Testicular Cancer: radiopathological correlation of testicular tumors in adulthood population. A review of 32 cases.

Poster No.: C-1085
Congress: ECR 2015
Type: Educational Exhibit
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Keywords: Patterns of Care, Metastases, Cancer, Diagnostic procedure, Ultrasound-Colour Doppler, Ultrasound, CT, Lymph nodes, Genital / Reproductive system male, Abdomen
DOI: 10.1594/ecr2015/C-1085

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Learning objectives

The purpose is to carry out a review of the principal features in ultrasonography techniques, the behaviour, the clinical presentation and histologic characteristics of testicular carcinoma.

Malignant tumor lesions of the testis represent about only 1% of all neoplasms in men, but they are the most common malignancy in the 15-34 year-old-age group. Germ cell tumors constitute 95% of all neoplasms and the sonographic appearance turn into their morphology and histologic characteristics.

Ultrasonography is the first imaging technique for evaluation any solid testicular lesion.
Background

Embryologic Reminder:

An adult normal testis is the product of development of different cell types, namely, testis is composed from cells came from three groups of embryonic tissues: mesenchyme, mesothelium, and germ cells.

- Sertoli cells: or supporting cells, those formed from the mesothelium. Sertoli cells secrete müllerian-inhibiting factor, which makes the paramesonephric ducts (müllerian ducts) regress.

- Leydig cells: interstitial cells. Leydig cells evolve from mesenchyme embryo and at approximately 8 weeks of gestational age, these cells begin to secret testosterone. Under this hormonal influence, mesonephric ducts (ducts of Wolff) are distinguished into the epididymis, vas deferens, seminal vesicles and ejaculatory ducts.

- Germ cells: during embryological development, primordial germ cells are formed in the yolk sac, next to the hindgut, and then migrate to the genital ridges to form the primitive sex cords (fig.1).

Anatomy features:

Normal adult testis is composed of 200 to 300 lobules, and a normal lobe contains 400-600 seminiferous tubules. The adult testis consists of densely packed seminiferous tubules, which are separated by fibrous septa and surrounded by a fibrous capsule, the tunica albuginea. The tunica albuginea is covered by a thin layer of mesothelium, the tunica vaginalis (fig.2).

Ducts, nerves and vessels entering and leaving the testicle through the testicular mediastinum, which is an area of thickened tunica albuginea in the testis is due.

Seminiferous tubules are composed of two cell types: Sertoli cells and the spermatogenic germ cells in different developmental stages, which are the predominant cell population. Spermatogenic germ cells finally mature in spermatozoa, and migrate to the center of the tubule.

Sertoli cells are nondividing cells that extend in the lumen of the tubule and aid in spermatogenesis by providing a way to supporting structure of ripening germ cells, as well as through the elimination of degenerating germ cells by phagocytosis.
The spaces between the seminiferous tubules is the interstitium, which is derived from mesenchyme. Leydig cells are included in the interstitium and are the main source of testosterone production in men.

**Ultrasonogram features of normal testis:**

Ultrasonography is done easily and proved to be almost 100% sensitivity in the identification of scrotal masses, combined by physical examination. For the testis evaluation is required high-frequency transducer (5-10MHz) that gives adequate penetration.

The normal testicle has a homogeneous, medium-level, granular echotexture (fig.3). Testicular mediastinum can be seen as an echogenic line emanating from the back of the testicle. The epididymis is isoechoic or slightly hyperechoic compared with the testis.

We must remember that it is very important to describe if an intratesticular mass is solid or cystic. With rare exceptions, solid intratesticular masses should be considered malignant.

The majority of testicular tumors are hypoechoic in comparison with the surrounding parenchyma. Other tumors can be very heterogeneous, with areas of increased echogenicity, calcifications and cysts formation. The use of color Doppler US is not much worth to characterize testicular tumors in adults. Increased vascularity of a lesion is not specific of testicular tumors.

