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Cell & Cellular Life Sciences Journal
ISSN: 2578-4811

Compilation and Embodiment-Leydig Cell Tumour Testis

Bajaj A*

Panjab University, India

***Corresponding author:** Anubha Bajaj, Panjab University, A.B. Diagnostics, A-1, Ring Road, Rajouri Garden, New Delhi-110027, India, Email: anubha.bajaj@gmail.com

Editorial

Volume 9 Issue 1

Received Date: January 02, 2024

Published Date: January 23, 2024

DOI: 10.23880/cclsj-16000197

Keywords: Leydig Cell Tumour; Cushing's Syndrome; Lymph Nodes; Pulmonary Parenchyma; Reinke's Crystals; Polygonal Cells

Abbreviations: SF: Steroid Genic Factor; HE: Haematoxylin Stain; UICC: Union for International Cancer Control; PLAP: Placental Alkaline Phosphatase; AR: Androgen Receptor.

Editorial

Leydig cell tumour is a commonly discerned sex cord stromal tumour arising within testes. Previously designated as interstitial cell tumour, the cellular tumefaction recapitulates non neoplastic Leydig cells. Nearly < 10% neoplasms appear overtly malignant. Neoplasm represents with diffuse or nodular pattern of tumour evolution. Constituent polygonal cells are pervaded with abundant, granular, eosinophilic cytoplasm, uniform spherical nuclei and prominent centric nucleoli. Intracytoplasmic Reinke's crystals may be discerned.

Upon cogent immunohistochemistry, tumour cells appear immune reactive to inhibin A, calretinin, Melan A, steroid genic factor 1(SF1) or androgen receptors. Morphological features categorizing malignant metamorphosis emerge as tumour magnitude > 5 centimetres, infiltrative tumour perimeter, occurrence of cytological atypical or tumour necrosis, frequent mitotic activity > 3 per 10 high power fields and vascular invasion. Cogent surgical resection appears curative for non-metastatic lesions. Orchiectomy is associated with superior prognostic outcomes and exhibits an overall 5 year survival > 90%.

Leydig cell tumour configures an estimated ~2% of adult testicular tumours and up to 6% of testicular tumours emerging within pre-pubertal male subjects. Neoplasm is predominantly sporadic and exceptionally associated with hereditary leiomyomatous and renal cell carcinoma syndrome. Although no age of disease emergence is exempt, tumefaction may appear within 10 years or between 30 years to 60 years [1,2]. Leydig cell tumour commonly emerges within testicular parenchyma. Exceptionally, sites as ectopic rests of Leydig cells confined to the epididymis may be incriminated [1,2].

Leydig cell tumour secretes androgens, predominantly testosterone with consequent syndromic effects. Tumour cells may secrete oestrogen as a consequence of direct production of oestradiol or on account of peripheral aromatization of testosterone [1,2].

Of obscure aetiology, Leydig cell tumour is infrequently concordant with germline mutations within fumarate hydratase gene, as observed with hereditary leiomyomatosis and renal cell carcinoma syndrome. Besides, activating mutations within luteinizing hormone receptor may occur. Frequently, neoplastic cells demonstrate gains within chromosome X, 19 or 19p and loss within chromosome 8 and 16. Besides, somatic guanine nucleotide binding protein alpha stimulating activity polypeptide 1 (GNAS) or activating mutation within R201S gene is documented.

Malignant Leydig cell tumour appears concurrent with DNA aneuploidy whereas benign Leydig cell tumour are diploid [2,3]. Majority (> 90%) of Leydig cell tumours appear benign and unilateral wherein bilateral lesions are infrequently encountered. Neoplasm represents with painless testicular enlargement. Incriminated paediatric subjects demonstrate precocious puberty due to androgen production and gynaecomastia with mammary tenderness due to oestrogen production [2,3].

Implicated adult subjects exhibit gynaecomastia, infertility, loss of libido or erectile dysfunction. Cushing's syndrome is exceptionally observed. Malignant Leydig cell

tumour may uncommonly represent with distant metastases, especially into retroperitoneal lymph nodes or pulmonary parenchyma [2,3].

