Extragonadal Seminoma Presenting as a Large Mass in the Pelvic Cavity Without c-kit-activating Mutations

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Extragonadal germ cell tumors are relatively rare tumors, which usually occur in the mediastinum or retroperitoneum. In this report, we present a case of primary seminoma arising in the pelvic cavity. A 58-year-old man with urinary retention and abdominal distension was admitted to our hospital. Computed tomography and magnetic resonance imaging demonstrated a large mass in the pelvic cavity. Histological examination of the specimens obtained by open biopsy revealed seminomatous malignant cells. Immunohistochemical studies detected vimentin, placental alkaline phosphatase and c-kit. Taking these results together with the patient’s other clinical manifestations, this case was diagnosed as extragonadal seminoma without c-kit-activating mutations, and chemotherapy followed by radiation therapy was successful. Primary seminoma in the pelvic cavity is extremely rare, but should be considered a cause of pelvic mass formation.

Key words: extragonadal germ cell tumor – seminoma – pelvic mass – c-kit-activating mutation

INTRODUCTION

Germ cell tumors (GCTs) are uncommon in elderly males, and male GCTs arise predominantly in the testes. However, 2–5% of GCT in males are of extragonadal origin (1). Extragonadal germ cell tumors (EGCTs) are most commonly found along the midline of the trunk, and primary retroperitoneal EGCT arise mainly in the space around the ventral aorta or postcava. Seminoma is a type of GCT that accounts for half of all cases. In this report, we present a case of extragonadal seminoma arising in the pelvic cavity of an elderly male, which presented as a large mass at the first medical examination.

CASE PRESENTATION

A 59-year-old male was admitted to the emergency unit of our hospital because of urinary retention and abdominal distension. Computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated a large mass in the pelvic cavity, which had dislocated the prostate and the urethra and extended outside the linea terminalis of the pelvis (Fig. 1). Urination was restored after insertion of a urethral catheter. Although transrectal needle biopsies of the tumor demonstrated small round malignant cells, the specimens obtained were insufficient for definitive diagnosis.
Histological examinations of the specimens obtained by biopsy during laparotomy revealed uniform tumor cells with sharply outlined cell membranes, small amounts of cytoplasm and large central nuclei. The tumor cells were typically arranged in nests surrounded by fibrous bands and detached from one another (Fig. 2a). However, tumorectomy was not performed because of massive bladder invasion.

The diagnosis of seminoma was established by the immunohistochemical studies of the neoplastic tissue. The tumor was positive for vimentin, placental alkaline phosphatase (PLAP) and c-kit (Fig. 2b–d). PLAP has been used as a representative surface marker of seminoma and c-kit is expressed in >90% of seminoma cases (2). In contrast, the tumor was negative for α-fetoprotein (AFP), inhibin, leukocyte common antigen (LCA/CD45), neuron-specific enolase, chromogranin (Fig. 2e), desmin, cytokeratin AE1/3 and for human chorionic gonadotrophin (hCG) (Fig. 2f). LCA/CD45 is expressed in almost every B-cell and T-cell lymphoma. Although some CD45-negative, cytokeratin-positive large cell lymphomas have been reported (3), both the surface markers were not expressed in our case. Therefore, we ruled out the possibility of malignant lymphoma. No tumors were found at any other site, including the testicles, mediastinum, abdominal cavity and other organs during physical or ultrasound examinations or CT scans. While the patient’s AFP (2.5 ng/ml) and carcinoembryonic antigen (1.4 ng/ml) levels were within normal limits, those of βhCG subunit (9.86 ng/ml) were high. Taking these results together with the patient’s other clinical manifestations; this case was diagnosed as primary extragonadal seminoma arising in the pelvic cavity.

We examined the patient’s neoplastic tissue to see whether it contained c-kit mutations in certain exons, since several studies have suggested that gain-of-function c-kit mutations and activation of its downstream signal transduction may contribute to tumorigenesis in a subset of seminoma (4,5) and a case of complete response after treatment with imatinib in pretreated disseminated testicular seminoma has been reported (6). However, we did not detect any mutations in our case.

Although we started chemotherapy with the bleomycin, etoposide and cisplatin regimen, the patient developed mechanical ileus on Day 2, which was caused by the tumor. After constructing an artificial anus, we carried out three courses of chemotherapy followed by radiation therapy (2 Gy/day;
radiation therapy to treat the residual tumor that remained after three courses of chemotherapy as it may have contained non-seminomatous components. However, only a minor change in tumor size was observed, and we performed repeated transrectal biopsies to confirm that no viable malignant cells were present.

Recently, it was reported that many kit-expressing human malignancies possess activating mutations in exons 9, 11, 13 and 17 of the c-kit gene (2). Since imatinib was found to be effective in treating gastrointestinal stromal tumor with c-kit-activating mutations, further efforts have been made to detect these mutations in other malignancies (15), and c-kit-activating mutations in exons 11 and 17 have already been reported to be commonly present in testicular seminomas (4,5) and intracranial germinoma (16). The positive rate of c-kit-activating mutations is 26–36% and 18%, respectively (4,5,16). On the other hand, Przygodzki et al. (17) reported that mutations are restricted to exon 17 in primary mediastinal seminoma, which displayed a mutation profile different from that of testicular seminoma with 50% positive rate. Although only one phase II study of imatinib has been performed thus far in chemotherapy refractory GCTs and has shown no evidence of significant antitumor activity of imatinib (18), newer drugs that specifically target imatinib-resistant c-kit protein may become clinically available (19). Therefore, these data on mutation profiles are important to future treatment of chemotherapy refractory seminomas. As we could not find any reports on extragonadal infradiaphragmatic seminoma in which c-kit gene mutations were analyzed despite the high frequency of mutations in seminoma at other sites, we assessed the c-kit mutations present in exons 9, 11, 13 and 17 of the patient’s neoplastic tissue. However, we could not detect a c-kit mutation in seminoma described in this report.

In conclusion, primary seminoma in the pelvic cavity is extremely rare, but should be considered for a differential diagnosis when an intrapelvic mass is detected, even in the absence of clinical symptoms. More epidemiological studies are needed to obtain insights into the risk factors for extragonadal seminoma in order to allow early diagnosis in symptom-free patients. The frequencies and locations of c-kit mutations and the differences between the clinicopathological factors of extragonadal infradiaphragmatic seminoma patients with and without mutations should be elucidated.

Conflict of interest statement
None declared.

References