**Epidemiology:**

Testicular cancer is the most common nonhematologic malignancy in men between 15 and 34 years, even in 15 - 49 years-old-age group. The disease is relatively rare (1% of all malignant neoplasms in males), but the incidence has more than doubled in the last four decades.

The average age of diagnosis is the fourth decade of life (about 33 years).

There are two major categories or subtypes of tumors: germ cell and stromal tumors. Germ cell tumors (GCTs) arise from spermatogenic cells and constitute 95% of testicular neoplasms; GCTs are typical tumor tissue types considered when discussing about testicular cancer.

GCT are further subdivided into seminoma and nonseminomatous GCT (NSGCT). This division plays a critical role in determining the approach to treatment. Seminoma is a tumor that is extremely sensitive to radiation, while NSGCTs respond better to chemotherapy and surgical approaches. Seminoma is the most common pure cell
histology of all tumors. However, the most common tumor type overall is a mixed GCT, which contains elements of multiple subtypes of GCT, including NSGCT and seminoma. Mixed tumors are treated as NSGCT even in the presence of seminomatous components.

Testicular tumors subtypes commonly present by age groups:

- **Seminoma**: the most common pure germ cell tumor (35-50% of all GCT). The rather large percentage ranges for both seminomas and mixed GCT stem from differences in pathologic reporting. Compared with nonseminomatous tumors, seminomas occur in a slightly older population (30-40 years the majority of cases, with an average patient age of 40.5 years). Around 75% of patients are presented with disease limited to the testicle, 20% have retroperitoneal adenopathy, and 5% have extranodal metastasis. Seminomas range in size from a small well-defined lesion to large masses that completely replace the testicle. The ultrasound characteristics of seminoma are quite predictable; these tumors are usually homogeneous and uniformly hypoechoic, they can be lobulated or multinodular (fig.4), but these nodules are most commonly in continuity with each other. In rare cases, true multifocal nodules can be seen (fig.5); multifocal seminomas are much more aggressive (fig.6) than classic seminoma. Bilateral tumors are also rare and occur in 2% of patients. Seminoma is a 5-years survival rate of 95%.

- **Embryonal carcinoma**: composed of primitive anaplastic epithelial cells resembling early embryonic cells. This tumor is present in 87% of the mixed GCT, although in its pure form, it accounts for only 2-3% of all testicular tumors. It is observed more frequently in a younger population than does seminoma (male aged between 25 to 30 years). Its size is usually smaller than seminoma, but tends to be more aggressive in behaviour (fig.7); the borders of the tumor are less distinct, often mixing imperceptibly into the adjacent parenchyma. In US images are more heterogeneous and ill-defined.

- **Yolk sac tumor**: the totipotencial germ cells that differentiate toward extraembryonic fetal membranes give rise to yolk sac tumor, also known as endodermal sinus tumor. It account for 80% of childhood testicular neoplasms, with most cases in kids younger 2 years old. In its pure form, yolk sac tumor is rare in adults; however, it is present in 44% of adult cases of mixed GCT. Imaging findings are nonspecific. The lungs are the most common site of recurrent disease.

- **Teratoma**: after yolk sac tumor, teratoma is the second most common testicular tumor in children (generally occurs in children less than 4 years of age). It is a complex tumor, composed for disorderly arrangement of adult and fetal tissues (with all three germ layers). In its pure form, teratoma is rare in adult; however, teratomatous elements occur in approximately half of all adult cases of mixed GCT (fig.8).
- **Choriocarcinoma**: is a rare germ cell tumor. In its pure form, occurs in less than 1% of cases; however, in mixed GCT it is seen in 8% of patients. The average age of diagnosis is third decade of life (20-30 years). Choriocarcinoma is a very highly malignant tumor (it is the most aggressive histologic subtype) and it is composed of a mixture of cytotrophoblastic and syncytiotrophoblastic cells. There is early widespread metastasis frequently. Patients may present with symptoms referable to advanced disease rather than a palpable testicular mass. Sites of metastases include the lung (fig. 9), liver, gastrointestinal tract and brain; primary tumor as well as metastases are often hemorrhagic. The levels of human chorionic gonadotropin (#-HCG) are elevated and causes gynecomastia in 10% of cases (fig. 10). Choriocarcinoma has the worst prognosis of any of the GCT; death usually occurs within 1 year of diagnosis.

