NON SEMINOMATOUS TUMORS OF THE TESTES.
AN UPDATE

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No financial relationships to disclose
Whats new after WHO 2016 in non seminomatous TGCT?

Updated pathogenetic model → restructuring of classification

Two main groups:

- Derived from GCNIS tumors
- Unrelated to GCNIS tumors

Preinvasive lesion: GCNIS

Spermatocytic tumor (seminoma)

Non-choriocarcinomatous tumors: new entities
Change in nomenclature
Old terms, neither represents the nature of the lesion

Not intraepithelial TIN

Not a carcinoma

Unclassified/Undifferentiated Confusing

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Sculley, Rosai, Mostofi, Kurman, et al, 1980
WHO classification 2004

Skakkebaek NE. Possible carcinoma-in-situ of the testis. Lancet; 1972; 2; 516–517.
Reedited: Histopathology 2002; 41; 2–3.
Gonocyte-like germ cells with ample clear cytoplasm in tubules with ↓ / absent spermatogenesis

Large angulated hyperchromatic nuclei with coarse chromatin clumps and prominent nucleoli

Confined to the basilar aspect of the seminiferous tubule: in the SPERMATOGONIAL NICHE
Embryonic GC markers

- OCT3/4
- PLAP
- CD117*
- D2-40
- NANOG
- SOX17*
- TSPY

* Also marks non neoplastic GC
Peritumoral parenchyma in 90% GCT in adults
Contralateral testis (2-6%)
Cryptorchid testis (2-5%)
Infertility biopsies (1%)
DSD (25%)

Dysgenetic testis with impaired Sertoli cells function

Supports the diagnosis of GCT
Diffuse distribution

Central–parabasal location in the seminiferous tubule

Absence of that cells in spermatogonial niche

GC with delay in maturation

Children beyond 6 months of age

DSD
CAIS / PAIS
Cryptorchidism

Morphology of primordial CG / gonocyte

Diffuse distribution

Central–parabasal location in the seminiferous tubule

Absence of that cells in spermatogonial niche
Positive for OCT3/4, CD117+, PLAP +
SCF negative
Likely give rise to GCNIS, but not invariably, so needs to be separated
A lesion intermediate between GC maturation delay and GCNIS

Cells resembling primordial germ cells/gonocytes

Location: central, parabasally and in the spermatogonial niche

OCT 3/4 and TSPY: heterogeneous expression

Expresión de SCF + (KIT ligand)

(=GCNIS, ≠ GC with maturation delay)

Ulbright TM. Arch Path Lab Med 2019; 143(6):711-721
Specific forms of Intratubular germ cell neoplasia

- Seminoma
- Embryonal carcinoma
- Trophoblast cells

Expanded tubules without residual Sertoli cells

Necrosis and calcification
Germ cell tumors – WHO 2016 Classification

Testicular Germ Cell Tumors

Unrelated to GCNIS

- Type I: Prepubertal-type
- Type III: Spermatocytic tumor

Derived from GCNIS

- Type II: Postpubertal-type

Different pathogenesis of TGCTs

Prepubertal-types can occur in postpubertal age

Postpubertal-types can occur in prepubertal age (DSD)

TGCTs represent the aberrant development of the physiological germ cell towards full spermatogenesis (at different phases of maturation)

Epidemiology GCNIS
- Increased incidence in 20th century Western lifestyle
- Dysgenetic testicular syndrome
  - Maternal hyperstrogenism
  - Hormonal disruptors
- Disorders of Sex Development
- Androgen insensitivity syndrome

Impaired Sertoli cell function → Testicular dysgenesis syndrome

Rajpert-De Meyts E. et al. Lancet 2016; 387: 1752-64
Primary Testicular Lesions are Associated With Testicular Germ Cell Tumors of Adult Men

Manuel Nival, MD, PhD,* ‡ Pilar Gonzalez-Peramato, MD, PhD, ‡ Javier Regadera, MD, PhD, ‡ Alvaro Serrano, MD, PhD, § Virginia Turin, MD,* and Maria P. De Miguel, PhD,*


2016 WHO Germ Cell Tumor Classification

Testicular Germ Cell Tumors

Occur in a background of dysgenetic testis
- Impaired spermatogenesis
- Sertoli cell-only pattern
- Immature Sertoli cells
- Leydig cell hyperplasia
- Hyalinized tubules
- Microlithiasis

