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From Gynecomastia to Unexpected Testicular Mass: Clinical Journey of a Young Male with a Mixed Non-Seminomatous Germ Cell Tumor

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ABSTRACT

A 20-year-old male presented to Breast Clinic with asymptomatic, bilateral gynecomastia. Thorough physical examination revealed an incidental finding of an enlarged left testicle. Further investigation led to the diagnosis of testicular cancer without evidence of distant metastasis. The patient underwent radical left orchiectomy. Final pathology revealed Stage IB mixed Non-Seminomatous Germ Cell Tumor (NSGCT) with lymphovascular invasion (pT2). Adjuvantly, he received a single cycle of chemotherapy that was well tolerated. Although the presentation of painless testicular mass was characteristic for a patient with this diagnosis, it ultimately was diagnosed by the surgeon when being evaluated for a chief complaint of gynecomastia. This case highlights the need for vigilance in thorough physical examination and detection of testicular tumors in the primary care setting.

INTRODUCTION

Testicular Germ Cell Tumors (GCTs) are a prevalent form of testicular cancer, particularly affecting young adult males. While testicular cancer represents a small proportion of all cancers, it is the most common cancer among men aged 15-35 [1]. Non-seminomatous Germ Cell Tumors (NSGCTs) are a specific subtype that typically present with advanced disease in 60% of patients, with an unfavorable prognosis in higher clinical stages [2]. This highlights the importance of detecting testicular GCTs early, as they are highly curable when diagnosed in earlier stages. The clinical presentation of testicular cancer is varied, which drives the importance of timely evaluation, detection, and referral for suspected testicular masses. Prompt diagnosis and management, including the use of serum tumor markers and appropriate imaging, are essential for optimizing patient outcomes with effective early intervention and recovery.

CASE PRESENTATION

A 20-year-old male presented to Breast Surgery Clinic as a referral from primary care for evaluation of gynecomastia. The patient stated he noticed development of breast tissue bilaterally and disliked the look and size of his chest. He reported an increase in areolar size, and an itchy sensation when both nipples were squeezed. He denied masses, nipple discharge and breast pain. He reported an unintentional 80-pound weight loss over the prior two years. He had no history of cancer, liver, thyroid, or renal disease. He was taking creatine as an over-the-counter supplement and did not use prescription medications. The patient reported no recent changes in diet and denied smoking, though he vaped nicotine in his teens with the last use several years ago. Family history included cancer on his maternal side, though he did not know specific details regarding the cancer. Upon further questioning, the patient reported sudden left testicular enlargement, three months prior to presentation. His only reported trauma was a fall from a height of approximately three feet. He was unsure if the timing of the fall correlated to the testicular enlargement. He denied scrotal or groin pain, palpable masses, discoloration, scrotal rash, fevers, chills, night sweats. He also denied urinary symptoms, including dysuria, hematuria, and penile discharge. The patient tested negative for HIV two months prior to the clinic visit. He was sexually active with one female partner. He denied any history of sexually transmitted infections. There was no history of cryptorchidism, testicular torsion, hydrocele, inguinal hernia, or orchiopexy. He had not previously sought medical attention for testicular enlargement.

The patient was a military servicemember with a recent thorough Military Entrance Processing Service physical performed 18 months prior to presentation, which revealed no significant findings. No environmental or occupational risk factors were reported.

On physical examination of the chest and axilla, the overlying skin appeared normal. There was no expressible nipple discharge. There was palpable, non-tender, subareolar firmness bilaterally, consistent with gynecomastia, that measured 2.5 cm on the right and 4.5 cm on the left. There were no other palpable masses. There were no palpable axillary lymph nodes.

The testicular examination demonstrated significant asymmetric enlargement of left testicle, measuring approximately 8 cm in diameter. There was no tenderness to palpation of the testicle, epididymis, or scrotum bilaterally. There were no right testicular masses. Additionally, there was no evidence of inguinal hernias or inguinal adenopathy.

Given the finding of painless left testicular enlargement with unintentional weight loss, the patient was informed of the necessity for further evaluation. Urgent labs and imaging were ordered, and he was immediately referred to Urology for management.

