JKKI
SCIENTIA EST BASIC VITAE

Jurnal Kedokteran dan Kesehatan Indonesia

Indonesian Journal of Medicine and Health

Journal homepage: https://journal.uii.ac.id/JKKI

Diagnostic challenges of gastrointestinal stromal tumour during transurethral resection of the prostate: A case report

Anandia Putriyuni*[1], Yevri Zulfiqar[2], Santy Saberko[3], Lila Indrati[4]

[1]Department of Pathology, Faculty of Medicine, Universitas Baiturrahmah/Dr. Rasidin General Hospital, Padang, Indonesia
[2]Division of Urology, Department of Surgery, Faculty of Medicine, Universitas Andalas/Dr. M. Djamil General Hospital, Padang, Indonesia
[3]Department of Pathology, M Natsir Regional General Hospital, Solok, Indonesia
[4]Department of Radiology, Faculty of Medicine/Universitas Andalas, Dr. M. Djamil General Hospital, Padang, Indonesia

Case Report

ARTICLE INFO

Keywords:
gastrointestinal stromal tumour, prostate, immunohistochemistry

***Corresponding author:**
anandia_putriyuni@yahoo.com

DOI: 10.20885/JKKI.Vol14.Iss3.art17

History:
Received: June 21, 2022
Accepted: December 8, 2023
Online: December 30, 2023

ABSTRACT

Mesenchymal prostate tumours are relatively rare compared to epithelial tumours. To diagnose mesenchymal tumours on transurethral resection of the prostate (TURP) specimen, doctors have to consider a few differential diagnoses, including gastrointestinal stromal tumour (GISTs). We reported a 63 years-old male patient, presented with urinary retention in one week. Based on an initial scan of the abdomen, a large lobulated mass in the pelvic cavity from the prostate pushed up the urinary bladder. Histopathologic examination demonstrated cellular spindle cell neoplastic proliferation, a moderate degree of atypia, and a mitotic count of >5 per 50 high-power fields (HPFs) with a fascicular growth pattern. Immunohistochemically, the tumour had positive expression for CD117 (c-KIT), CD34, and discovered on Gist-1 (DOG-1), while smooth muscle actin (SMA) and S-100 were negative. The pathological report was consistent with a high-risk group of GISTs in the prostate. Subsequent imaging revealed that the tumour mass was centrally located between the rectum and prostate, infiltrating bladder and liver metastases. Comprehensive differential diagnoses of mesenchymal tumours involving the prostate are necessary because of the inadequacy of specific clinical signs, symptoms, and unexpected location. Diagnoses of GISTs was performed based on spindle cell pattern and the positive immunohistochemistry expression for CD117, CD34, and DOG-1. The tumour mass involved in the prostate with spindled morphology should be considered as a GIST, assisted with appropriate immunohistochemistry marker panel. It is a challenge to diagnose the GIST particularly involving the prostate.

Tumor mesenkim prostat relatif jarang terjadi dibandingkan dengan tumor epitel. Diagnosis tumor mesenkim pada spesimen TURP harus mempertimbangkan beberapa diagnosis banding, termasuk GIST. Kami melaporkan seorang pasien laki-laki usia 63 tahun yang memiliki gejala retensi urin sejak seminggu yang lalu. Pencitraan abdomen awal ditemukan massa besar berlobus-lobus pada rongga pelvis berasal dari prostat yang mendorong vesika urinaria. Pemeriksaan histopatologis menunjukkan proliferasi sel spindel neoplastik yang selular, atipik derajat sedang, dan jumlah mitosis > 5 per 50 lapang pandang besar dengan pola pertumbuhan fasikular. Didapatkan ekspresi positif dari pemeriksaan imunohistokimia untuk CD117 (c-KIT), CD34, and DOG-1 sedangkan SMA dan S-100 negatif. Laporan patologi sesuai dengan GIST dengan kelompok risiko tinggi pada prostat. Pemeriksaaan pencitraan berikutnya menemukan massa tumor yang berpusat antara rektum dan prostat, menyusup ke vesika urinaria dan metastasis ke hepar. Diagnosis banding yang komprehensif untuk tumor mesenkim yang melibatkan prostat diperlukan karena kurangnya tanda dan gejala yang spesifik, dan lokasi yang tidak terduga. Diagnosis GIST ditegakkan berdasarkan pola sel spindel dan ekspresi positif imunohistokimia untuk CD117, CD34 dan DOG-1. Massa tumor yang melibatkan prostat dengan morfologi sel spindel harus dipertimbangkan sebagai

GIST, dengan dibantu panel penanda imunohistokimia yang tepat. Suatu tantangan mendiagnosis GIST yang terutama melibatkan prostat.