GCNIS-derived

Not GCNIS-derived

Normal testicular parenchyma
Absence of dysgenetic changes
Not associated with cryptorchidism
The World Health Organization 2016 classification of testicular germ cell tumours: a review and update from the International Society of Urological Pathology Testis Consultation Panel

Semioma
Embryonal carcinoma
Somatic malignancy
Choriocarcinoma / Others trophoblastic tumors
Sarcomatoid YST / sarcoma NOS
Yolk sac tumor Postpubertal-type
Teratoma Postpubertal-type
Mixed GCT
Regressed GCT

Type II GCNIS-derived

Germ Cell Tumors

Type III
Spermatocytic tumor
Chrom 9 amplification: DMRT1 gen

Type I
Spermatocytic tumor with sarcoma
Yolk sac tumor Prepubertal-type
Gain / losses chromosomes

Indolent behavior

Type III
Spermatocytic tumor

Malignant behavior

Type II
GCNIS-derived

Determines prognosis and treatment

No genetic abnormalities

Choriocarcinoma / Others trophoblastic tumors

Dermoid cyst Epidermoid cyst Carcinoid tumor

Chrom 9 amplification:
DMRT1 gen

Gain / losses chromosomes

Somatic malignancy

Mixed GCT

Regressed GCT

Somatic malignancy

Type I
Teratoma Prepubertal-type

Choriocarcinoma / Others trophoblastic tumors

Dermoid cyst Epidermoid cyst Carcinoid tumor
Yolk sac tumor

Malignant GCT that differentiates structures similar to extraembryonic structures (yolk sac, allantoids and extraembryonic mesenchyme)

98%: ***AFP*** > 100 ng/ml

![Glypican 3](image)

Yolk sac tumor

Postpubertal-type

GCNIS-derived

Germ Cell Tumors

Not GCNIS-derived

Yolk sac tumor

Prepubertal-type

Adults

99% in mixed GCT

i(12p)

Metastasis (30% in stage I)

Lymphatic based-distribution of metastasis

In the first 2y of life (48-52%), not congenital

Most are pure (teratoma)

Gain (1q, 3, 8q24, 12 (p13), 20q, 22) / losses (1p36, 4, 6q, 16q and 20p) of whole or portions of several chromosomes

Less apt to metastasize (16% in stage I)

Hematogenous distribution of metastasis

Arch Pathol Lab Med. 2019;143:711–721
Pre-pubertal type YST

- Solid pattern
- Glandular pattern

Same morphology

- Myxomatous pattern
- Macrocystic pattern

Post-pubertal type YST

- Schiller-Duval or glomeruloid bodies
- Endodermal sinus pattern: 20%

- Hepatoid pattern
Yolk sac tumor

Pre- and post-pubertal type

Architectural patterns

- Microcystic / Reticular (vacuolated): 80%
- Solid
- Myxomatous
- Macrocystic
- Glandular / alveolar
- Endodermal sinus (feston)
- Hepatoid
- Papillary
- Sarcomatoid
- Parietal (AFP -)
- Polyvesicular vitelline

Chemo-resistence
Mixed patterns

Clues

Cuboid cells, intermediate size between seminoma and embryonal carcinoma

Intercellular basement membrane

Hyaline globules PAS+
It is the TGCT that most often goes unnoticed
47% of overall errors: failure to diagnose YST


Serum AFP ↑

Necklace pattern (double layer + EC) (7%) → Mixed GCT

Positive for:
- AFP (80%)
- Glypican 3 (100%)
- CD117 (60% solids)
- SALL4
- GATA 3
- AE1/AE3
- CDX2 !!!!

Negative for:
- OCT 3/4
- CD30
- Inhibin

Poliembrioma-like → Mixed GCT

Yolk sac tumor, postpubertal -type
GCT composed elements resembling somatic tissues derived from one or more germinal layers (endoderm, mesoderm, and ectoderm)

Mature elements

Immature elements

NOT affect overall prognosis

Germ Cell Tumors

GCNIS-derived

Teratoma

Postpubertal-type

Somatic malignancy

Teratoma

Prepubertal-type

Dermoid cyst

Epidermoid cyst

Carcinoid tumor

Not GCNIS-derived

Somatic malignancy

Adults

Pure GCT (2.7-7%)

Mixed GCT (50%)

Malignant

Metastasis (22-37%)

Mostly in children (< 6 y)

Also in adults

Pure neoplasm

Benign

No recurrence/metastasis

Conservative treatment

Adults

Pure GCT (2.7-7%)

Mixed GCT (50%)

Malignant

Metastasis (22-37%)

 Mostly in children (< 6 y)

Also in adults

Pure neoplasm

Benign

No recurrence/metastasis

Conservative treatment
Prepubertal-type teratoma

Organoid arrangement
Cysts
Squamous / ciliated epith.
Smooth muscle
Occasional salivary gland/pancreas acinar cells
No necrosis

Normal parenchyma
Prepubertal-type teratoma in postpubertal patients

Postpubertal age: 59 years-old
Present in childhood?

