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Teaching cases

An intrapelvic extraintestinal gastrointestinal stromal tumor of undetermined origin: Diagnosis by prostate needle biopsy

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ABSTRACT

We herein report a case of intrapelvic gastrointestinal stromal tumor (GIST) of undetermined origin in a 48-year-old male who presented with dysuria. An enlarged tumor was detected on digital rectal examination. Imaging studies showed a solid and lobular homogenous tumor of 7.0 cm in diameter. The tumor was attached to the right dorsal aspect of the prostate with compression of the seminal vesicles and rectum. It was considered that the tumor had arisen from the prostate, although the patient's serum prostate-specific antigen level was low (0.436 ng/mL). The histological diagnosis by prostate needle biopsy was a spindle cell tumor. At cystoprostatectomy, the tumor was confirmed to be separated from the prostate by a fibrous band, and showed spindle cells with a fascicular growth pattern, but without necrotic areas. Mitotic figures were noted in 12 of 50 high-power fields. The tumor cells were immunoreactive for the KIT protein (CD117), CD34, Discovered on GIST-1 (DOG-1), and vimentin. In contrast, they were negative for desmin, α-smooth muscle actin, pancytokeratin (AE1/AE3), and S100 protein. The Ki-67 labeling index was 5%. The genetic analyses targeting the c-kit gene revealed a point mutation at codon 559 (GTT → GAT). The diagnosis of GIST was confirmed on the basis of the morphological features, immunoprofile, and results of the molecular analyses. Since extraintestinal GIST can resemble a prostatic tumor clinically, KIT (CD117) and DOG-1 should be considered for inclusion in the immunohistochemical panel for spindle cell tumors obtained by prostate needle biopsy.

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common gastrointestinal mesenchymal tumors [1–4]. It has been suggested that GISTs originate from the interstitial cells of Cajal (ICC), which are regarded as pacemaker cells in the gut, or from less differentiated stem cells which then develop into ICC [5–7]. GISTs predominantly occur in the gastrointestinal tract [2,8,9], but occasionally develop in the extragastrointestinal region as primary tumors [10–13]. It has also been reported that GISTs are present in the omentum, mesentery, and retroperitoneum, where ICC have yet to be identified [12,14,15]. There have been several reports of GISTs which involved the anorectal region and led clinicians to perform a prostate needle biopsy due to significant urological symptoms [2,8]. Such cases may be difficult to distinguish from other spindle cell tumors by prostate needle biopsy [2].

We herein report a rare case of GIST of undetermined origin in the pelvic area, which was interpreted to have arisen from the prostate on imaging studies.

Case report

A 48-year-old male presented with dysuria, and a large prostatic tumor was suspected based on a digital rectal examination. The patient's serum prostate-specific antigen level was low (0.436 ng/mL). Pelvic computed tomography (CT) and magnetic resonance imaging (MRI) confirmed the presence of a tumor measuring 7.0 cm in the right dorsal aspect of the prostate and *levator ani* muscle (Fig. 1). The seminal vesicles and rectum were compressed to the anterior side of the pelvic area by the tumor. The tumor showed parenchymal intensity with a lobular shape, and the boundary of the tumor was clearly defined. No changes in bowel habits or bloody stools had been noted. Colonoscopy and cytoscopy demonstrated an intact rectal wall and urinary bladder wall with no evidence of tumor involvement. No metastatic tumors were

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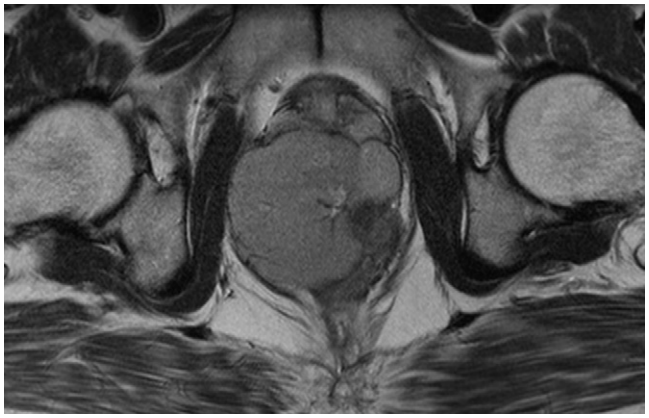

Fig. 1. Magnetic resonance imaging showed a large tumor with a lobular and asymmetrical shape in the pelvic area. The tumor was located in the right dorsal aspect of the prostate and showed a clear boundary.

detected by additional imaging studies, including chest X-ray, and all laboratory test values were normal.

Pathological findings

A transrectal prostate needle biopsy of the tumor was performed, which histologically resulted in the diagnosis of a spindle cell tumor. The tumor showed a 'patternless pattern', or focal nuclear palisading pattern of uniform spindle cells with a background of collagen. Immunohistochemically, the tumor cells were positive for CD34, and negative for desmin, α-smooth muscle actin, estrogen receptor, progesterone receptor, and pancytokeratin (AE1/AE3). The Ki-67 labeling index was approximately 5%. The spindle cell tumor was suggested to be a stromal tumor of uncertain malignant potential (STUMP) or a malignant solitary fibrous tumor (SFT).