A bilateral scrotal ultrasound was ordered to further evaluate the dimension and characteristics of the mass with abnormalities noted in the left scrotal ultrasound (Figures 1-2). The right scrotal ultrasound was noted to be normal (Figures 3-4). CT pelvis further assessed the mass and local metastasis (Figures 5-6). CT chest/abdomen ordered to assess for distant metastases (Figures 7-8).

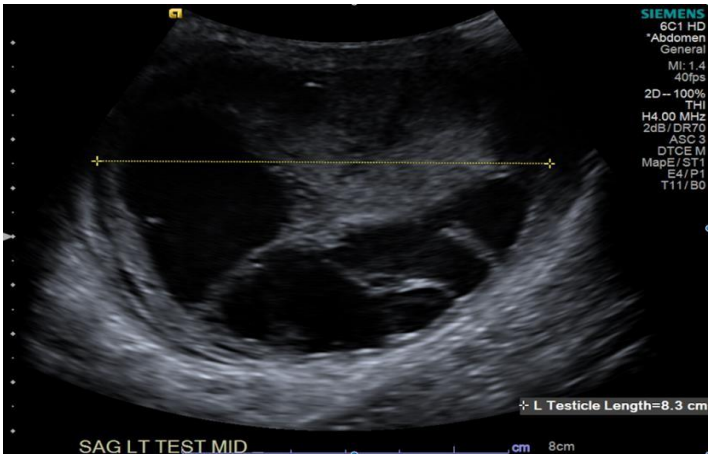

Figure 1: Heterogenous cystic and solid mass measuring at least 7.7 cm × 5.6 cm × 8.3 cm within the left testicle.

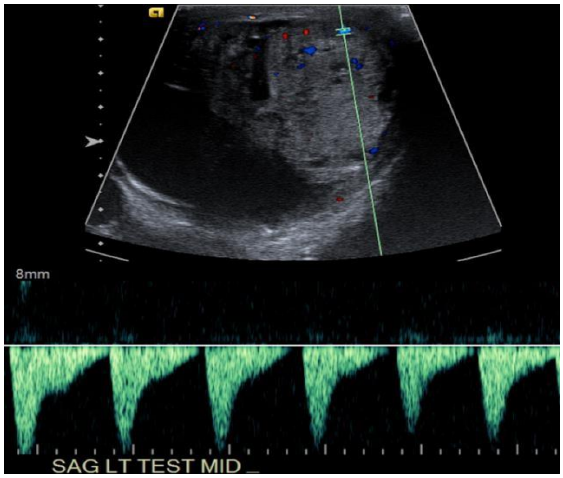

Figure 2: Internal arterial and venous waveforms are identified within the solid portion of the mass.

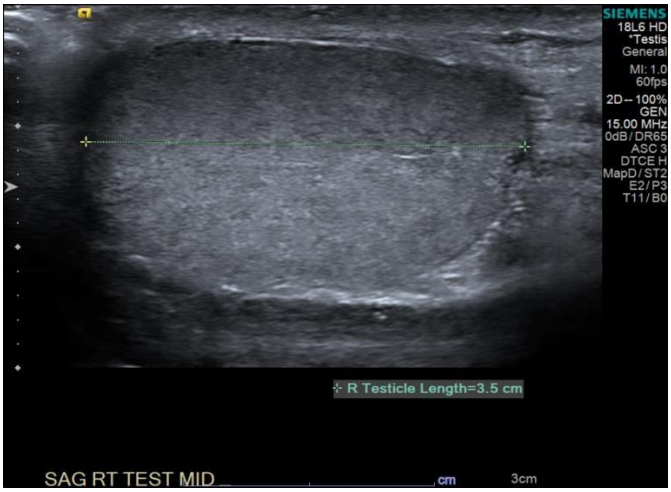

Figure 3: The right testicle is normal in size, morphology, and echotexture, measuring 3.5 cm × 2.4 cm × 3.3 cm.