- No cytologic atypia
- No immature tissues
- No scars / dysgenetic changes
- Diploid → No (i)12p
- No GCNIS

Normal spermatogenesis
Prepubertal-type teratoma in postpubertal patients

Evidence Supporting the Existence of Benign Teratomas of the Postpubertal Testis
A Clinical, Histopathologic, and Molecular Genetic Analysis of 25 Cases
Chen Zhang, MD, PhD; Daniel M. Berney, FRCPath; Michelle S. Hirsch, MD, PhD; Liang Cheng, MD, and Thomas M. Ulbright, MD


Dermoid Cyst of the Testis
A Study of Five Postpubertal Cases, Including a Pilomatrixoma-Like Variant, With Evidence Supporting Its Separate Classification From Mature Testicular Teratoma
Thomas M. Ulbright, M.D., and John R. Srigley, M.D.


University Hospital La Paz for 20 years
72 teratomas- (19 prepubertal-type: 26%)
8 (42%) older 15 y (10 mo-58 y)
12 epidermoid cysts, 2 dermoid cysts, 5 Prepubertal-type T
Follow-up (5-19y): No recurrence or metastases

Carcinoid tumours of the testis
Otto B. Stroosma and Karl P.J. Delacre
Department of Urology, Asylum Medical Centre, Heerlen, the Netherlands

Primary Carcinoid Tumors of the Testis: A Clinicopathologic Study of 29 Cases
Wenle P. Wang, PhD; Charles Guo, MD; Daniel M. Berney, MD; Thomas M. Ulbright, MD; Donna E. Hansel, PhD; Rulong Shen, MD; Tehminah Ali, MD; and Jonathan I. Epstein, MD


10 dermoid cysts
15 non dermoid teratomas
23 skin and other elements
18 analyzed: no 12p
17 with follow-up: alive, 11 disease-free
**Prepubertal-type teratoma in postpubertal patients**

### Dermoid cyst
Unilocular cyst, mural protuberance  
Keratinized squamous epithelium  
Adnexal structures, Hair  
Other tissues: glands, muscle, cartilage..  
Lipogranulomas

### Epidermoid cyst
Unilocular cyst  
Keratinized squamous epithelium  
No adnexal structures or other tissues

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Teratoma, Postpubertal-type

Well circumscribed nodules
Complex masses, solid-cystic
Cartilage, calcification, fibrosis

GCNIS and testicular dysgenetic changes in peritumoral parenchyma
Epithelium: squamous with / without keratin, glandular, intestinal, respiratory

Mesenchmal: Fibrous, smooth muscle, adipous, neuroglía, cartilage, bone, retin

Rangedly distribution

Organoid arrangement: Less frequent
Hypercellular and atypical cartilage not sufficient for sarcoma
Rare

**Adults** with teratomas who develop overgrowth of a secondary malignant somatic-type neoplasm excluding other elements

In the testes or more frequently after chemotherapy (Chemoslection) in metastasis (poor prognosis). Chemoresistence.

- Angiosarcoma, Rhabdomyosarcoma (embrionary or alveolar), liposarcoma
- Neuroblastoma, nephroblastoma, PNET
- Adenocarcinomas
- Squamous carcinoma

**Size criteria:** at least a 4X field or 5 mm in diameter
Several years after treatment
AFP normal or slightly elevated
Myxoid or fibrocolagenous nodules
Fusocellular or epithelioid cells

Basement membrane material
AE1/AE3 y Glypican 3 +
SALL4 +
AFP -
Muscle differentiation
**2016 WHO Germ Cell Tumor Classification**

- **Seminoma**
- **Embryonal carcinoma**
- **Yolk sac tumor Postpubertal-type**
- **Teratoma Postpubertal-type**
- **Sarcomatoid YST / sarcoma NOS**
- **Somatic malignancy**
- **Mixed GCT**
- **Regressed GCT**
- **Choriocarcinoma / Others trophoblastic tumors**

