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Rudimentary and Incipient-Yolk Sac Tumour- Testis

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Short Communication

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Abstract

Yolk sac tumour of testis configures as a germ cell neoplasm comprised of cellular articulations or structures simulating embryonic or foetal yolk sac, allantois and extra-embryonal mesenchyme. Testicular yolk sac tumour is pre-eminently comprised of prepubertal subtype which is non-concordant to germ cell neoplasia in situ, emerges as a 'pure' neoplasm and demonstrates multiple gains within chromosome 1q, 20q or 22 and losses within chromosomes 1p, 4 or 6q. Postpubertal subtype is concurrent to germ cell neoplasia in situ (GCNIS), preponderantly configures as a component of 'mixed tumour' and occurs due to testicular dysgenesis syndrome, subfertility or as single nucleotide polymorphism (SNP) variants within KITLG, SPRY4 or DMRT1 genes and expounds gain of isochromosome 12p. Upon microscopy, neoplasm may configure distinctive configurations as microcystic or reticular pattern, macrocystic pattern, myxomatous pattern, sarcomatoid or spindle shaped cellular pattern, solid pattern, glandular or alveolar pattern, endodermal sinus or perivascular pattern, hepatoid pattern, papillary pattern, parietal pattern or poly-vesicular vitelline pattern. Yolk sac tumour appears immune reactive to alpha fetoprotein (AFP), glypican 3, SALL4, pancytokeratin, villin or CK7. Neoplastic cells appear immune non-reactive to OCT3/4, CD30, CD117, placental alkaline phosphatase (PLAP), podoplanin (D2-40), inhibin, GATA3 or p63. Testicular yolk sac tumour requires segregation from neoplasms as teratoma, seminoma, embryonal carcinoma, rete testis with hyaline globules and microcystic leydig cell tumour. Tumefaction preponderantly depicts elevated levels of serum alpha fetoprotein (AFP). Testicular yolk sac tumour may be optimally subjected to surgical manoeuvers as orchiectomy.

Keywords: Embryonic or Foetal Yolk Sac; Allantois and Extra-Embryonal Mesenchyme; Prepubertal; Postpubertal

Abbreviations: GCNIS: Germ Cell Neoplasia in Situ; AFP: Alpha Fetoprotein; SNP: Single Nucleotide Polymorphism; PLAP: Placental Alkaline Phosphatase; PASD+: Periodic Acid Schiff's Stain with Diastase.

Introduction

Yolk sac tumour of testis configures as a germ cell neoplasm comprised of cellular articulations or structures simulating embryonic or foetal yolk sac, allantois and extra-embryonal mesenchyme. Initially scripted by Gunnar Teilum and subsequently by Aleksander Talerman, neoplasm is additionally designated as primitive endodermal tumour, yolk sac carcinoma, endodermal sinus tumour, mesoblastoma vitellinum, orchioblastoma, and polyvesicular vitelline tumour, adenocarcinoma of the infant testis or extraembryonic mesoblastoma. Nomenclature of malignant endothelioma of perithelioma type appears obsolete.

Testicular yolk sac tumour is pre-eminently comprised of distinct entities as:

- Postpubertal subtype or tumefaction concurrent to germ

cell neoplasia in situ (GCNIS) which preponderantly configures as a component of 'mixed tumour'.

- Prepubertal subtype which is non-concordant to germ cell neoplasia in situ and emerges as a 'pure' neoplasm.

Postpubertal subtype of yolk sac tumour pre-eminently configures as a constituent of mixed tumour wherein 44% tumours are non-seminomas and 'pure' neoplasms are extremely exceptional. As envisaged with germ cell neoplasia in situ concordant tumours, the variant arises within 15 years to 40 years [1,2]. With amplifying neoplastic incidence, disease emergence may be triggered by environmental, genetic and epigenetic factors.

Prepubertal subtype is infrequently encountered and pre-eminently configured of 'pure' neoplastic articulations, Mixed tumours concordant with teratoma are exceptionally observed [1,2]. Neoplasm is preponderantly observed within paediatric population < 6 years with median age of disease emergence at 16 months to 20 months. In contrast to Postpubertal subtype, epidemiological variations appear absent [1,2]. Postpubertal subtype is derived from germ cell neoplasia in situ and represents a continuum of primordial germ cells or gonocytes with arrested maturation → germ cell neoplasia in situ → reprogramming → extra-embryonal differentiation. Tumefaction articulates type II germ cell tumour. Prepubertal subtype is non-concordant with germ cell neoplasia in situ and is posited to arise from teratoma. Tumefaction configures as type I germ cell tumour [2,3].

Postpubertal subtype may emerge due to:

- Environmental factors as testicular dysgenesis syndrome, subfertility.
- Genetic factors as single nucleotide polymorphism (SNP) variants within KITLG, SPRY4 or DMRT1 genes [2,3].

