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Upper Gastrointestinal Bleeding Due to a Duodenal Metastasis from Primary Testicular Squamous Cell Carcinoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 57-year-old
Final Diagnosis: Metastatic squamous cell carcinoma
Symptoms: Dizziness • fatigue • melena • testicular mass
Medication: —
Clinical Procedure: Esophagogastroduodenoscopy • surgery and radiotherapy
Specialty: Gastroenterology and Hepatology • Oncology • Surgery • Urology

Objective: Rare disease

Background: Primary squamous cell carcinoma of the testis (tSCC) is exceptionally rare. To date, only 5 cases have been described in the literature. We report the first case of upper gastrointestinal bleeding due to a duodenal metastasis from tSCC.

Case Report: We report a male patient who presented with marked swelling of his left scrotum. Inguinal orchiectomy demonstrated keratinizing squamous cell carcinoma (SCC). All surgical margins were negative, and germ cell neoplasia *in situ* was not identified. PET/CT showed retroperitoneal metastasis. He underwent surgical resection. Three months later, surveillance imaging revealed progression of metastatic disease, including a mass between the transverse duodenum and inferior vena cava invading the duodenal wall without obstruction. Two days later, he presented to the hospital due to gastrointestinal bleeding. CT of the abdomen was negative for a retroperitoneal bleed or intraluminal bleed with stable metastatic retroperitoneal lymph nodes. Esophagogastroduodenoscopy (EGD) showed a fungating and oozing mass in the second portion of the duodenum. Biopsies confirmed metastatic SCC. Palliative radiation and adjuvant chemotherapy were initiated.

Conclusions: tSCC, though rare, is an aggressive malignancy and requires prompt and aggressive combined oncological treatment. Most of the cases have been reported to develop from an epidermal cyst, chronic hydrocele, or epididymis. This malignancy can lead to unexpected phenomena such as gastrointestinal bleeding or intestinal obstruction due to its unique metastatic pattern.

MeSH Keywords: Carcinoma, Squamous Cell • Gastrointestinal Hemorrhage • Neoplasm Metastasis • Testicular Neoplasms • General Surgery • Chemotherapy, Adjuvant • Radiotherapy, Adjuvant

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/922007

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Background

A painless testicular mass is the most common initial presentation of testicular cancer [1]. Germ cell tumors (GCTs) account for more than 90% of testicular cancer. Clinically, these tumors are classified as either seminoma or nonseminoma [2]. The remaining 5–10% of tumors are generally sex cord-stromal tumors, derived from cells involved in the generation and maturation of sperm [1,3]. Primary testicular squamous cell carcinoma (tSCC) is extremely rare, and metastasis from other organs should be excluded first [3]. Lymphoma and prostate cancer are the most frequent diseases to metastasize to the testicles [4]. Among SCC, lung is the most common primary site [5]. To date, only 5 cases of tSCC have been described in the literature [6–10]. Gastrointestinal manifestation of GCTs is uncommon (5%), with duodenal involvement seen in only 1.4% of cases [11]. We report the first case of upper gastrointestinal bleeding due to a duodenal metastasis from tSCC.

Case Report

A 57-year-old male patient with past medical history of major depression, essential hypertension, and coronary artery disease status post drug-eluting stent placement presented for initial evaluation in the Genitourinary Medical Oncology Clinic. He reported that 10 years ago, he had some trauma while playing soccer and developed bruising in his right upper thigh and had some shrinkage of his right testis afterward, but his left testis actually increased in size at that time. He underwent an ultrasound, which was negative. He had no further difficulty until February 2018, when he noted marked swelling of his left scrotum.

