

Cylinders and Assemblage- Sertoli-Leydig Cell Tumour -Ovary



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Guest Editorial

Sertoli-Leydig cell tumour is an exceptionally discerned, ovarian neoplasm composed of sex cord or Sertoli cells admixed with stromal component expounded by Leydig cells. Sertoli-Leydig cell tumour may occur in association with DICER1 syndrome or emerge as a sporadic phenomenon. Sertoli-Leydig cell tumour manifests as well differentiated, moderately differentiated or intermediate grade and poorly differentiated neoplasms. Additionally, categories such as Sertoli-Leydig cell tumour with heterologous elements or retiform variant of Sertoli-Leydig cell tumour may be expounded. Majority of paediatric Sertoli-Leydig cell tumours are moderately differentiated or poorly differentiated, concur with DICER1 syndrome and frequently display heterologous elements or retiform tumour configuration. Histological categorization of neoplasms with enhanced tumour grade appears challenging [1,2].

Well differentiated tumefaction exhibits distinctive Sertoli cell and Leydig cell components. Moderately differentiated or minimally differentiated neoplasms appear devoid of well-formed Sertoli cell tubules with scant Leydig cells [1,2].

The infrequent, paediatric, preponderantly unilateral ovarian neoplasm is commonly delineated within young females with mean age of tumour emergence at 25 years although postmenopausal women may be implicated. Retiform tumour configuration or germline DICER1 mutations occur in neoplasms occurring in younger females [1,2].

Sertoli-Leydig cell tumour is associated with DICER1 syndrome which is an exceptional, tumour predisposition syndrome engendered by germline mutations within DICER1, a gene which encodes RNase III enzyme confined to microRNA maturation pathway.

Germline mutation expounds as a truncating mutation which may comprehensively incriminate the gene. Second hit somatic mutation occurs as focused, hotspot missense mutation implicating RNase IIIb domain of DICER [1,2].

Sertoli-Leydig Cell Tumour Exhibits Distinctive Molecular Subtypes as

- DICER1 mutant wherein moderately differentiated or poorly differentiated tumour exemplifies heterologous elements or retiform configuration and incriminates young subjects [1,2].
- FOXL2 c.402C>G (p.Cys134Trp) mutant wherein moderately differentiated or poorly differentiated tumefaction is devoid of retiform component or heterologous elements and incriminates postmenopausal women [1,2].
- DICER1 / FOXL2 wildtype wherein well differentiated neoplasm appears devoid of retiform component or heterologous elements and implicates middle aged women.
- somatic hotspot DICER1 mutations are frequently associated with germline DICER1 mutations [1,2].
- DICER1 mutations commonly appear within moderately differentiated or poorly differentiated neoplasms. In contrast, well differentiated tumours are devoid of DICER1 mutations [1,2].
- Sporadic, moderately differentiated or poorly differentiated Sertoli-Leydig cell tumours harbour somatic mutations within hotspot of DICER1 gene. FOXL2 mutation may concur with DICER1 mutations [1,2]. Clinical symptoms of hormonal or androgenic activity are discerned. However, certain representative features may concur or recede, as denominated with characteristic androgenic symptoms or tumour emergence within elderly, peri-menopausal or postmenopausal women. Clinical manifestations as pelvic pain or pelvic tumefaction may be discerned. Ascites or tumour rupture is exceptional [1,2]. Androgenic hormonal symptoms or virilisation is commonly represented as hirsutism, clitoromegaly, breast atrophy, menstrual irregularities or amenorrhoea [1,2]. Oestrogenic hormonal manifestations are infrequently observed. Histological subtype and tumour grade are concordant to clinical behaviour [1,2]. Upon gross examination, predominantly unilateral tumefaction may

demonstrate a cystic component, foci of heterologous elements or retiform configuration. Poorly differentiated neoplasms exhibit foci of tumour necrosis. Tumour magnitude varies from < 1 centimetre to ~ 35 centimetres with mean diameter of 12 centimetres to 14 centimetres. Characteristically, cut surface is solid and tan to yellow [1,2]. Frozen section exemplifies an admixture of Sertoli cell tubules or compressed cellular cords variably intermingled with Leydig cell clusters. Intracytoplasmic Reinke crystals may be delineated [1,2].