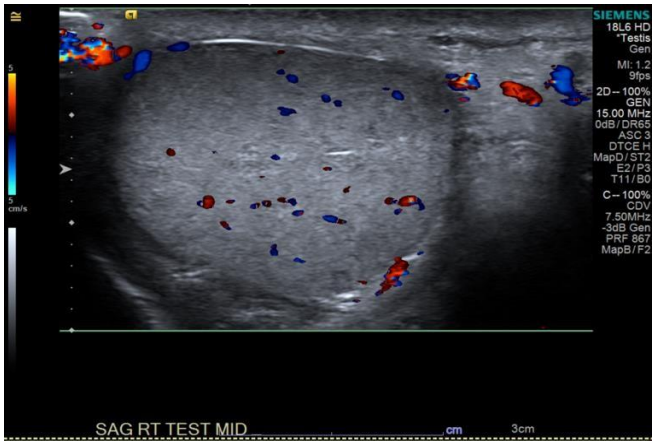

Figure 4: Right testicular arterial and venous waveforms are detected.

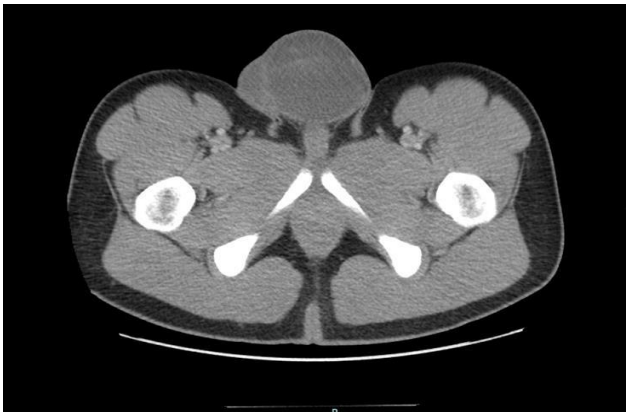

Figure 5: Partially visualized large mixed cystic and solid left testicular mass, measuring up to 8.2 cm × 7.8 cm.

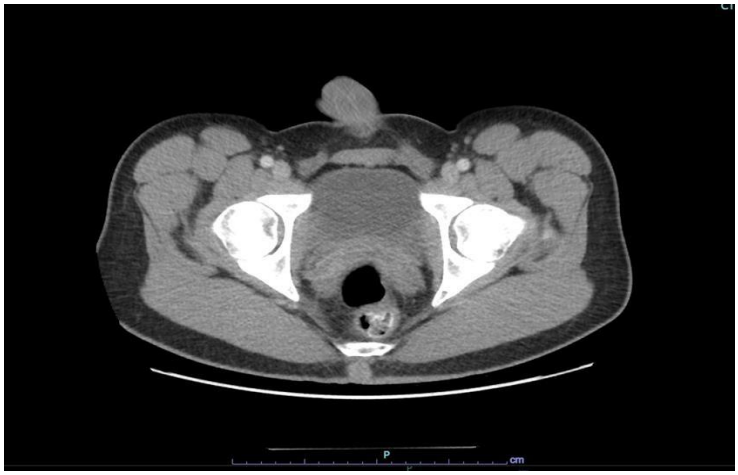

Figure 6: Few prominent bilateral inguinal lymph nodes and retroperitoneal nodes, with the most conspicuous measuring 3mm. Bladder is unremarkable and there is no evidence of metastatic disease in pelvis.

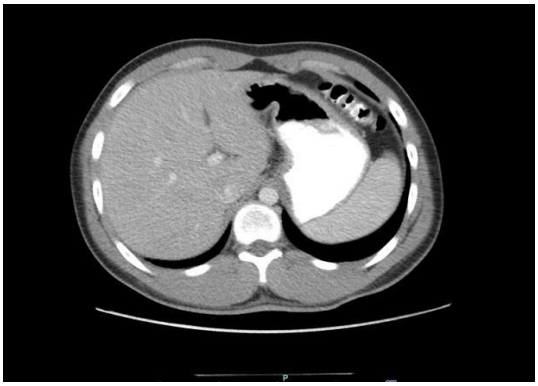

Figure 7: No evidence of metastatic disease within the chest or abdomen.