Scrotal ultrasound showed a hypoechoic solid mass measuring 5.6×5.1×5.2 cm with large left hydrocele, and a clinical exam noted no skin lesions. Tumor markers included alpha-fetoprotein (AFP) 2.8 ng/ml (0–8), beta human chorionic gonadotropin (beta-hCG) <2 mIU/ml (<5), lactate dehydrogenase (LDH) 157 IU/L (120–240). Computed tomography (CT) of chest, abdomen, and pelvis demonstrated enlarged para-aortic lymph node (LN) measuring 1.6 cm in short axis. He subsequently underwent left inguinal orchiectomy, which demonstrated a 6.5-cm solid and cystic mass composed of invasive moderately-differentiated keratinizing SCC involving the testicular parenchyma, epididymis, and hilar soft tissue **(**Figure 1). A separate, noncontiguous 1.8-cm mass of keratinizing SCC was present in the proximal spermatic cord. Germ cell neoplasia *in situ* was not identified, and all surgical margins were negative. PET/CT was strongly suggestive of retroperitoneal metastasis (Figure 2).

Due to the uncommon diagnosis of tSCC and no clear standard therapy, surgical resection was indicated with the possibility of being curative. At the end of May 2018, he underwent retroperitoneal lymph node dissection, which showed an extensive retroperitoneal mass invading the mesentery of the descending colon, a gonadal vein tumor with extension into the left renal vein and left ureter, completely encased by the tumor. The procedure included ureterolysis, cord excision, mobilization, and resection of a portion of the descending colonic mesentery and serosa, with lysis of adhesions. The postoperative course was complicated by retroperitoneal bleeding and abdominal compartment syndrome, from which he recovered completely. Pathology from the abdominal surgery revealed keratinizing SCC extensively involving soft tissue, with invasion of and tumor thrombus within large veins, and metastatic keratinizing SCC was present in 1 of 44 retroperitoneal lymph nodes. Given lack of clear evidence of adjuvant chemotherapy or radiation, we began surveillance with a planned repeat CT of the chest, abdomen and pelvis in approximately 3 months.

Approximately 3.5 months after surgery, a CT of the abdomen and pelvis revealed progression of metastatic disease with multiple new centrally necrotic soft tissue masses involving the retroperitoneum and mesentery. There was a left retroperitoneal mass invading the wall of the descending colon, resulting in luminal narrowing but no upstream obstruction. Another mass sized 2.9×2.8 cm between the transverse duodenum and inferior vena cava was reported, which was invading the duodenal wall without any obstruction **(**Figure 3**)**. At least 5 regional disease deposits >1 cm were also present. A CT chest was notable for an indeterminate 5-mm (previously 3 mm) nodule along the right diaphragmatic pleura. We planned to present his case to the Tumor Board.

Two days later, he came to the hospital due to new-onset dizziness and fatigue, and was found to have a hemoglobin of 7.5 g/dl (baseline 12.6). He reported no obvious bleeding. On arrival, he had an episode of melena, and his hemoglobin decreased further to 6.2 g/dL, for which he received 1 unit of packed red blood cells. A CT abdomen and pelvis was negative for a retroperitoneal bleed or intraluminal bleed, with stable metastatic retroperitoneal and mesenteric LNs. EGD demonstrated a 2-cm fungating and oozing mass in the second portion of the duodenum. Colonoscopy showed a submucosal, non-obstructing, 3-cm mass in the sigmoid colon, causing external compression at 35-cm from the anal verge. No bleeding was present. Mucosa overlying the mas was normal. A biopsy from the duodenum confirmed metastatic keratinizing SCC (Figure 4). Palliative radiation to 30 Gy in 10 fractions for approximately 2 weeks was initiated to control local gastrointestinal bleeding. After radiation, he completed 2 cycles of cisplatin and 5-fluorouracil combination chemotherapy but had disease progression.