- Well differentiated Sertoli-Leydig cell tumour expounds open or compressed Sertoli cell tubules admixed with clusters of Leydig cells accumulated within intervening stroma. Cellular and nuclear atypia or mitotic activity is absent [1,2]. Sertoli cells appear as low, columnar to cuboidal cells with spherical to elliptical nuclei, nuclear grooves and miniature nucleoli. Leydig cells demonstrate abundant, eosinophilic cytoplasm with characteristic Reinke crystals, lipofuscin pigment and spherical nuclei [1,2].

- Moderately differentiated Sertoli-Leydig cell tumour characteristically depicts diffuse or lobulated architecture with alternating hypo-cellular and hyper-cellular areas. Sertoli cells configure compressed tubules, cords or diffuse sheets wherein cells are imbued with hyperchromatic, elliptical or spindle-shaped nuclei. Mild to moderate nuclear atypia and mitotic figures ~ 5 per 10 high power fields are discerned. Exceptionally, miniature clusters of Leydig cells appear commingled with Sertoli cell component. Discernible follicular differentiation may simulate juvenile granulosa cell tumour [1,2].

- Poorly differentiated Sertoli-Leydig cell tumour is constituted of diffuse sheets of immature, sarcomatoid Sertoli cells with configuration of infrequent, indistinct cords. Nuclear atypia is moderate to marked. Mitotic activity is significant with ~ 20 mitoses per 10 high power fields. Undiscernible Leydig cells are represented by few, miniature clusters, characteristically accumulated upon periphery of tumour nodules [1,2].

- Sertoli-Leydig cell tumour with heterologous elements is constituted of epithelial or mesenchymal elements represented within moderately differentiated, poorly differentiated or retiform Sertoli-Leydig cell tumour. Benign, borderline or malignant intestinal or gastric type mucinous epithelium is a common heterologous element. Trabecular or goblet cell carcinoid tumour may arise from heterologous mucinous epithelium. Heterologous mesenchymal elements as cartilage or skeletal muscle are uncommon. Focal differentiation into hepatic parenchyma and elevated serum α -fetoprotein (AFP) levels is infrequent [1,2].

- Retiform variant of Sertoli-Leydig cell tumour demonstrates focal or diffuse retiform pattern with configuration of anastomosing, slit-like, irregular spaces or multi-cystic, sieve-like or papillary architecture [1,2].

Sertoli-Leydig cell tumour is immune reactive to general sex cord proteins as inhibin, calretinin, SF1, FOXL2, CD56, WT1, CD99, vimentin, pancytokeratin, Melan A/MART1, CK20, CDX2, AFP,

arginase or HepPar1 [3,4]. Sertoli-Leydig cell tumour is immune non-reactive to CK7 or EMA.

Neoplasm is devoid of histochemical staining with reticulin.

Sertoli-Leydig cell tumour requires segregation from neoplasms such as endometrioid adenocarcinoma, adult granulosa cell tumour, fibroma or tubular Krukenberg tumour emerging from metastatic signet ring cell carcinoma. Retiform variant of Sertoli-Leydig cell tumour necessitates distinction from yolk sac tumour or low grade, borderline serous carcinoma ovary. Sertoli-Leydig cell tumour with heterologous elements mandates distinction from carcinosarcoma, teratoma and primary or metastatic ovarian mucinous neoplasms [3,4].

Sertoli-Leydig cell tumour can be assessed with pertinent clinical examination of young women manifesting features such as virilisation with elevated testosterone levels. An ovarian or pelvic tumefaction can be detected upon imaging. Intraoperative frozen section is optimal for cogent tumour evaluation and adoption of relevant surgical procedures. Incriminated subjects depict elevated serum testosterone levels. Sertoli-Leydig cell tumour can be appropriately investigated with imaging of pelvic cavity with techniques as ultrasonography, computerized tomography or magnetic resonance imaging. Upon imaging, a preponderantly solid or solid and cystic adnexal tumefaction is denominated [3,4].

Genetic counselling and assessment of germline DICER1 mutation is recommended [3,4].