Cytological smears obtained with fine needle aspiration appear optimal for evaluating tumour metastasis into lymph nodes. Cellular smears are comprised of dis-cohesive cells pervaded with abundant, eosinophilic, granular cytoplasm, spherical, eccentric nuclei, uniformly disseminated nuclear chromatin and prominent nucleoli. Naked nuclei are commonly observed. Vacuolated cytoplasm may occur due to lipid accumulation [3,4].

Focal nuclear grooves, bi-nucleated cells or multi-nucleated cells, nuclear pseudo-inclusions and Reinke's crystals may be exemplified. Cogent cytological features segregating Leydig cell tumour from nodular Leydig cell hyperplasia appear absent [3,4]. Upon frozen section, tumour is composed of diffuse sheets of uniform, polygonal cells impregnated with spherical nuclei, centric nucleoli, abundant granular, eosinophilic cytoplasm and rectangular to club shaped Reinke's crystals [3,4]. Touch imprint preparations and scrape smears may be optimally adopted to appropriately discern Reinke's crystals [3,4].

Grossly, a well circumscribed, solid, homogeneous, tumefaction < 5 centimetre magnitude is encountered. Cut surface is golden brown or greenish brown. Foci of hyalinization or calcification may be discerned. Macroscopic features indicative of malignant metamorphosis emerge as enlarged tumefaction>5 centimetre magnitude, infiltrative tumour perimeter, focal haemorrhage, necrosis or extra-testicular neoplastic extension [3,4].

Upon microscopy, neoplasm exhibits specific tumour architecture as diffuse or nodular. Tumour parenchyma is traversed with fibrous tissue septa. Uncommonly, tumour patterns as insular, trabecular, pseudo-tubular, ribbon-like, spindle shaped cells or micro-cystic configurations may be encountered. Tumefaction is composed of polygonal cells incorporated with abundant, eosinophilic, granular cytoplasm, uniform, spherical nuclei and prominent centric nucleoli.

Exceptionally, ground glass nuclei may be expounded [3,4]. Infrequently, neoplastic cells may be imbued with scanty or foamy cytoplasm. Spindle shaped cellular component is exceptionally discerned. Bi-nucleated or multi-nucleated cells may emerge.

Intracytoplasmic lipofuscin pigment may appear as golden yellow granules upon haematoxylin stain (H&E) stain and red purple granules upon Periodic acid Schiff's (PAS) stain [3,4]. The pathognomonic, intracytoplasmic Reinke's crystals are detected in ~30% neoplasms and are configured due to cellular degradation or dissolution associated with formalin fixation. Extracellular crystals may be exceptionally expounded [3,4].

Mitotic figures are infrequently encountered. Nuclear atypia is mild. Occasionally, psammoma bodies, calcification, osseous metaplasia or adipocytic metaplasia may be discerned [3,4].

Microscopic features indicative of malignant metamorphosis emerge as

- Tumour magnitude > 5 centimetres
- Infiltrative tumour perimeter
- Cytological atypical
- Frequent mitoses > 3 mitosis per 10 high power fields
- Foci of vascular invasion
- Focal tumour necrosis

Generally, occurrence of >2 features are a pre-requisite for malignant transition (Figure 1) [3,4]. Ultrastructural examination exhibits the pathognomonic Reinke's crystals wherein morphology is contingent to plane of sectioning and crystals may articulate as a prism, hexagonal lattice or hexagonal microtubules configuring parallel lines. Predominantly intracytoplasmic, crystals may be confined to nucleus or interstitial tissue. Additionally, abundant smooth endoplasmic reticulum, mitochondria with tubulo-vesicular cristae, innumerable lipid droplets and lipofuscin granules may be discerned (Figure 2) and (Table 1) [3,4].