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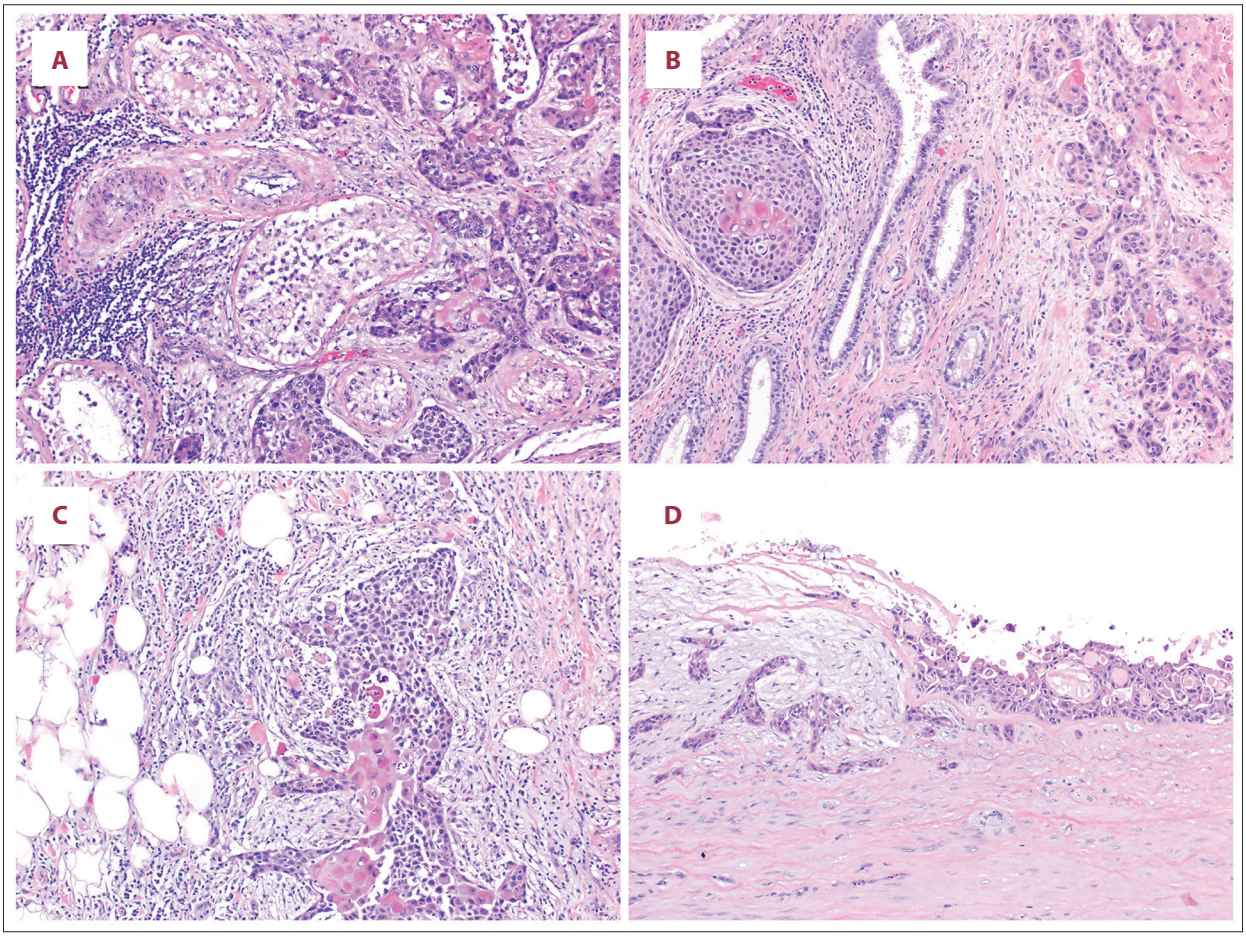

Figure 1. Primary testicular squamous cell carcinoma. (**A–D**) Hematoxylin and eosin (H&E) images of invasive moderately-differentiated keratinizing squamous cell carcinoma involving testicular parenchyma (**A**), epididymis (**B**), and hilar soft tissue (**C**). Cystic areas of the primary tumor were lined by atypical keratinizing squamous epithelium (right in **D**) with adjacent invasive carcinoma showing stromal desmoplasia (left in **D**). Objective magnification=10×.

On January 2019, a repeat CT of chest, abdomen, and pelvis showed enlargement of the previously evident solid-appearing mass in the left abdominal mesentery (5.2×3.7 cm from 4.1×3.5 cm) without evidence of high-grade bowel obstruction (Figure 5). Due to inability to sequence the small duodenal biopsy, he underwent an interventional radiology-guided biopsy of the abdominal mass. One week later, he was readmitted due to gastrointestinal bleeding. A repeat EGD showed a non-bleeding duodenal ulcer with no stigmata of recent bleeding on the second portion of the duodenum. Colonoscopy was deferred due to high risk of perforation. Bleeding was treated with radiation again. Due to his recurrent gastrointestinal bleeding and need for transfusions, he was not a candidate for any clinical studies with CDK4/6 inhibitors, so the decision was made to start docetaxel chemotherapy.