Optimally, Sertoli-Leydig cell tumour occurring in young women is treated with fertility sparing surgical techniques. Sertoli-Leydig cell tumour can be appropriately managed with conservative, fertility sparing surgical procedures as unilateral salpingo-oophorectomy. Cogent tumour staging along with or devoid of regional lymph node dissection can be performed in young women exemplifying stage I tumours. Incriminated elderly females, where fertility preservation is unnecessary, can classically be subjected to bilateral salpingo-oophorectomy, total abdominal hysterectomy and comprehensive surgical staging of tumefaction. Platinum based adjuvant chemotherapy is beneficial in treating moderately differentiated or poorly differentiated tumours and neoplasms with heterologous mesenchymal elements, advanced tumour stage or tumour rupture [3,4].

Biological behaviour is contingent to histological subtype and tumour grade. Well differentiated Sertoli-Leydig cell tumours are essentially benign neoplasms whereas ~ 10% of moderately differentiated and ~59% of poorly differentiated tumours demonstrate malignant biological behaviour. Occurrence of heterologous elements, retiform tumour configuration, tumour rupture, tumour dissemination beyond ovary, stage II or advanced stage neoplasms delineate an adverse prognostic outcome. Neoplasms demonstrating germline DICER1 mutations exhibit favourable prognosis, in contrast to tumours with singular somatic DICER1 mutation [3,4] (Figure 1,2).

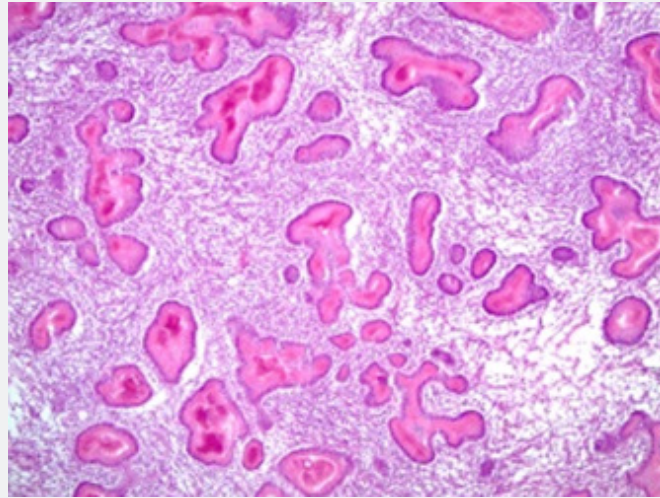


Figure 1: Sertoli-Leydig cell tumour depicting numerous well formed glandular articulations interspersed with aggregates of Leydig cells disseminated within a fibrotic stroma [5].

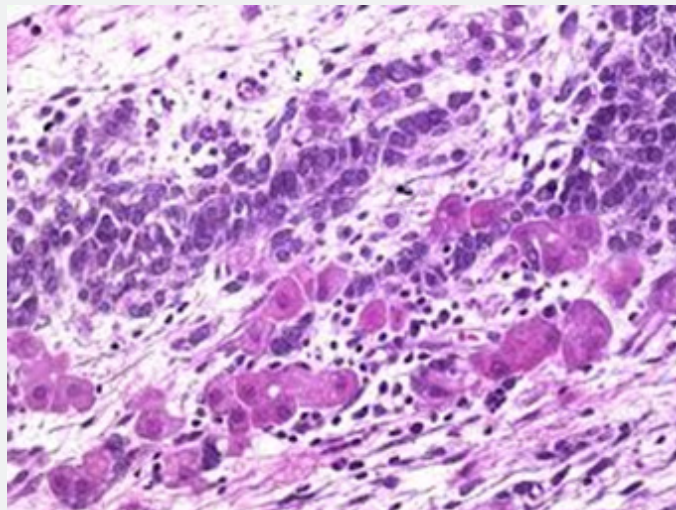


Figure 2: Sertoli-Leydig cell tumour enunciating moderately differentiated, epithelium layered tubules intermingled with aggregates of Leydig cells with abundant, granular, eosinophilic cytoplasm and circumscribing fibrous tissue stroma.

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