- **Mixed GCT**: contain more than one germ cell component. Of the nonseminomatous GCT, they are much more common than any of the pure histologic forms, representing even 60% of all. Virtually any combination of cell types can occur (embryonal carcinoma is the most common component). The medium age of presentation is 30 years. US imaging findingss are variable, reflecting the diversity of this group if tumors (figs.11-12).

**Patterns of Spread:**

Metastases can spread by both lymphatic and hematogenous routes. Direct extension through the tunica albuginea with involvement of the scrotal skin is a rare and late finding. Most GCT spread first via the lymphatics drainaged rather hematogenously, but a notable exception is choriocarcinoma, which has a proclivity for early hematogenous spread.

Lymphatic spread describe a predictable pattern. Testicular lymphatic drainage follows testicular veins. For the right testis, the first node level is in the interaortocaval chain at the second lumbar vertebral body (fig.13). In the case of the left testis, the first rank node is in the left paraaortic nodes in an area bounded by the renal vein, aorta, ureter and inferior mesenteric artery (fig.14). A lymphatic level crossing can occurs in a right-to-left chains following the normal drainage pattern to the cisterna chyli and thoracic duct. From the thoracic duct, tumor can spread to the left supraclavicular nodes and subsequently to the lungs. Left-to-right crossover is rare. (fig.15)

**Staging:**

The staging systems commonly used are the American Joint Committee on Cancer (AJCC) (fig.16) and the Internatinal Germ Cell Tumor Consensus Conference Classification.

**Extragonadal GCT:**
Primary germ cell tumors can occur outside the gonads and should be differentiated from regressed germ cell tumor with metastasis. Primary extragonadal GCTs can appear in the retroperitoneum, mediastinum (fig.17), sacrococcygeal area and pineal gland. They may result from aberrant migration of the germ cells from the yolk sac or represent persistent pluripotential cells that remained in primitive rests during somatic development.

**Testicular Microlithiasis:**

Testicular microlithiasis is a relatively uncommon finding in the general population (0.6%); historically, was initially considered to be an innocuous incidental finding. However, the association between microlithiasis and testicular carcinoma is clear (risk increase x40). The microcalcifications may result from an underlying abnormal testis, or perhaps the microcalcifications themselves trigger damage. Several findings have been demonstrated in association with microlithiasis, including cryptorchidism, infertility, Klinefelter syndrome, Down syndrome, atrophy,...

On US images, microlithiasis appears as punctate, nonshadowing, hyperechoic foci within the usually homogeneous testicle (fig.18).
Fig. 1: Embryologic Development

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**Fig. 2:** Cross-sectional drawing illustrates the anatomic components of the normal testis.

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Fig. 3: Imaging ultrasounds of a normal adult testis (longitudinal -left- and transverse -right- US image) showing a homogeneous echogenic, medium-level, granular echotexture.

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Fig. 4: Seminomas (a-b) A 33 years old man (left testicle). Multiple well-marginated, hypoechoic, homogeneous nodules with scant normal remaining parenchyma; we can see a slightly increase of the vascularization (b). (c-d) Multinodular homogeneously hypoecogenic mass surrounding by normal testicular tissue in right testis of a 27 years old man. (e-f) Large seminoma; longitudinal US image of the right testis shows a homogeneously hypo- isoechogetic enlarged right testis with no normal remaining parenchyma (a 32-years-old man). In all cases there is no extratesticular disease.

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Fig. 5: A 26 years old man, with lumbar pain and low-grade fever; physical examination and testis size were normal (a-b) Multifocal seminoma; longitudinal US images of the left testicle show some well-defined, hypoechoic nodules, with size less than 1cm. Note the presence of testicular microlithiasis. (c) Abdominal transverse US image shows retroperitoneal mass (adenopathy) (d-e) Extranodal metastasic disease (pulmonary nodes). The patient died in 8 months after diagnosis.