Discussion

tSCC is an extremely rare entity, with only 5 cases reported in the literature so far (Table 1). Therefore, it is crucial to rule out a secondary involvement of the testicles. In the literature, all the reported patients were middle-aged (over 50 years old) except for 1 young patient who was 27 years old; this young patient was reported to have tSCC arising from the epididymis and was much more aggressive than the other cases [6].

Trauma can play a role in the pathogenesis of tSCC. It is proposed that prolonged inflammation contributes to squamous metaplasia of the lining cells, progressing to dysplasia, carcinoma *in situ,* and, ultimately, invasive squamous carcinoma [7,8]. Most of the patients presented with enlarged testicles for a lengthy period of time but were brought to medical attention when pain occurred. One patient underwent removal of the testicle as a part of other urological surgery, and was incidentally found to have tSCC developed in chronic

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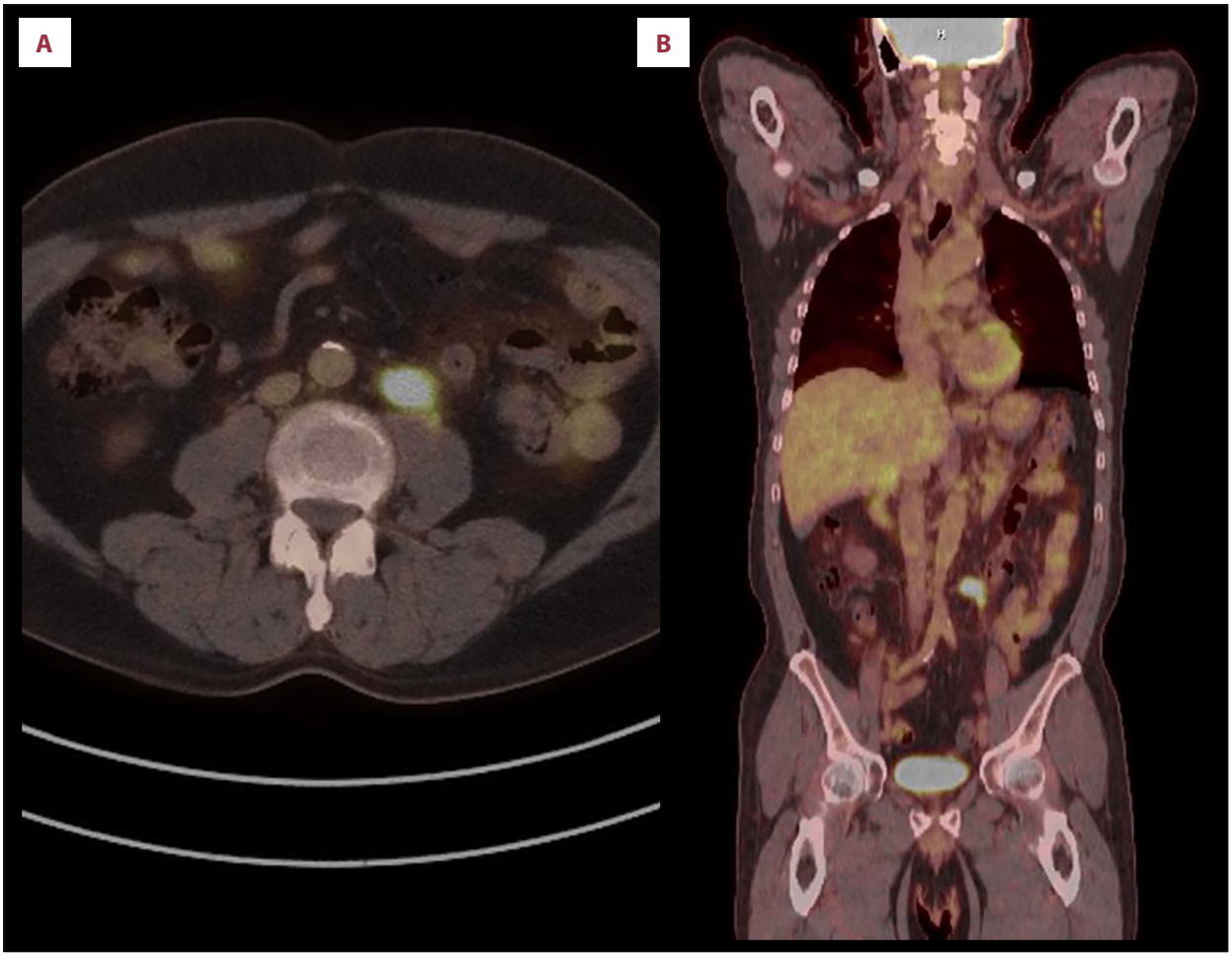

