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·*Case Report*·

Extragastrointestinal stromal tumor presenting as a scrotal mass: an unusual case

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Abstract

We describe an unusual case of extragastrointestinal stromal tumor (EGIST) presenting as a scrotal mass. A 71-year-old man presented with a gradually enlarging scrotal mass with a 20-year duration. Physical examination revealed a huge (as large as volleyball), round, nontender mass occupying the whole scrotum, which was resected completely. Clinical and radiological findings did not comply with any other primary site disease. Under histological examination, the tumor showed a spindle cell pattern with low cellularity, absence of necrotic and mitotic features. Immunohistochemical anlaysis revealed the tumor reactive for CD117 and CD34, while negative for smooth muscle actin, desmin and S-100 protein. To our knowledge, this is the first reported case of an EGIST involving the scrotum. *(Asian J Androl 2007 Mar; 9: 275–279)*

Keywords: extragastrointestinal stromal tumor; scrotum; immunohistochemistry

1 Introduction

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors that arise from the wall of the gastrointestinal tract expressing CD117 and/or CD34 [1]. Similar tumors in the soft tissue of the abdomen are called extragastrointestinal stromal tumors (EGIST). We report a case of a huge left scrotal mass in a 71-year-old man, which was treated with complete surgical resection. Histological assessment showed a spindle cell neoplasm, which was positive for CD117 and CD34 on immunohistochemical analysis, consistent with an EGIST. To our knowledge, there has been no report of a primary GIST in the scrotum.

2 Case report

A 71-year-old man was admitted to our department because of a huge scrotal mass, which had enlarged gradually over a 20-year period. Physical examination revealed a huge, round, nontender mass, approximate to the size of a volleyball, occupying the whole left scrotum and several tortuous engorged blood vessels on the distended scrotal wall (Figure 1). Laboratory findings showed the level of serum tumor markers, including alpha-fetoprotein, human chorionic gonadotropin and lactic acid dehydrogenase, were within the normal range. Scrotal ultrasonography showed a huge, heteroechogenic

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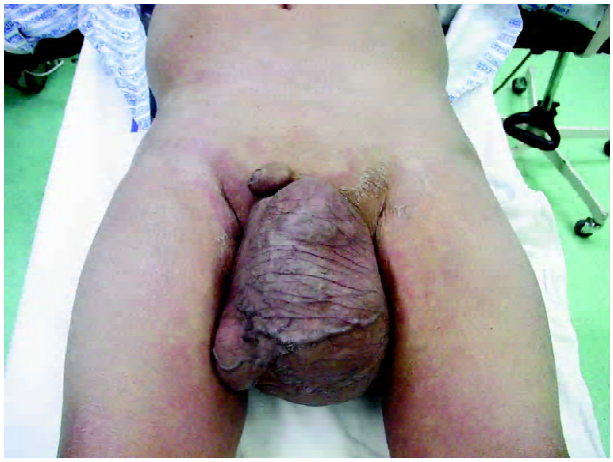

Figure 1. Physical examination revealed a huge (as large as volleyball), round, non-tender mass occupying whole the left scrotum, with several tortuous engorged blood vessels on the distended scrotal wall

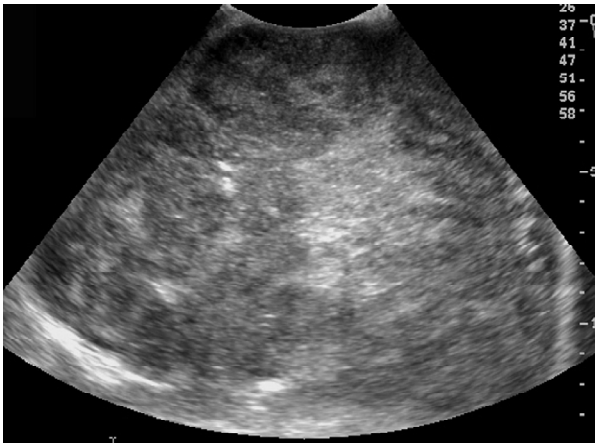

Figure 2. Transverse scan of the scrotum with a 2–5 MHz convex array transducer shows a heterogeneously echogenic mass in the scrotum.

lesion in the left scrotum, but there was no abnormal finding in both testis and epididymis (Figure 2). Preoperative magnetic resonance imaging revealed a 12 × 15 × 18 cm-sized, well demarcated mass in the left scrotum. The mass showed a slightly high signal intensity on both the T1 and T2 weighted images (Figure 3). Multiple flow void with intense enhancement indicated vasculature within the mass. There was a non-enhancing central portion of the mass that was considered necrotic, with a high signal intensity on the T2 weighted image and low signal intensity on the T1 weighted image. Both testes were normal and showed good separation from the mass. There was no evidence of lymph node enlargement or ascites. Computed tomography scans of the chest, abdomen and pelvis failed to reveal other mass lesions.