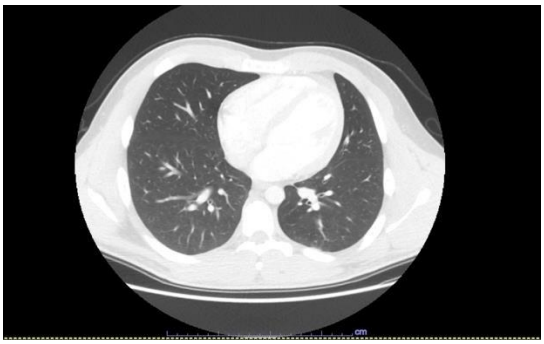

Figure 8: No evidence of metastatic disease within the chest or abdomen.

TREATMENT

The patient underwent a successful radical left orchiectomy via an inguinal approach one week after the initial presentation (Figure 9). The patient was subsequently followed in the outpatient setting by Medical Oncology for further treatment.

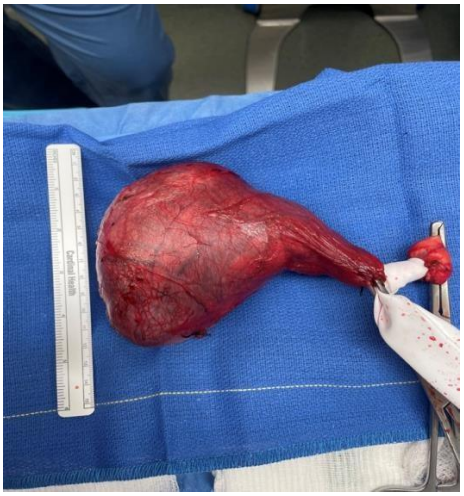

Figure 9: Left testicle and spermatic cord post-orchiectomy. Measuring 8.5 cm × 6.5cm × 5.1 cm.

The resected mass was diagnosed as a stage IB mixed Non-Seminomatous Germ Cell Tumor (NSGCT) 80% yolk sac + 20% teratoma [3]. The tumor was confined to the testis with Lymphovascular Invasion (LVI) present, pathologic grade T2 (Figure 10-11). There was no evidence of retroperitoneal nodal or distant metastatic disease on CT imaging of the chest, abdomen, and pelvis (Figures 5-8).

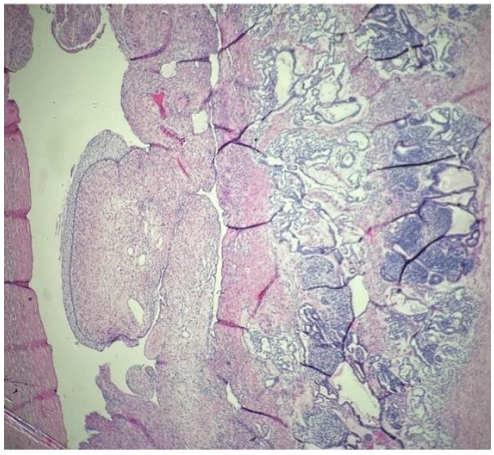

Figure 10: H&E image at 4X magnification showing a mixed germ cell tumor with teratoma and yolk sac components.

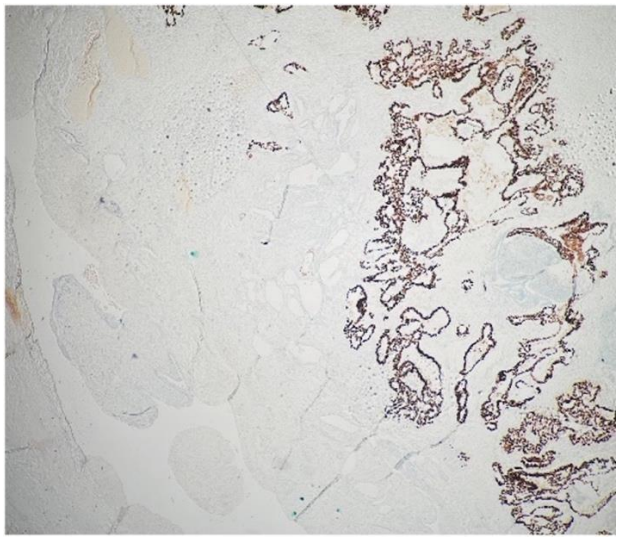

Figure 11: Pan-keratin (AE1/AE3) highlighting both yolk sac component and epithelial portions of teratoma component.

