetic outcomes. Nevertheless, tumour reoccurrence is commonly observed, especially within lesions with unidentifiable and untreated contributory factors [7,8]. Neoplasm may reappear where concurrent contributory factor remains unaddressed. However, lesion appears non concordant with enhanced possible emergence of carcinoma breast. An estimated 3% to 46% of carcinoma male breast are concordant with gynecomastia [7,8].

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9. Image 1 Courtesy: Wikipedia.com.

10. Image 2 Courtesy: Teach me surgery.com.