**Not GCNIS-derived**

- **Spermatocytic tumor**
  - **Spermatocytic tumor with sarcoma**
- **Yolk sac tumor Prepubertal-type**
- **Teratoma Prepubertal-type**
  - **Dermoid cyst**
  - **Epidermoid cyst**
  - **Carcinoid tumor**
Trophoblastic tumors

Changes

**WHO 2004**
- Choriocarcinoma
- Trophoblastic neoplasms other than choriocarcinoma
  - Monophasic choriocarcinoma
  - Placental site trophoblastic tumor

**WHO 2016**
- Choriocarcinoma
  - Monophasic choriocarcinoma
- Non-choriocarcinomatous trophoblastic neoplasms
  - Placental site trophoblastic tumor
  - Epithelioid trophoblastic tumor
  - Cystic trophoblastic tumor

Absence of biphasic pattern
Lower levels of β-hCG
Less aggressive than choriocarcinoma
Analogous to uterine counterparts
Age: 2nd-3rd decade

Mixed GCTs: 6.4 - 17.8%

Pure forms: <1% (in metastasis)

Hematogenous metastasis at presentation (lung, brain, GI) → more aggressive GCT

↑ ↑ ↑ ↑ β-hCG > 50,000 UI/L → bad response to treatment and poor prognosis

Pure and > 50% → Poor prognosis and survival (10-13 months)
OCT3/4 - **Syncytiot**: βHCG+, glypican 3+, inhibin+
**Cytot**: SALL4 +, p63+, GATA3+,

### Table 1 Percent positivity of CK7, inhibin, p63, and β-hCG in testicular GCT subtypes

<table>
<thead>
<tr>
<th>GCT subtype</th>
<th>%</th>
<th>CK7</th>
<th>Inhibin</th>
<th>p63</th>
<th>β-hCG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choriocarcinoma</td>
<td></td>
<td>100</td>
<td>89</td>
<td>85</td>
<td>96</td>
</tr>
<tr>
<td>Embryonal carcinoma</td>
<td></td>
<td></td>
<td>52</td>
<td>0</td>
<td>55</td>
</tr>
<tr>
<td>Yolk sac tumor</td>
<td></td>
<td>84</td>
<td>0</td>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>Teratoma</td>
<td></td>
<td>59</td>
<td>0</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Seminoma</td>
<td></td>
<td>0</td>
<td>0</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>ETT</td>
<td></td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>33</td>
</tr>
</tbody>
</table>

Fig. 2  Choriocarcinoma and embryonal carcinoma metastatic to an axillary lymph node (original magnifications ×10 for all images). Positivity for CK7, inhibin, and p63 differentiated choriocarcinoma from embryonal carcinoma, whereas β-hCG did not. A, Hematoxylin and eosin staining with choriocarcinoma (bottom) and embryonal carcinoma (top). B, Diffuse, nonspecific β-hCG reactivity in both choriocarcinoma and embryonal carcinoma. C, CK7 was positive in choriocarcinoma and negative in embryonal carcinoma. D, Inhibin was positive in choriocarcinoma and negative in embryonal carcinoma. E, p63 was positive in choriocarcinoma and negative in embryonal carcinoma.
Placental site trophoblastic tumor

- Discohesive proliferation
- **Pleomorphic** implantation-type intermediate trophoblast
- Tendency to invade vascular walls → fibrinoid reaction
- Human placental lactogen +, p63 -, GATA 3 +
- Chemoresistant → surgery

DD: Hepatoid pattern of YST

**Nonchoriocarcinomatous Trophoblastic Tumors of the Testis**

The Widening Spectrum of Trophoblastic Neoplasia

Muhammad T. Idriss, MBBS, MD,* Chiu-Sui Kao, MD,* Jonathan I. Epstein, MD;† and Thomas M. Ullrich, MD*


Associated with teratoma
Epithelioid trophoblastic tumor

Original Article

Nonchoriocarcinomatous Trophoblastic Tumors of the Testis
The Widening Spectrum of Trophoblastic Neoplasia
Muhammad T. Idrees, MBBS, MD,* Chia-Shi Kao, MD,* Jonathan I. Epstein, MD,† and Thomas M. Ulbright, MD*

Primary tumor
Post chemotherapy metastasis
Associated teratoma or mixed GCT

Cohesive nests and cords
Intermediate trophoblast
**Squamoid** mononucleated cells
**Apoptotic hyaline cellular debris**
Fibrinoid deposits in vascular walls surrounding cells
Lymphocytes at periphery
Human placental lactogen –, p63 +
Inhibin+ GATA 3 +