The patient underwent a complete gross excision of the mass with a vertical left scrotal incision extending to the left lower inguinal area. At surgery, there were many engorged blood vessels to the mass and we ligated all of these during excision. The mass displaced the left testis to the upper lateral scrotum but the left testis and epididymis appeared normal. After excising and trimming the remnant scrotal wall for cosmetic purposes we orchiopexied the left testis.

Grossly, the surgical specimen consisted of an ovoid, whitish-gray, firm lobulated mass, measuring 19.5 × 12.5 × 12 cm and weighing 1.8 kg. It was encapsulated well and cut sections showed yellowish fibrotic

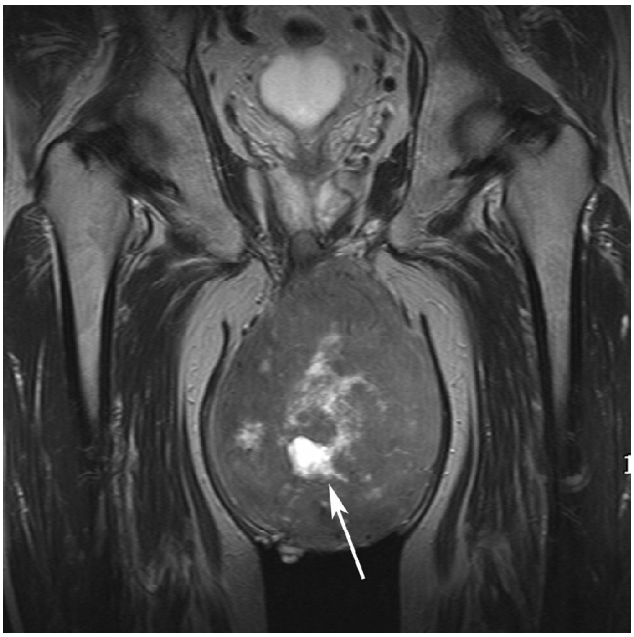

Figure 3. Coronal T2 weighted MR image of the pelvis shows a large mass with heterogeneous signal intensity in the scrotum. A focal necrosis (arrow) is seen with high signal intensity at the center of the mass.

lobulated tissue with focal calcification. A 2.5 × 1.5 cm cystic change, not necrotic, was noted in the central portion of the mass. Microscopically, the tissue was composed of a densely packed spindle cell proliferation. The cells were predominantly arranged in short, inter-

weaving fascicles with multifocal hyalinization and calcification. Individual cells showed oval, uniform nuclei without any mitosis per 50 high power field and clear cytoplasm. The Ki-67 labeling index was also less than 5%. Immunohistochemical stains demonstrated strong positivity for both c-kit (CD117) and CD34. However, the stains were negative for smooth muscle actin, desmin, or the S-100 protein (Figure 4). After an uneventful postoperative course, the patient was discharged 7 days after surgery. There was no recurrence of the tumor during the 7-month follow-up examination.

3 Discussion

Gastrointestinal stromal tumors are nonepithelial neoplasm that usually arise in the muscular layer of the digestive tract, particularly in the stomach and small intestine. Stromal tumors that arise outside the gastrointestinal tract are extremely rare and these lesions are known as EGIST. EGIST are generally considered similar to their gastrointestinal counterpart histologically and immunohistochemically. However, because of their rarity, the clinicopathological features of the EGIST are not well documented.

Reith *et al*. [2] reported 48 cases of EGIST. In their study, 40 tumors arose within the abdominal cavity, where they involved the omentum or mesentery. The remaining 8 tumors were located in the retroperitoneum. Other unusual sites of reported occurrence include the bladder [3], the inguinal hernia sac [4], and the vagina [5]. In a previously reported case of EGIST, Froehner *et al*. [6] showed that GIST might involve the scrotum by direct extension from the abdominal wall. Our patient presented with a huge left scrotal mass, which caused difficulty in identification of left testes. Clinical and radiological findings did not identify any other primary site of disease nor obvious direct extension from the hernia sac. Moreover, the patient did not present any abdominal pain, or change in bowel or urinary habits.

The diagnosis of GIST and their extragastrointestinal variants are now specifically diagnosed by the demonstration of a specific marker profile with expression of CD 117 and CD34 [7]. It was found that most GIST expressed KIT, a receptor tyrosin kinase encoded by protooncogene *c-kit*. In normal gastrointestinal wall, KIT is expressed by interstitial cells of Cajal (ICC), which are a pacemaker for autonomous gastrointestinal movement. Because both GIST and ICC are double-positive for KIT and CD34, and because familial and multiple GIST appear to develop from diffuse hyperplasia of ICC, GIST are considered to originate from ICC [8]. It has also been found that approximately 90% of sporadic GIST have somatic gain-of-function mutations of the *c-kit* gene, and that patients with familial and multiple GIST have germline gain-of-function mutations of the *c-kit* gene [1]. These facts strongly suggested that the *c-kit* gene mutations are a cause of GIST. Approximately half of the sporadic GIST without *c-kit* gene mutations have been demonstrated to have gain-of-function mutations in platelet-derived growth factor receptor-α (*PDGFRA*) gene that encodes another receptor tyrosine kinase [9, 10]. Because KIT is immunohistochemically negative in a minority of GIST, especially in *PDGFRA* gene mutation-harboring GIST, mutational analyses of *c-kit* and