Post-operative Alpha-Fetoprotein (AFP) levels were markedly decreased to 2.7 ng/mL (Table 1,2), indicating a significant reduction in tumor marker levels.

The patient was considered a candidate for a single cycle of BEP chemotherapy (bleomycin, etoposide, cisplatin) for relapse reduction. Baseline pulmonary, renal function and audiology tests were performed prior to initiating each cycle of chemotherapy to monitor for potential side effects.

Table 1: Basic endocrine studies (estradiol, FSH, LH, testosterone total, TSH, free T4) were ordered and all found to be within normal limits.

Endocrine Studies (pre- treatment)	Value	Reference
Estradiol	48.3 pg/mL	-
FSH	2.6 mIU/mL	-
LH	4.0 mIU/mL	-
Testosterone total	459.0 mg/dL	-
TSH	1.9	-
Free T4	1.18 ng/mL	-

Table 2: Further initial laboratory studies revealed an elevated AFP of 172.0 ng/mL, without elevations in beta-HCG and LDH. Reference for AFP: (0-5.7 ng/mL).

Tumor markers	Pre-resection	Post resection
LDH	151 U/L	265 U/L
Beta HCG	<2.42 mIU/mL	<1 mIU/mL
AFP	172.0 ng/mL	2.7 ng/mL

Outcome and follow-up

The patient recovered well from the radical left orchiectomy and returned to full daily functioning. A Mediport was placed for administration of a single cycle of BEP chemotherapy, which was well-tolerated. The patient experienced manageable side effects, including nausea and reflux. These symptoms were responsive to Compazine and famotidine, respectively, and resolved completely after the completion of chemotherapy.

The patient experienced infrequent tinnitus without accompanying hearing loss. Follow-up with audiology is planned for post-cisplatin monitoring. No signs of neuropathy or pulmonary toxicity were observed during the treatment course.

According to NCCN guidelines for stage IB non-seminomatous germ cell tumor, the patient will have follow-up as follows [4]: laboratory markers every 3 months for the first two years, every 6 months for the next two years, and then annually in year 5. Annual CT scans of the chest, abdomen, and pelvis for the first two years, and subsequently as clinically indicated.

DISCUSSION

Non-Seminomatous Germ Cell Tumors (NSGCTs) encompass several subtypes including embryonal carcinoma, yolk sac tumor, teratoma, and choriocarcinoma. Embryonal carcinoma is known for its aggressive nature and often presents with mixed growth pattern [5]. Yolk sac tumors, typically found in younger patients, may secrete Alpha-Fetoprotein (AFP). Choriocarcinoma is highly aggressive and is characterized by elevated Human Chorionic Gonadotropin (hCG) levels. Teratomas are composed of mature or immature tissue from the three germ layers

(ectoderm, mesoderm, and endoderm). Unlike seminomas which are less aggressive and more responsive to radiation therapy, NSGCTs manifest with advanced disease in 60% of patients [2]. The development of these tumors often involves genetic mutations and chromosomal abnormalities, such as isochromosome 12p which is found in 80% of germ cell tumors regardless of the histologic type [5].