INTRODUCTION

Mesenchymal prostate tumours are relatively rare compared to epithelial tumours and have been reported for less than 1% of all prostatic neoplasm. Mesenchymal tumours on TURP specimen have to consider a few differential diagnoses, such as smooth muscle tumours, GISTs, neural tumours, stromal tumours of uncertain malignant potential (STUMP), prostatic stromal sarcoma, solitary fibrous tumour (SFT), inflammatory myofibroblastic tumour, and rhabdomyosarcoma.[1,2]

The most common gastrointestinal tract mesenchymal malignancy is GISTs, but it only occupies 1-2% of all gastrointestinal tract malignancies.[3,4] GISTs have KIT gene mutations in approximately 80% of cases and 5-7% platelet-derived growth factor receptor-alpha (PDGFRA) mutations.[5] Mesenchymal tumours, that arise outside of the gastrointestinal tract and that most frequently originate from the mesentery, omentum, and retroperitoneum, are referred to as extra-GISTs (E-GISTs). They represent less than 5% of all GIST cases, but primary prostatic GISTs are extremely rare. If the specimen is a GIST in the prostate, it considers the possibility of a primary or secondary lesion (extension from another site such as rectum).[6,7,8] It needs examinations to confirm the diagnoses with radiology and immunohistochemistry. The investigation of rectal GIST suspected by radiological examination is challenging due to their rarity. The crucial immunohistochemical hallmark to identify GISTs from other mesenchymal tumours is CD117, CD34, and DOG-1.[2,8] Due to the rarity of mesenchymal tumours in the prostate, particularly GISTs, we report a GIST case found in specimens derived from TURP and discuss how to approach the diagnostic challenges in such case.

CASE DESCRIPTION

A 63 years-old male experienced urine retention in one week. Dysuria, hesitancy, urinary frequency, and nocturia were felt in the past sixth months and got worse. He had no history of haematuria, urethral catheterization, or urinary tract stones. Physical examination was unremarkable, and systemic examination was essentially normal. Rectal toucher examination found a markedly enlarged prostate gland with a smooth and bulging surface, firm consistency, and nontender. Haematology tests and urinalysis were normal. Prostate-specific antigen level was 0.11 ng/ml (cut off ≤ 4 ng/ml). An enlarged prostate was 11.46 cm in diameter from ultrasonographic. The abdominal computerized tomography (CT) scan represented a large lobulated mass in the pelvic cavity extended to posterior and pushing up the urinary bladder. The scan also pointed out an is Odense mass with poorly defined parts and multiple calcifications. It also showed multiple lesions in the liver (Figure 1).

A gross examination on the mass collected from TURP procedure revealed pieces of white tissue with brown parts. The pieces measured 2.5 x 2.5 x 2.5 cm in size and displayed elastic-solid consistency. Histopathological examination showed proliferation of cellular neoplastic spindle cells with a fascicular growth pattern, moderate degree of atypia with eosinophilic cytoplasm, indistinct cell borders, and a mitotic count of >5 per 50 HPFs (Figure 2). There was some necrotic area with calcification. The pathological report was a malignant spindle cell tumour with differential diagnoses such as leiomyosarcoma, GISTs, malignant peripheral nerve sheath tumour (MPNST), and prostatic stromal sarcoma. Immunohistochemically, the positive expressions in tumour cells were CD117 (c-kit), CD34, and DOG-1, while SMA and S-100 were negative. There was about 10% expression of the Ki-67 proliferation index (Figure 3). The diagnose was consistent with a high-risk group of GISTs in the prostate.

The patient was referred to the central hospital and obtained contrast CT scan of abdomen approximately three months after surgery. The scan showed an isodense and inhomogeneous mass centrally located between the rectum and the prostate, measuring 12.8 x 9 x 21.8 cm with a poorly circumscribed and irregular border. The mass extended to posterior and constricted the pre-rectal space (Figure 4A). There were multiple hypodense and inhomogeneous nodules in the liver (Figure 4B). There was no regional lymphadenopathy. The patient lastly was presented with haematuria, and a repeat contrast