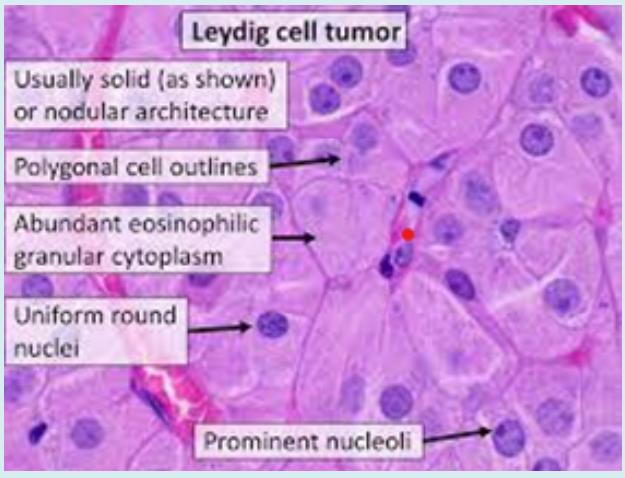

Figure 1: Leydig cell tumour delineating solid aggregates composed of polygonal cells incorporated with abundant, granular, eosinophilic cytoplasm and uniform nuclei with prominent nucleoli [5].

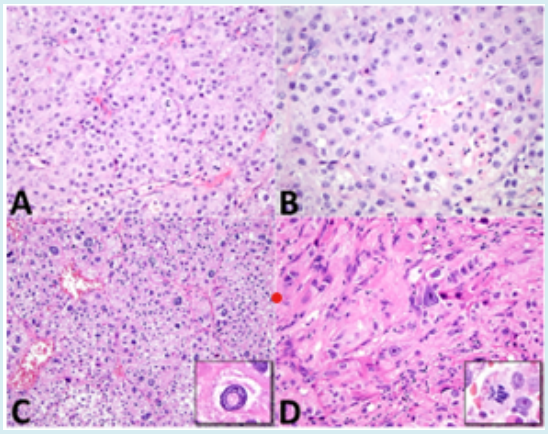

Figure 2: Leydig cell tumour demonstrating variable morphology with solid cellular nests pervaded with abundant, granular, eosinophilic cytoplasm and uniform nuclei with prominent nucleoli [6].

Stage	T	N	M	S
Stage 0	Tis	N0	M0	S0
Stage I	T1-T4	N0	M0	SX
Stage IA	T1	N0	M0	S0
Stage IB	T2-T4	N0	M0	S0
Stage IS	Any T/TX	N0	M0	S1-S3
Stage II	Any T/TX	N1-N3	M0	SX
Stage IIA	Any T/TX	N1	M0	S0
	Any T/TX	N1	M0	S1
Stage IIB	Any T/TX	N2	M0	S0
	Any T/TX	N2	M0	S1
Stage IIC	Any T/TX	N3	M0	S0
	Any T/TX	N3	M0	S1
Stage III	Any T/TX	Any N	M1a	SX
Stage IIIA	Any T/TX	N1-N3	M0	S0
Stage IIIB	Any T/TX	Any N	M1a	S1
	Any T/TX	N1-N3	M0	S2
	Any T/TX	Any N	M1a	S2
Stage IIIC	Any T/TX	N1-N3	M0	S3
	Any T/TX	Any N	M1a	S3
	Any T/TX	Any N	M1b	Any S

Table 1: Prognostic Groups of Testicular Cancer as per Union for International Cancer Control (UICC) [4].

- Stage IA is comprised of primary neoplasms confined to testis and epididymis. Microscopic evidence of neoplastic vascular or lymphatic invasion appears absent. Clinical examination or imaging demonstrates absence of distant metastasis. Following orchidectomy, serum levels of tumour markers appear within normal limits.
- Stage IB is constituted of neoplasms demonstrating localized invasion of primary tumour with an absence of distant metastasis.
- Stage IS delineates persistent elevation or enhancing serum levels of tumour markers following orchidectomy, thereby indicating subclinical metastatic disease or a germ cell tumour confined to contralateral testis.