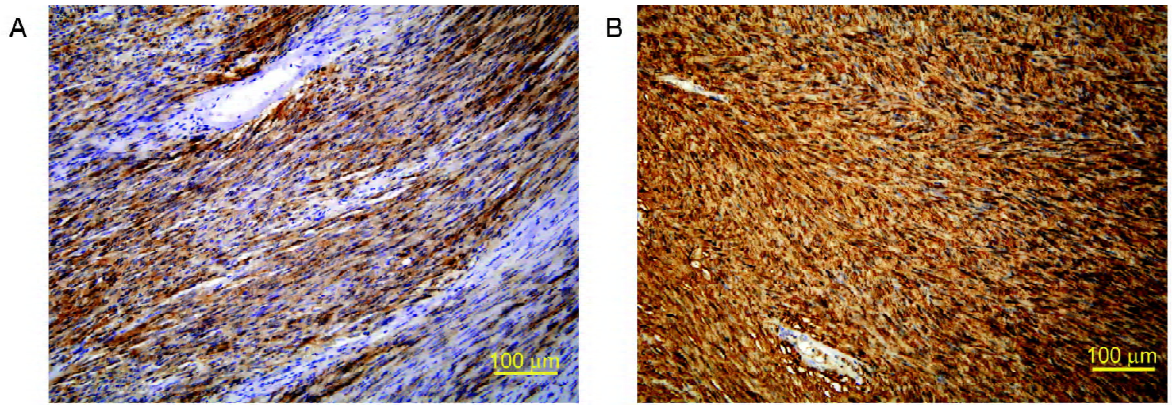

Figure 4. Immunohistochemical stain demonstrates positivity (A): for CD117; (B): for CD34.

PDGFRA genes might be required to diagnose such GIST with certainty [8]. Histologically, GIST generally shows one of three patterns: spindle cell, epitheloid or mixed. The spindle cell pattern, as present in the current case, is the most common type, accounting for 70% of reported cases [7].

There is growing evidence that despite the fact that virtually all stromal tumors express the c-kit receptor, they display various site-specific differences. Most importantly, the behavior of stromal tumors differs by location, and there seems to be a general trend for increasingly aggressive behavior as one proceeds distally along the gastrointestinal tract [11, 12]. For example, the minority of GIST located in the stomach have a good prognosis, whereas those in the small intestine have a significantly worse prognosis.

Predicting the prognosis of EGIST is not easy, but EGIST are usually presumed to have a more aggressive course resembling small intestinal tumors from the viewpoint of location. The National Institute of Health consensus conference has proposed a risk classification of GIST based on tumor size and histopathological mitotic count [7]. If the tumor is less than 5 cm and the mitotic count is below 5 per 50 high power field (HPF), the risk of malignancy is considered to be low. Ando *et al*. [13] report that the presence of mitotic cells and the Ki-67 labeling index are significant predictive factors for malignant GIST. Recently, Reith *et al*. [2] assess the histopathologic prognostic factors of EGIST. In their report, cellularity, mitotic activity (> 2 per 50 HPF), and necrosis are associated with statistically significant increases in the risk for an adverse outcome. Overall, 5% of patients who had none or one of the above three risk factors developed adverse outcomes (metastasis and/or death from a complication of their tumor), compared with 92% of patients who had two or three risk factors. In the present case, there were no risk factors (low cellularity, absent mitosis per 50 HPF without nuclear pleomorphism and absent necrosis), suggesting good prognosis. The Ki-67 labeling index also showed less than 5%. Besides, the risk of malignancy might be low based on his scrotal mass, which had enlarged gradually over a 20-year period.

The current definitive treatment for GIST is complete surgical resection. Lymphadenectomy is not necessary, because lymph-node metastasis of GIST is very rare [14]. Conventional chemotherapy and radiation therapy have been reported to be ineffective in the treatment of GIST. Imatinib (a tyrosine kinase inhibitor) has been confirmed to be an effective treatment against metastatic and unresectalbe GIST [15]. In the treatment of EGIST, complete surgical resection is recommended; however, the role of imatinib is unclear. In our case, complete surgical resection of the tumor was performed successfully. Imatinib was not used because no primary site was found, except scrotal mass on clinical and radiologic evaluation, nor any adverse prognostic factor detected on histological examination. There was no recurrence of the tumor during the 7-month follow-up examination, but close follow up is be required because of the huge tumor size. The 7-month follow-up is too short to completely rule out an extrascrotal primary tumor, especially given the slow growth of this tumor.

In summary, the current case emphasizes the possibility that this rare tumor can involve the scrotum as a primary site. Further studies will be necessary to clarify the management and biologic behavior of these unique tumors.

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