Postpubertal subtype of yolk sac tumour exhibits gain of isochromosome 12p. Generally, genomic imprinting is obliterated. Prepubertal subtype of yolk sac tumour enunciates multiple gains within chromosome 1q, 20q or 22 and losses within chromosomes 1p, 4 or 6q. However, gain within chromosomal region 12p is absent. Genomic imprinting within paternal and maternal genes may concur. Prepubertal subtype is engendered due to obscure factors. Yolk sac tumour exemplifies a unilateral, painless testicular mass [2,3]. Postpubertal subtype is an aggressive neoplasm wherein 40% tumours configure as stage I disease. Distant metastasis occurs in 33% tumefaction. Stage III tumours delineating yolk sac elements are associated with inferior prognostic outcomes. Delayed tumour relapse is associated with augmented disease prevalence and resistance to chemotherapy [2,3]. Prepubertal subtype is minimally aggressive. Nearly 80% tumours configure stage I disease. Singular monitoring with neoplastic surveillance displays minimal tumour reoccurrence of 6%. Metastasis into retroperitoneal lymph nodes may be exempt whereas haematogenous dissemination is significant, in contrast to postpubertal subtype [2,3].

Yolk sac tumour is commonly enunciated within testis, ovary or diverse extra-gonadal sites confined to midline. Tumour delineates significant morphological variations and may be misinterpreted as or recapitulated by diverse testicular neoplasms. Yolk sac component is associated with elevated serum alpha fetoprotein (AFP) levels [2,3]. Cytological examination exhibits cellular clusters of variable magnitude, occasional glomeruloid structures and globs of metachromatic basement membrane substance. Enlarged tumour cells with elevated nucleocytoplasmic ratio appear enmeshed within mucoid substances and hyaline globules immune reactive to Periodic acid Schiff's stain [2,3].

Grossly, postpubertal subtype is comprised of non-encapsulated, inadequately circumscribed, predominantly solid, grey/white, yellow or tan tumefaction. Cut surface is gelatinous with foci of haemorrhage, necrosis and cystic areas. Prepubertal subtype emerges as a solid or mucoid, homogeneous, grey/white or yellow, lobulated neoplasm. Cut surface is bulging wherein foci of haemorrhage and necrosis are uncommonly observed [4,5]. Upon microscopy, neoplasm depicts significant heterogeneity and multitudinous patterns. Frequently, an amalgamation of morphological variations is encountered.

Neoplasm may configure:

- Microcystic or reticular pattern which is frequently discerned and comprised of anastomosing cords of flattened epithelial cells articulating a 'honeycomb' or 'spider web' meshwork enunciating spaces incorporated with mucoid or basophilic material.
- Macrocystic pattern delineating coalescence of miniature cystic spaces which configure the microcystic pattern.
- Myxomatous pattern simulates microcystic pattern and is constituted of minimally disseminated spindle shaped or stellate cells enmeshed within a myxoid background frequently commingled with a prominent capillary network, designated as the angioblastic pattern. Tumefaction may infrequently demonstrate focal differentiation into cartilage or skeletal muscle, in contrast to teratoma [4,5].
- Sarcomatoid or spindle shaped cellular pattern is associated with progression of myxomatous configuration with elevated quantifiable and dense aggregates of spindle shaped or stellate cells immune reactive to cytokeratin. Few tumours categorized as somatic malignant neoplasm with configuration of sarcoma may represent as sarcomatoid pattern of yolk sac tumour.
- Solid pattern is constituted of sheets and nodules of

polygonal, clear to amphophilic cells with a distinct cellular membrane.

- Glandular or alveolar pattern is constituted of glands or tubular structures. Occasionally, tumour cells exhibit sub-nuclear vacuoles, akin to secretory endometrium or intestinal epithelium.
- Endodermal sinus or perivascular pattern is endowed with a predominance of Schiller-Duval bodies [4,5].
- Hepatoid pattern exhibits sheets, solid areas, nests or trabeculae of polygonal, eosinophilic cells permeated with enlarged nuclei and prominent nucleoli, reminiscent of hepatocytes. Tumour cells are intensely immune reactive to alpha fetoprotein.
- Papillary pattern is composed of papillary formations along with or devoid of fibro-vascular cores bulging into cystic spaces. Hobnail morphology is frequently observed. Tumour cells display enhanced nucleocytoplasmic ratio. Exfoliated tumour cells exhibit cellular clusters abutting tumour parenchyma.
- Parietal pattern is constituted of an extensive, dense, eosinophilic basement membrane material encompassing neoplastic cells.
- Poly-vesicular vitelline pattern essentially concurs with diverse neoplastic patterns. Tumour is composed of vesicles, occasionally with constrictions or articulating figure of 8 structures which appear enmeshed within an oedematous or fibrous stroma [4,5].

Aforesaid tumour patterns display variable cytological atypia, commonly observed within solid, sarcomatoid or glandular patterns. An estimated 50% neoplasms exhibit 'Schiller-Duval' bodies exemplifying papillary structures permeated within cystic spaces which are layered with cuboidal to columnar epithelial cells and a distinctive, centralized vascular structure [4,5]. Characteristically, tumour parenchyma enunciates intracytoplasmic and extra-cytoplasmic, refractile, eosinophilic hyaline globules which appear immune reactive to alpha-1 antitrypsin and Periodic acid Schiff's stain with diastase (PASD+) [4,5]. Ultrastructural examination exhibits epithelial cells with adherent tight junctional complexes, apical microvilli along with extracellular deposits of basal lamina and glycogen [4,5].