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Fig. 6: Multifocal seminoma; (f-h) axial and coronal chest CT images show some bilateral nodules consistent with pulmonary metastases. (i) Abdominal CT image shows large retroperitoneal mass. (j-k) Metastatic cerebral disease.

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Fig. 7: A 39 years old man with embryonal carcinoma (a) Longitudinal US image shows a heterogeneus, hypoechoic, well-defined mass in right testis (note some punctate hyperechoic foci -microlithiasis-). (b-c) Transverse US image (b) and CT abdominal image (c) show retroperitoneal lymphadenopathy (red arrows). (d-e) Radiograph of chest (d) and corresponding coronal chest CT image (e, lung window) show innumerable bilateral nodules. (f) Metastasic cerebral disease.

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Fig. 8: A 32 years old man with mixed GCT (composed from 98% mature teratoma and 2% embryonal carcinoma) in left testis. (a-e) US images show a very enlarged left testis with no normal remaining parenchyma; normal tissue is replaced by a big, heterogeneous lesion whit cysts or anechoic areas. (f) CT chest image shows bilateral nodes consistent with pulmonary metastases (red arrows).

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Fig. 9: A 32 years old man with choriocarcinoma. (a-d) US images show a heterogeneous isoechoic mass in the superior half of the right testis, with a slightly increased vascularity (b / d). It appears to invade the tunica albuginea (blue arrow). (e-f) PA and lateral chest radiograph show countless bilateral pulmonary nodes.

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**Fig. 10:** Same patient; (a) Liver metastases. (b) Retroperitoneal lymphadenopathy. (c-f) Chest CT images (d-f lung windows) show incontrollable necrotic pulmonary nodules. Gynecomastia is also noted (f, yellow arrow). (g-h) Unenhanced brain CT images show some hemorrhagic metastases with surrounding edema. Patient die 15 months after diagnosis.

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Fig. 11: A 21 years old man with mixed GCT in right testis. (a-c) Longitudinal US images show a heterogeneous isoechoic mass with some areas of hypoechogenicity and limited normal parenchyma in superior testis pole. In this case, note the obvious increased vascularity (b).

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Fig. 12: A 32 years old man with GCT (80% classic seminoma and 20% embryonal carcinoma) in left testicle. (a-b) Longitudinal US images show a heterogeneously hypoechogetic, enlarged left testis with no normal remaining testicular tissue. (c-e) Abdominal CT enhanced images show a big retroperitoneal mass (red arrow) with internal necrotic areas.

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Fig. 13: Abdominal CT images (coronal image -left- and axial section -right-) show lymphatic involvement in the interaortocaval chain at the second lumbar vertebral body (L2 level) in a 21 years old man with embryonal carcinoma in right testicle.

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Fig. 14: A 31 years old man with mixed GCT in left testis. Note a big necrotic retroperitoneal mass (a-c) at the left paraaortic nodes. Pulmonary metastases were present in diagnosis.

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**Fig. 15:** A 26 years old man with mixed GCT in left testis. (a-b) CT abdominal images show extensive retroperitoneal lymphadenopathy. Left-to-right crossover has produced.