Tumour cells appear immune reactive to inhibin A, calretinin, Melan A, androgen receptor (AR), steroidogenic factor 1 (SF1) and variably immune reactive to insulin-like 3 (INSL3). Besides, CD99 or MIC2 exhibit membranous staining. Neoplastic cells appear immune non-reactive to SALL4, OCT4, β catenin, cytokeratin, chromogranin, synaptophysin, S100 protein or placental alkaline phosphatase (PLAP) [7,8].

Testicular Leydig cell tumour requires segregation from neoplasms as testicular tumour of adrenogenital syndrome or testicular adrenal rest tumour, Leydig cell hyperplasia, granular cell tumour, large cell calcifying Sertoli cell tumour, seminoma or malakoplakia. Subjects with gynecomastia necessitate distinction from conditions such as obesity, hyperthyroidism, hepatic disorders, Klinefelter syndrome, adrenal neoplasms or reaction from drugs as ACE inhibitors, marijuana or spironolactone [7,8].

Individuals representing with hypogonadism mandate distinction from conditions as primary hypogonadism associated with Klinefelter syndrome, testicular trauma, infection or exposure to radiation and secondary hypogonadism arising due to prolactin-secreting pituitary tumour, Kallman syndrome or hypogonadotropic hypogonadism.

Intra-testicular lesions discerned upon scrotal ultrasonography require distinction from germ cell tumours as seminoma, teratoma, yolk sac tumour, embryonal carcinoma or choriocarcinoma and non-germ cell tumours as Sertoli cell tumour, granulosa cell tumour, gonadoblastoma and intra-testicular haematoma [7,8]. Leydig cell tumour can be appropriately categorized with histological assessment and precise immunohistochemistry.

Biochemical assay exhibits elevated serum testosterone and oestrogen levels. Neoplasm is associated with decimated sperm concentration, reduced total sperm count and decreased sperm motility. Upon imaging, neoplasm depicts nonspecific features. Ultrasonography exhibits a well-defined, homogeneous, hypoechoic, miniature, solid, hyper-vascular tumour mass with focal cystic areas [7,8].

Benign Leydig cell tumour can be appropriately subjected to surgical manoeuvres as orchidectomy. Miniature neoplasms may be optimally managed with testis sparing surgical options. Malignant Leydig cell tumour is suitably managed with surgical procedures as orchiectomy in accompaniment with retroperitoneal lymph node dissection.

Adoption of radiation therapy or chemotherapy appears inefficacious. Benign Leydig cell tumour alleviated with surgical intervention is associated with superior prognostic outcomes [7,8].

In contrast, malignant Leydig cell tumour exemplifies inferior survival outcomes. Majority of subjects delineate distant metastasis with augmented tumour associated mortality [7,8].

References

1. David J, Chumbalkar V, Chadha J (2023) An insight into metastatic Leydig cell tumors: A case report. SAGE Open Med Case Rep 11: 2050313X231184180.

2. Yamamoto Y, Taiji R, Takewa M, Kitatsuji W, Okura A, et al. (2023) Leydig cell tumor of the testis with characteristic contrast patterns of tumor and non-tumorous testicular parenchyma on MRI: a case report. Abdom Radiol (NY) 48(8): 2477-2482.

3. Untan I (2023) Coexistence of Leydig Cell Tumour and Sertoli Cell-Only Syndrome with an Incompatible Hormone Profile and Azoospermia. Acta Endocrinol (Buchar) 19(2): 252-255.

4. Kapoor M, Leslie SW (2023) Sex Cord Stromal Testicular Tumor. In: Stat Pearls International, Treasure, Florida.

5. Image 1 Courtesy: Wikipedia.

6. Image 2 Courtesy: Nature.com.

7. Meyts ERD, Aksglaede L, Bandak M, Toppari J, Jorgensen N, et al. (2023) Testicular Cancer: Pathogenesis, Diagnosis and Management with Focus on Endocrine Aspects. In: Feingold KR, Anawalt B, et al. (Eds.), Endotext, South Dartmouth (MA): MDText.com, Inc.

8. Pomajzl AJ, Siref LE (2023) Leydig Cell Cancer. In: Stat Pearls International, Treasure Island, Florida.