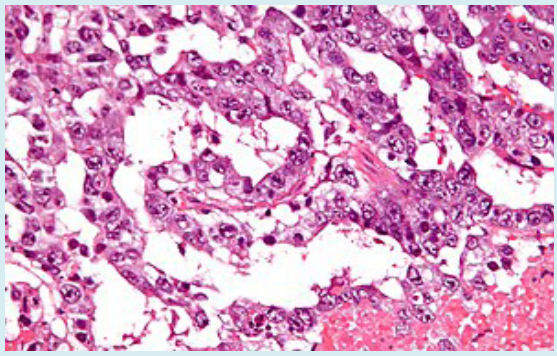

Figure 1: Yolk sac tumour delineating Schiller-Duval bodies with papillary projections into cystic spaces layered with columnar epithelium and centric, vascular structure [6].

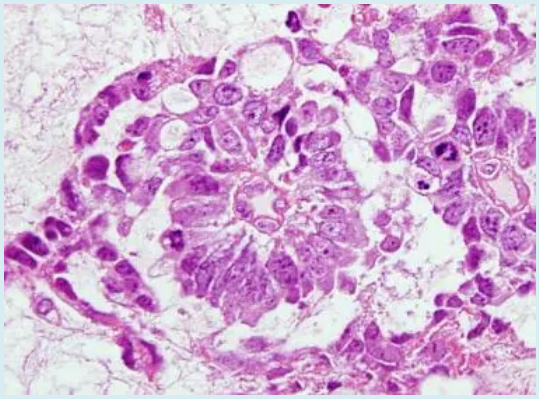

Figure 2: Yolk sac tumour demonstrating Schiller-Duval bodies with papillae confined to cystic spaces and layered with columnar epithelium with a centric vascular structure [7].

Germ Cell Tumours Derived from Germ Cell Neoplasia in Situ
Non-invasive lesions as germ cell neoplasia in situ / gonadoblastoma
Germinoma
Seminoma, pure
Seminoma with syncitiotrophoblastic cells
Non seminomatous germ cell tumour, pure
Embryonal carcinoma
Yolk sac tumour, postpubertal type
Trophoblastic tumours, choriocarcinoma
Teratoma, postpubertal or teratoma with somatic type transformation
Non seminomatous mixed germ cell tumours
Regressed germ cell tumour
Germ Cell Tumours Unrelated to Germ Cell Neoplasia in Situ
Spermatocytic tumour
Prepubertal (paediatric) tumours
Teratoma, prepubertal type
Dermoid cyst
Epidermoid cyst
Yolk sac tumour, prepubertal type
Prepubertal type testicular neuroendocrine tumour
Mixed prepubertal type tumours

Table 1: World Health Organization of Testicular Germ Cell Tumours [4].

Yolk sac tumour appears immune reactive to alpha fetoprotein (AFP), glypican 3, SALL4, pancytokeratin, villin or CK7. Neoplastic cells appear immune non-reactive to OCT3/4, CD30, CD117, placental alkaline phosphatase (PLAP), podoplanin (D2-40), inhibin, GATA3 or p63 [8,9].

Testicular yolk sac tumour requires segregation from neoplasms as teratoma, seminoma, embryonal carcinoma, rete testis with hyaline globules and microcystic leydig cell tumour. Testicular yolk sac tumour can be ascertained with cogent physical examination, testicular ultrasonography and biochemical assessment of serum tumour markers [8,9]. Majority (98%) of tumefaction depict elevated levels of alpha fetoprotein (AFP), in contrast to neoplasms as teratoma with hepatoid differentiation. Besides, occurrence of mucinous glands is associated with raised AFP in 25% instances. Notwithstanding, neonates exemplify physiological augmentation of serum alpha fetoprotein for up to 6 months [6,7]. Upon ultrasonography, tumefaction demonstrates heterogeneous echogenicity with intra-tumour calcification. Cystic spaces are frequently observed. Tumour perimeter is inadequately defined. Precise histological evaluation of an orchiectomy specimen may categorically detect and classify the neoplasm [8,9]. Testicular yolk sac tumour may be optimally subjected to surgical manoeuvers as orchiectomy. Adjuvant chemotherapy with cisplatin may or may not be adopted [8,9].

Factors contributing to prognostic outcomes of testicular germ cell tumours, especially concurrent with tumour staging as per International Germ Cell Cancer Collaborative Group is designated as:

- Postpubertal mixed tumours are constituted of enhanced proportionate yolk sac tumours configuring as stage I or stage II neoplasms.
- Stage I prepubertal yolk sac tumours with magnitude > 4.5 centimetres, concordant invasion of rete testis or epididymis along with discernible tumour necrosis expound inferior prognostic outcomes [8,9].

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