Figure 2. Positron emission tomography/computed tomography: (**A**) Axial and (**B**) coronal view of left retroperitoneal lymph node with increased metabolic activity.

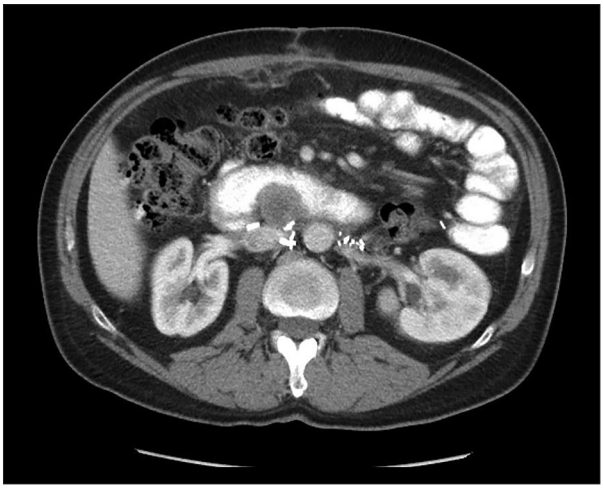

Figure 3. Computed tomography of abdomen and pelvis with contrast showing a 2.9×2.8 cm mass between the transverse duodenum and inferior vena cava. This mass likely invades the duodenal wall without evidence of obstruction.

hydrocele [7]. All the patients who were diagnosed with tSCC were diagnosed on histopathological examination after radical orchiectomy. Therefore, it is almost impossible to diagnose tSCC based on non-invasive testing. Three cases originated from epididymal cysts – one case from epididymis and another from a chronic hydrocele.

Tumor markers such as ALP, b-hCG, and LDH are generally not elevated [6,8,10]. Carcinoembryonic antigen was reported to be minimally elevated in 1 case [9]. In gross appearance, these tumors appear to arise as thick-walled cystic masses filled with cheesy or brown pus-like material [8,9]. These masses sometimes replace all the testicular tissue and also invade testicular layers [8]. A similar cystic appearance can be seen on imaging with ultrasonography or CT.

Previous to tSCC diagnosis, it is imperative to rule out any secondary causes of squamous cell metastasis to the testicles such as lung or head and neck cancer. Furthermore, the entire gross specimen needs to be examined for elements of