Testicular Mixed Germ Cell Tumors (TMGCTs) are composed of at least two different histologic types. These compromise approximately one-third of germ cell tumors [5]. These mixed forms mainly include embryonal carcinoma in combination with teratoma [6]. Interestingly, teratoma identified in a mixed germ cell tumor has deceptively benign morphology with underlying hidden malignant features [5]. Although the proportion of each germ cell tumor type is variable, they exhibit histologic features corresponding to the pure form. The main cause of TMGCTs is the limited differentiation of a single seminoma into the components of a nonseminoma [2]. Tumors markers Alpha-Fetoprotein (AFP), human Chorionic Gonadotropin (hCG), and Lactate Dehydrogenase (LDH) all play a vital role in tumor diagnosis and management. Non-seminomatous germ cell tumors, such as yolk sac tumor or MGCT, predominantly have elevated levels of AFP. Elevated hCG levels are linked to choriocarcinoma and other non-seminomatous germ cell tumors, including embryonal carcinoma, and can also be elevated in seminomas, though less frequently [6]. LDH, a non-specific marker, may be elevated in various cancers, including testicular germ cell tumors, and is used to assess tumor burden and response to treatment [6]. Histologic confirmation by immunohistochemistry becomes important regarding the proportions of each germ cell type involved in the final diagnosis.

Testicular germ cell tumors typically present as a palpable, firm, non-tender mass in the testicle, however, presentations can vary. Some post-pubertal patients may experience atypical symptoms such as testicular pain, swelling, gynecomastia, or an abdominal mass [7]. Oftentimes in prepubertal males, GCTs can present as testis torsion, trauma, or hydrocele [7]. If the disease is advanced enough, symptoms of metastasis may occur.

Studies suggest that a significant proportion of testicular germ cell tumors are initially detected in the primary care setting or by patients themselves, often before metastasis has occurred. Between 1973 and 2014, the percentage of testicular tumors diagnosed at a localized stage increased from 55% to 68% in the US [8]. At present, less than 15% of men present with stage III disease, with metastasis to the pulmonary, nonpulmonary, or non-regional lymph nodes [9]. This stage migration in the last 40 years is presumably due to increased awareness and thus earlier diagnosis. Early detection of testicular cancer is crucial as it is associated with a higher cure rate and less aggressive treatment. Testicular cancer detected at Stage I has a 5-year survival rate exceeding 95% [9], compared to lower survival rates for more advanced stages. However, lack of awareness is a significant barrier to early detection.

The American Academy of Family Physicians (AAFP) recommends a routine testicular examination for any patient needing a breast evaluation for gynecomastia and further testicular ultrasound for those with palpable testicular masses, gynecomastia larger than 5cm, or otherwise unexplained gynecomastia [10]. It is important to understand that the possibility of a testicular tumor must be evaluated in any male patient presenting with a complaint of gynecomastia.

Routine screening for testicular cancer in asymptomatic men is not recommended per the American Cancer Society [11]. However, the ACS acknowledges that testicular self-examination may be considered for highrisk individuals, such as those with a history of cryptorchidism or a family history of testicular cancer [11]. The American Urological Association (AUA) guidelines indicate that a solid mass in the testis identified by physical exam or imaging should be managed as a malignant neoplasm until proven otherwise [8]. Scrotal ultrasound with Doppler should be obtained in patients with a unilateral or bilateral scrotal mass suspicious for neoplasm and tumor markers should be obtained and measured prior to any treatment [8].

These guidelines are based on evidence that survival rates for early-stage testicular cancer are high with standard therapy. However, disease progression is highly dependent on early assessment. Managing a scrotal mass of unknown etiology urgently facilitates prompt evaluation by a Urology specialist. Primary care providers should not only inform patients about the importance of timely evaluation, but also coordinate communication with the urology department to expedite referrals. Streamlining the referral process and coordinating care between primary care and urology can enhance turnaround times and patient management.

CONCLUSIONS

The clinical presentation of testicular cancer can vary which makes diagnosis challenging. Standard physical exam for gynecomastia must include testicular evaluation in the primary care setting before referral to specialists. Early-stage testicular cancer is highly treatable and associated with excellent outcomes; therefore early detection is very important. Prompt Urology referral is important to guide staging, surgical planning, and surveillance. Scrotal ultrasound and serum tumor markers can be ordered concurrently with urology referral. Although there are no standard guidelines for screening of testicular cancer, prevention of tumor growth to extraordinary dimensions is dependent on deliberate examination in the primary care setting in addition to patient awareness.

DECELERATION

Data availability

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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