FIGURE 1. A. ETT with prominent fibrinoid material around vessels. B. Cystic change in ETT (adjacent to teratoma) with peripheral small clusters and single trophoblastic cells infiltrating stroma with a dense lymphocytic infiltrate. C. Solid sheet of trophoblastic cells with prominent cytoplasmic membranes, nuclear pleomorphism, multinucleation, apoptosis, and intracytoplasmatic and extracellular hyaline globular material. D. Small clusters and single trophoblastic cells in fibrous and fibrinoid background with prominent vessels. Positive immunoreactivity in ETT including GATA3 (f), p63 (f), inhibin (G), and Ki67 (h) in trophoblastic cells.
Cystic Trophoblastic Tumor

After chemotherapy
After cisplatin-based Cht
Retroperitoneum LN
Teratoma associated
β-hCG normal / slight ↑

Little aggressive potential
No evolution to choriocarcina.
Clinical significance similar to residual teratoma
Managed expectantly

Multifocal small circumscribed cysts lined by mononucleated trophoblasts; +/- intracytoplasmic lacunae

TABLE 2. Differential Features of Cystic Trophoblastic Tumor (CTT) Versus Choriocarcinoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CTT</th>
<th>Choriocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Small (mean, 2.7 mm)</td>
<td>Usually large (&gt;1 cm)</td>
</tr>
<tr>
<td>Architecture</td>
<td>Cystic</td>
<td>Nodular/nested</td>
</tr>
<tr>
<td>Biphasic pattern</td>
<td>Absent</td>
<td>Often present</td>
</tr>
<tr>
<td>Mitotic figures</td>
<td>Infrequent</td>
<td>Frequent</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>Absent</td>
<td>Usually present</td>
</tr>
<tr>
<td>Necrosis</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Infiltrative growth</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>hCG immunoreactivity</td>
<td>Usually focal</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Metástasis post cisplatin: 17 cases
Primary Cystic Trophoblastic Tumor of the Testis
A Study of 14 Cases

Dibson D. Gondim, MD, Thomas M. Ulbright, MD, Liang Cheng, MD, and Muhammad T. Idrics, MD, MBBS


De novo in testes (primary)
Nontreated (9)
In mixed GCT

Chorioca in regression?
Chorioca → teratoma?

Cystic trophoblastic tumor

**TABLE 3. Characteristics of CTT of Testis**

<table>
<thead>
<tr>
<th>No.</th>
<th>Characteristics</th>
<th>No. Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cystic component</td>
<td>14/14 (100)</td>
</tr>
<tr>
<td>2</td>
<td>Association with teratoma</td>
<td>14/14 (100)</td>
</tr>
<tr>
<td>3</td>
<td>Multilocality</td>
<td>7/14 (50)</td>
</tr>
<tr>
<td>4</td>
<td>Mitotic figures</td>
<td>2/14 (18)</td>
</tr>
<tr>
<td>5</td>
<td>Hemorrhagic background</td>
<td>1/14 (7)</td>
</tr>
<tr>
<td>6</td>
<td>hCG immunoreactivity</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>7</td>
<td>Fibrinoid changes</td>
<td>14/14 (100)</td>
</tr>
<tr>
<td>8</td>
<td>Association with choriocarcinoma*</td>
<td>6/14 (43)</td>
</tr>
<tr>
<td>9</td>
<td>Well-circumscribed growth</td>
<td>12/14 (86)</td>
</tr>
<tr>
<td>10</td>
<td>Solid foci</td>
<td>5/14 (36)</td>
</tr>
</tbody>
</table>

*Clinical suspicion due to markedly increased hCG. Only 1 case of choriocarcinoma was identified on microscopy after chemotherapy.
Mixed Germ Cell Tumors

Non seminomatous

Report percentage of each component

Heterogeneous

Syncytiotrophoblast

Teratoma

EC
2016 WHO Germ Cell Tumor Classification

Seminoma

Embryonal carcinoma

Yolk sac tumor Postpubertal-type

Sarcomatoid YST / sarcoma NOS

Somatic malignancy

Teratoma Postpubertal-type

Choriocarcinoma / Others trophoblastic tumors

Germ Cell Tumors

Not GCNIS-derived

Spermatocytic tumor

Spermatocytic tumor with sarcoma

Yolk sac tumor Prepubertal-type

Teratoma Prepubertal-type

Dermoid cyst Epidermoid cyst Carcinoid tumor
Spermatocytic tumor

Cytogenetic profile:
- Gain 9p (*DMRT1*), 1.20
- Loss 22

Unique Clinical-pathological entity → no relationship with seminoma

Bilateral: 9% cases

Older group (+ 50-60 years-old; 19-92y)