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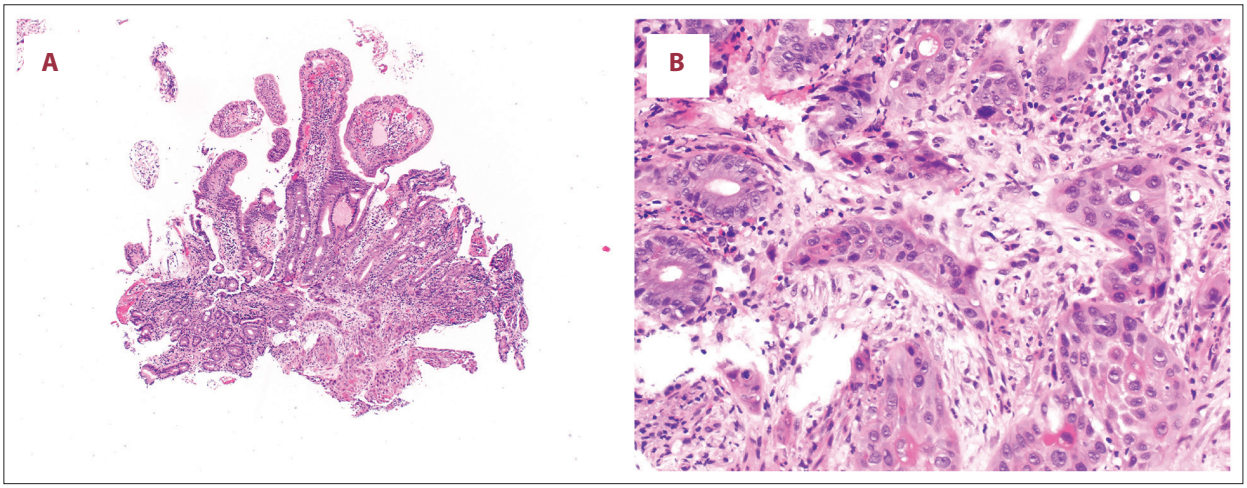

Figure 4. Metastatic testicular squamous cell carcinoma involving the duodenum. (**A, B**) Hematoxylin and eosin (H&E) images of metastatic keratinizing squamous cell carcinoma involving duodenal mucosa. Objective magnification=4× (**A**) and 20× (**B**).

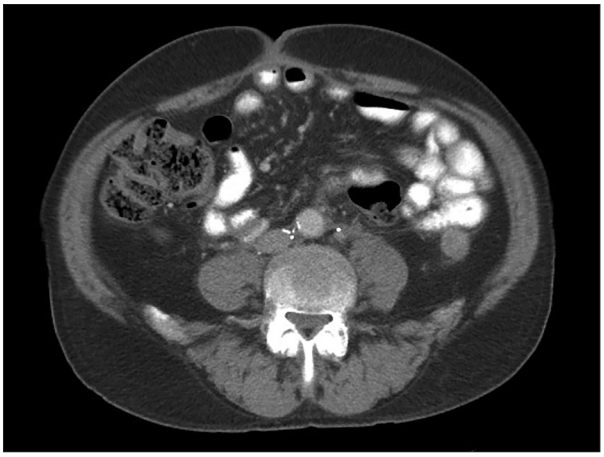

Figure 5. Computed tomography of abdomen and pelvis with contrast showing a heterogenous solid-appearing mass in the left abdominal mesentery measuring 5.2×3.7 cm.

teratomas. In case of well-defined cystic structure, the cystic lining needs to be examined for teratomatous components such as appendages, nails, and teeth. Histologically, the lining of malignant cystic structures may contain components of squamous metaplasia, dysplasia, *in situ* SCC, and invasive SCC [7]. The central cheesy or gray material of the masses is keratinous in nature [8,9].

Artemyeva et al. reported a case of tSCC with poor differentiation, along with necrosis and hemorrhage without keratinization [6]. Immunohistochemically, markers of SCC are positive [8].

Negative immunoreactivity with placental ALP, b-HCG, and AFP can be helpful in differentiating primary SCC from mixed GCTs [8]. As all these patients may have had testicular swelling for years and may also have had an epidermal cyst for a prolonged period of time, which led to the squamous dysplasia with subsequent malignant transformation into SCC of the testicle, originating from the epidermal cyst.

In regard to treatment, all patients underwent radical orchiectomy. However, the stage of tSCC is not well-defined. LN involvement was reported in 2 patients at the time of diagnosis [6,8]. Only 1 patient had been reported to undergo chemotherapy after radical orchiectomy, reported by Artemyeva et al., with cisplatin+5-Flurouracil [6], but this patient was reported to have received only 1 cycle of chemotherapy. Long-term follow-up or surveillance data that could have provided insight into the prognosis of tSCC were also not available in these patients. Only 1 out of 5 patients was reported to have a 6-month follow-up, and that patient was alive and without evidence of any recurrence at time of publication [10].