Since the tumor was large, at 7.0 cm in diameter determined by imaging, and was diagnosed as malignant, the microscopic invasion of the tumor to the urinary bladder was suspected. Subsequently, the patient underwent a cystoprostatectomy, together with tumor excision. Macroscopically, the tumor was adherent to the prostate and seminal vesicles. However, the tumor was separated from the prostate by a thin fibrous capsule (Fig. 2A). As observed on imaging studies, the wall of the urinary bladder was intact (Fig. 2B). The encapsulated tumor was clearly separated from both the urinary bladder and rectum. The tumor was yellowish-white, but without necrosis. Microscopically, it was clear that the thin fibrous capsule had compressed the boundary of the prostate, but no prostatic tissue was observed in the tumor (Fig. 3A). The tumor consisted of spindle cells with a fascicular growth pattern and characteristic cytoplasmic vacuoles indenting the nuclear poles (Fig. 3B). Some tumor cells showed epithelioid features, including a variable amount of densely collagenous stroma (Fig. 3B). The tumor cells had oval to elongated nuclei with a mild degree of pleomorphism. The chromatin patterns were granular, with at least one small nucleolus. The mitotic rate was 12 mitoses per 50 high-power fields. The seminal vesicles showed no tumor cell infiltration. Immunohistochemically, the tumor cells were strongly positive for the KIT protein (CD117) and CD34, and weakly positive for Discovered on GIST-1 (DOG-1) (Fig. 3C), but negative for desmin, α-smooth muscle actin, S100 protein, and pancytokeratin (AE1/AE3). The Ki-67 labeling index was approximately 5%. The spindle cells on needle biopsy specimens were also immunohistochemically positive for KIT (CD117) and DOG-1, and the tumor was confirmed to be GIST retrospectively (Supplementary Fig. 1).

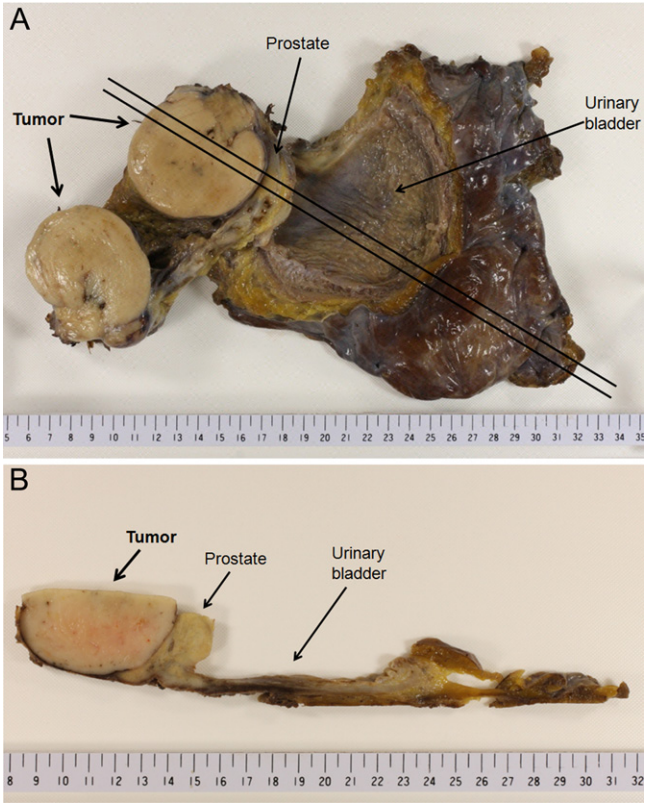

Fig. 2. Gross findings of the resected tumor by cystoprostatectomy. (A) The tumor was separated from the prostate by a thin fibrous capsule. The urinary bladder, urethra, and bilateral ureters were intact. (B) The tumor was clearly observed to be separated from the prostate on a cross-sectional view (parallel lines on the middle of the resected specimen in (A)) of cystoprostatectomy.

Tumor DNA was extracted from a paraffin block that was subjected to polymerase chain reaction amplification and sequence analysis for exon 11 of the c-kit gene. A genetic analysis demonstrated a point mutation at codon 559 (GTT → GAT) (Fig. 4), and confirmed a diagnosis of high-risk GIST [16,17]. Postoperatively, imatinib mesylate therapy was administered. The patient has been observed for two years postoperatively, and has shown no sign of recurrence or metastases.

Discussion

GISTs are thought to be derived from ICC, which are considered pacemaker cells of the gut, and commonly occur in the gastrointestinal tract, whose motility is regulated by the Cajal cells [18,19,20]. However, in recent years, ICC or ICC-like cells have also been observed in extraintestinal organs [21]. In the genitourinary tract, KIT-positive specialized pacemaker cells have been described in the bladder, urethra, uterus, and prostate [22–26]. The presence of these cells in various organs or soft tissue could provide an explanation for the rare cases of GISTs that occur as primary tumors outside the gastrointestinal tract, such as in the mesentery, omentum, retroperitoneum, liver, gallbladder, vagina, uterus, urinary bladder, or prostate [10–13,22,27–33]. In some of these extragastrointestinal stromal tumors, the origin remains unclear.

A total of 20 pelvic GIST cases diagnosed by prostatic tissue examination, including prostatic biopsy, have been reported and were summarized in a table including the tumor size/location and prognoses by Anagnostou et al. [34]. In most of these cases, the rectum and/or prostate was involved by the tumors, which were regarded as primary rectal neoplasms extending to the prostate. Ten cases of pelvic GIST involved or occurred in the prostate, and