There are no prepubertal cases

Never described outside the testicle

- No ovarian or extragonadal counterpart

Clinically benign except sarcomatous transformation → 50% metastasis and death

Treatment: orchidectomy without adjuvant

Exceptionally metastatic (5 cases; < 50y; 3 with 12p)

Pathogenesis different from the rest of GCT

- Not associated with cryptorchidism
- Not associated with GCNIS
- Always purely (not other TCGs)
- It is not associated with 12p anomalies
- Gain 9p (*DMRT1*), 1.20, loss 22

Similar to spermatogenesis

Negative serological markers


Seminoma

CGT derived from postpubertal-type GC, resembling spermatogonias or primary spermatocytes
Spermatocytic tumor

- Well circumscribed
- Multilobated or multinodular
- Soft, friable, cystic
- Mucoid or gelatinous surface

Diffuse solid pattern (simulates lymphoma)
- Pseudocystic pattern / Edema
- Scarce fibrous septa / Low lymphoid infiltrate

- Trabeculae-nests-loose cells
- No granulomas

Rare extratesticular extension
Polymorphous (monomorphous)
Three cell types
High mitosis rate, atypical
Apoptosis
Intratubular growth
DD GCNIS
Spermatocytic Seminoma

A Report of 85 Cases Emphasizing Its Morphologic Spectrum Including Some Aspects Not Widely Known

Rong Hu, MD, PhD,* Thomas M. Ulbright, MD;† and Robert H. Young, MD*

Negative markers:
- OCT3/4
- PLAP (rare focal)
- CD30
- AFP
- hCG
- Vimentin
- NSE
- NSE
- CEA
- LCA

Positive markers:
- SALL4 +
- CD117 + (50%) !!!!!!!
- NUT, MAGEA4, GAGE7 y NY-ESO1
- DMRT1 +
- FGFR3, HRAS

<table>
<thead>
<tr>
<th>Morphologic Feature</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-power pattern</td>
<td>51</td>
</tr>
<tr>
<td>Multinodular</td>
<td>49</td>
</tr>
<tr>
<td>Diffuse</td>
<td></td>
</tr>
<tr>
<td>Peripheral rim of fibrin around nodules</td>
<td>20</td>
</tr>
<tr>
<td>Edema fluid</td>
<td>87</td>
</tr>
<tr>
<td>Pseudofollicles</td>
<td>24</td>
</tr>
<tr>
<td>Irregular spaces</td>
<td>39</td>
</tr>
<tr>
<td>Microcysts</td>
<td>15</td>
</tr>
<tr>
<td>Anastomosing insular growth</td>
<td>19</td>
</tr>
<tr>
<td>Cords at periphery</td>
<td>21</td>
</tr>
<tr>
<td>“Tripartite” cellular populations</td>
<td>100</td>
</tr>
<tr>
<td>Relatively monomorphic cell population with vesicular chromatin and prominent nucleoli</td>
<td>6</td>
</tr>
<tr>
<td>Clusters of lymphocytes</td>
<td>38</td>
</tr>
<tr>
<td>Rare</td>
<td>8</td>
</tr>
<tr>
<td>Prominent</td>
<td>8</td>
</tr>
<tr>
<td>Striking granulomatous inflammation</td>
<td>1</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>11</td>
</tr>
<tr>
<td>Tumor necrosis</td>
<td>8</td>
</tr>
<tr>
<td>Intratubular tumor spread</td>
<td>64</td>
</tr>
<tr>
<td>Intertubular growth</td>
<td>39</td>
</tr>
<tr>
<td>Atrophy in adjacent parenchyma</td>
<td>62</td>
</tr>
<tr>
<td>Sarcomatous transformation</td>
<td>2</td>
</tr>
</tbody>
</table>
What's new after WHO 2016 in non seminomatous TGCT?

Conclusions

Updated pathogenetic model of GCT

Classification that synthesizes pathogenesis-morphology-molecular characteristics

GCNIS: new term

Restructuring of classification: GCNIS derived / GCNIS unrelated GCT

Yolk sac tumor and Teratoma: Postpubertal-type vs prepubertal-type

New entities: Non-choriocarcinomatous trophoblastic tumors

Spermatocytic tumor: new term
Acknowledgement:
Dr Manuel Nistal

Thank you for your attention

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