Gastrointestinal involvement in testicular cancer is very uncommon (5%), with only 1.4% of cases demonstrating duodenal metastases [12]. To date, this represents the first case of tSCC with gastrointestinal involvement reported in the literature. Previous reviews have demonstrated that non-seminoma germ cell tumors are more likely to have gastrointestinal involvement than seminomas (60% *vs.* 20%) [13,14]. The most common gastrointestinal manifestations are abdominal pain (46%), melena (44%), and hematemesis/hematochezia (24%). Mean hemoglobin was 6.8 g/dl with patients requiring large-volume transfusion to maintain hemodynamic stability [13,14].

Our patient is also similar to the other cases reported in terms of age (57 years old), longstanding history of testicular enlargement, with rapid growth and negative tumor markers. Similar to other cases, our patient may have had an epidermal cyst or hydrocele for a long time, which transformed into SCC, leading to rapid growth. In contrast, our patient had extensive tumor burden due to lymphovascular invasion and

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Table 1. Literature review of case reports of squamous cell carcinoma of the testicles.

Author, year	Age	Presentation	Origin	Pathology	Lymph nodes, distant metastasis	Treatment	Follow-up
Bryan et al., 1990 [7]	85-YoM	Chronic scrotal swelling	Chronic hydrocele	Moderately-differentiated	–LNs	• Surgery: RO	Not reported
Shih et al., 1996 [9]	64-YoM	Enlarged testicle with painful swelling	Epidermal cyst	Keratinized	–LNs	• Surgery: RO	Not reported
Kim et al., 2010 [8]	51-YoM	Enlarged testicle and scrotal pain	Epidermal cyst	Keratinized moderately-differentiated	+LNs	• Surgery: RO	Lost to follow-up
Artemyeva et al., 2018 [6]	27-YoM	Enlarged testicle with rapid growth	Epididymis	Non-keratinized poorly-differentiated	+LNs, lungs	• Surgery: RO • Chemo: cisplatin+ 5-fluorouracil	
Kasahara et al., 2019 [10]	50-YoM	Painless scrotal mass	Epidermal cyst	Keratinizing well-differentiated	–LNs	• Surgery: RO	Alive at 6 months, no recurrence
Gonzalez et al., 2019	57-YoM	Enlarged testicle with rapid growth	Origin?	Keratinizing moderately-differentiated	+LNs, retroperitoneal mass with invasion of mesentery, left renal vein/left ureter involvement	• Surgery: RO, retroperitoneal LNs dissection and resection of tumor burden • Radiations: palliative to control gastrointestinal bleeding • Chemo: cisplatin+ 5-flurouracil followed by docetaxel	

YoM – Year-old-Male; Yr. – year; RO – radical orchiectomy; LNs – lymph nodes.

underwent RPLN dissection with the excision of a tumor with curative intent. However, the tumor had rapid metastatic progression after 3 months, leading to intestinal bleeding requiring palliative radiation on 2 separate occasions and ongoing systemic chemotherapy. Our experience with this patient suggests that aggressive treatment approaches should be adopted from the beginning in an attempt to achieve better patient-related outcomes.

Conclusions

tSCC, though rare, is an aggressive malignancy and needs aggressive management. Most of the cases have been reported to develop from epidermal cyst, chronic hydrocele, or epididymis. Longstanding history of testicular enlargement with rapid growth points toward acute-on-chronic pathogenesis in the development of tSCC. Patients with chronic testicular enlargement due to cystic changes may need removal of the cyst before it transforms into a malignancy, especially in middle-aged men. Experience with our case denotes the significance of aggressive treatment approaches from the beginning of diagnosis. Even after the surgical excision of metastatic masses, adjuvant therapy can be beneficial in cases of lympho-vascular invasion because microscopic disease can emerge as gross disease burden in the near future. tSCC can lead to unexpected phenomena such as gastrointestinal bleeding or intestinal obstruction due to its unique metastatic pattern. Guidelines need to be developed to manage such malignancies.

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