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### TNM Staging Classification of Testicular Cancer (American Joint Committee on Cancer)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor (pT)*</td>
<td>Primary tumor cannot be assessed (if no radical orchiectomy has been performed, TX is used)</td>
</tr>
<tr>
<td>pTX</td>
<td>No evidence of primary tumor (e.g., histologic scar in testis)</td>
</tr>
<tr>
<td>pT0</td>
<td>Intratubular germ cell neoplasia (carcinoma in situ)</td>
</tr>
<tr>
<td>pTis</td>
<td>Tumor limited to the testis and epididymis without vascular or lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis</td>
</tr>
<tr>
<td>pT1</td>
<td>Tumor limited to the testis and epididymis with vascular or lymphatic invasion or tumor extending through the tunica albuginea with involvement of the tunica vaginalis</td>
</tr>
<tr>
<td>pT2</td>
<td>Tumor invades the spermatic cord with or without vascular or lymphatic invasion</td>
</tr>
<tr>
<td>pT3</td>
<td>Tumor invades the scrotum with or without vascular or lymphatic invasion</td>
</tr>
<tr>
<td>pT4</td>
<td>Tumor invades the spermatocord or with or without vascular or lymphatic invasion</td>
</tr>
<tr>
<td>Regional lymph nodes (pN)</td>
<td>Unknown nodal status</td>
</tr>
<tr>
<td>pNX</td>
<td>No regional node involvement</td>
</tr>
<tr>
<td>pN0</td>
<td>Node mass or single nodes ≤ 2 cm; ≤ 5 nodes involved (no node &gt; 2 cm)</td>
</tr>
<tr>
<td>pN1</td>
<td>Node mass &gt; 2 but &lt; 5 cm; or &gt; 5 nodes involved, none &gt; 5 cm; or evidence of extranodal tumor</td>
</tr>
<tr>
<td>pN2</td>
<td>Node mass &gt; 5 cm</td>
</tr>
<tr>
<td>Distant metastasis (M)</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>MX</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M0</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Nonregional nodal or pulmonary metastasis</td>
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<tr>
<td>M1a</td>
<td>Distant metastasis other than to nonregional lymph nodes and lungs</td>
</tr>
<tr>
<td>M1b</td>
<td>Serum tumor markers (S)*</td>
</tr>
<tr>
<td>SX</td>
<td>No marker studies available</td>
</tr>
<tr>
<td>S0</td>
<td>All marker levels normal</td>
</tr>
<tr>
<td>S1</td>
<td>LDH &lt; 1.5 × N1, plus hCG, &lt; 5,000 mIU/mL, plus AFP, &lt; 1,000 mg/mL</td>
</tr>
<tr>
<td>S2</td>
<td>LDH, 1.5-10 × N1, or hCG, 5,000-50,000 mIU/mL, or AFP, 1,000-10,000 ng/mL</td>
</tr>
<tr>
<td>S3</td>
<td>LDH, &gt; 10 × N1, or hCG, &gt; 50,000 mIU/mL, or AFP, &gt; 10,000 ng/mL</td>
</tr>
</tbody>
</table>

Source: American Joint Committee on Cancer. T = tumor, N = node, M = metastases.

*The extent of primary tumor is classified after radical orchiectomy.

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**Fig. 17:** A 32 years old man come in Emergency because of progressive dyspnea and chest pain. (a) Radiograph of chest reveals a thoracic center mass with left predominance. (b-c) Chest CT images; heterogeneous, well-defined, lobulated bulky mass located in mediastinum (probably anterior mediastinum) with necrotic internal areas. Pathological anatomy study confirmed mediastinal seminoma.

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**Fig. 18:** Testicular microlithiasis; Longitudinal US images of different patients show multiple, hyperechoic, nonshadowing foci scattered throughout the parenchyma. (a) A 28 years old man with seminoma in right testis; patient had only one testis (cryptorchidism, left testicle was no descended). (b) Longitudinal sonogram image of a 32 years old man with history of left testicle seminoma in the past (5 years before). Is recommended close follow-up of these patients.

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Findings and procedure details

Our results: we inspect a serie of 32 male patient in the 17-43 year-old age group who were diagnosed in testicular carcinoma, finding 9 cases of seminoma (28%), 14 cases of mixed GCT (44%), and 9 cases of nonseminomatous GCT (including 2 cases of mature teratoma -6%-, 5 cases of embryonal carcinoma -16%-, and 2 cases of choriocarcinoma -6%-).

All patient were suitably diagnosed in solid tumoral lesion by ultrasonography of the scrotum.
Conclusion

Ultrasounds are the gold standard imaging technique in the evaluation of the testis. Ultrasonography is done easily and proved to be almost 100% sensitivity in the identification of scrotal masses, combined by physical examination. Only seminomas show a homogeneously, hypoechoic uniform pattern and their imaging features are quite predictable.
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