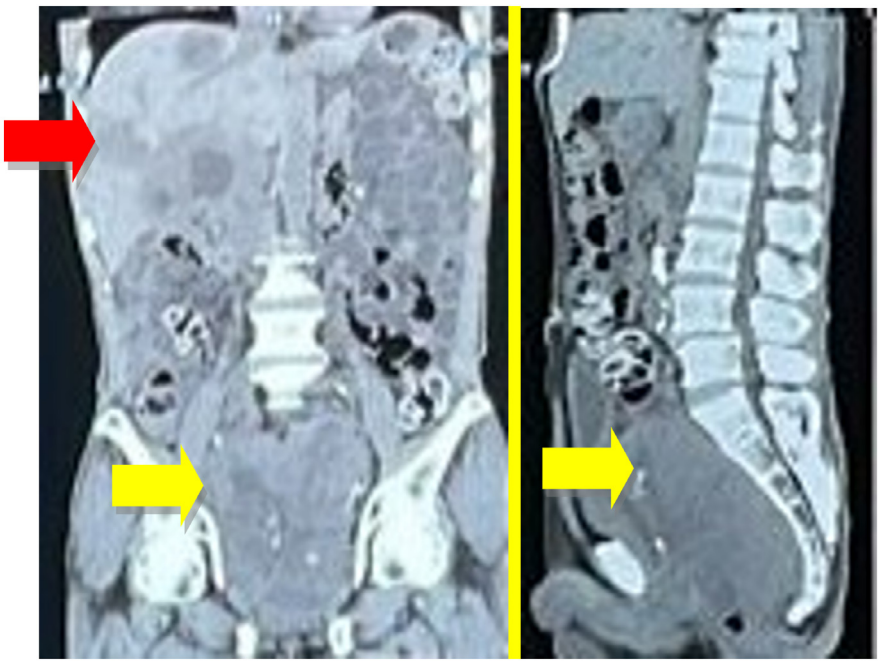

Figure 1. Abdominal non-contrast computerized tomography (CT) scan. A large lobulated mass in the pelvic cavity extended to posterior (yellow arrow) and multiple lesions in the liver (red arrow).

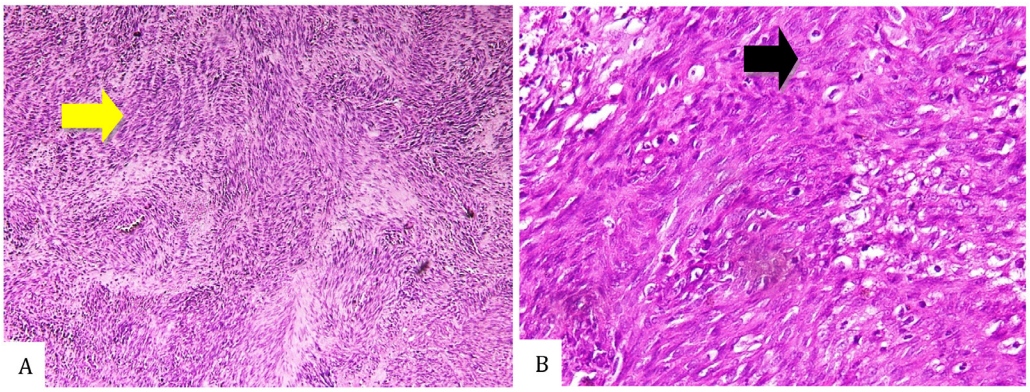

Figure 2. Histopathological examination. (A) Cellular spindle cells tumour with a fascicular growth pattern (yellow arrow); (B) The spindle cell tumors had moderate degree of atypia with eosinophilic cytoplasm and indistinct cells borders (black arrow) (Hematoxylin-Eosin, x100 & x400).

CT scan was performed with added result of no clear boundary of mass between the prostate and rectum (Figure 4C). This imaging shows trilobed feature and there is no normal prostatic tissue (Figure 4D). Posterior wall of bladder was thick with infiltrating mass. The imaging impressed that the primary tumor was from the prostate.

DISCUSSION

The GISTs originate from Cajal interstitial cells, the intestinal pacemaker cells of gut motility. Extra-GISTs were found growing in areas lacking of the Cajal, such as mesentery, omentum, retroperitoneum, urinary bladder, liver, adrenal, pancreas, and prostate.[3,9,10] The presence of GISTs in the rectum is infrequent, only 5% of all GISTs.[11] According to Khan et al. (2000-2018), the most common primary site of GISTs were the stomach (63%), small intestine (30%), rectum (3%), and oesophagus (0.7%).[3] Then Ceausu et al. observing 57 cases with GISTs in Sf. Pantelimon Emergency Clinical Hospital Bucharest (2011-2020) found that most tumour locations were stomach (49.12%) and sigmoid (3.5%) but no rectum.[12]

Mesenchymal tumours of the prostate with spindle cell patterns required a comprehensive differential diagnosis. This case lacked specific clinical signs and symptoms, as well as laboratory findings. The case is rare and has an unexpected anatomic location. Imaging may vary for each

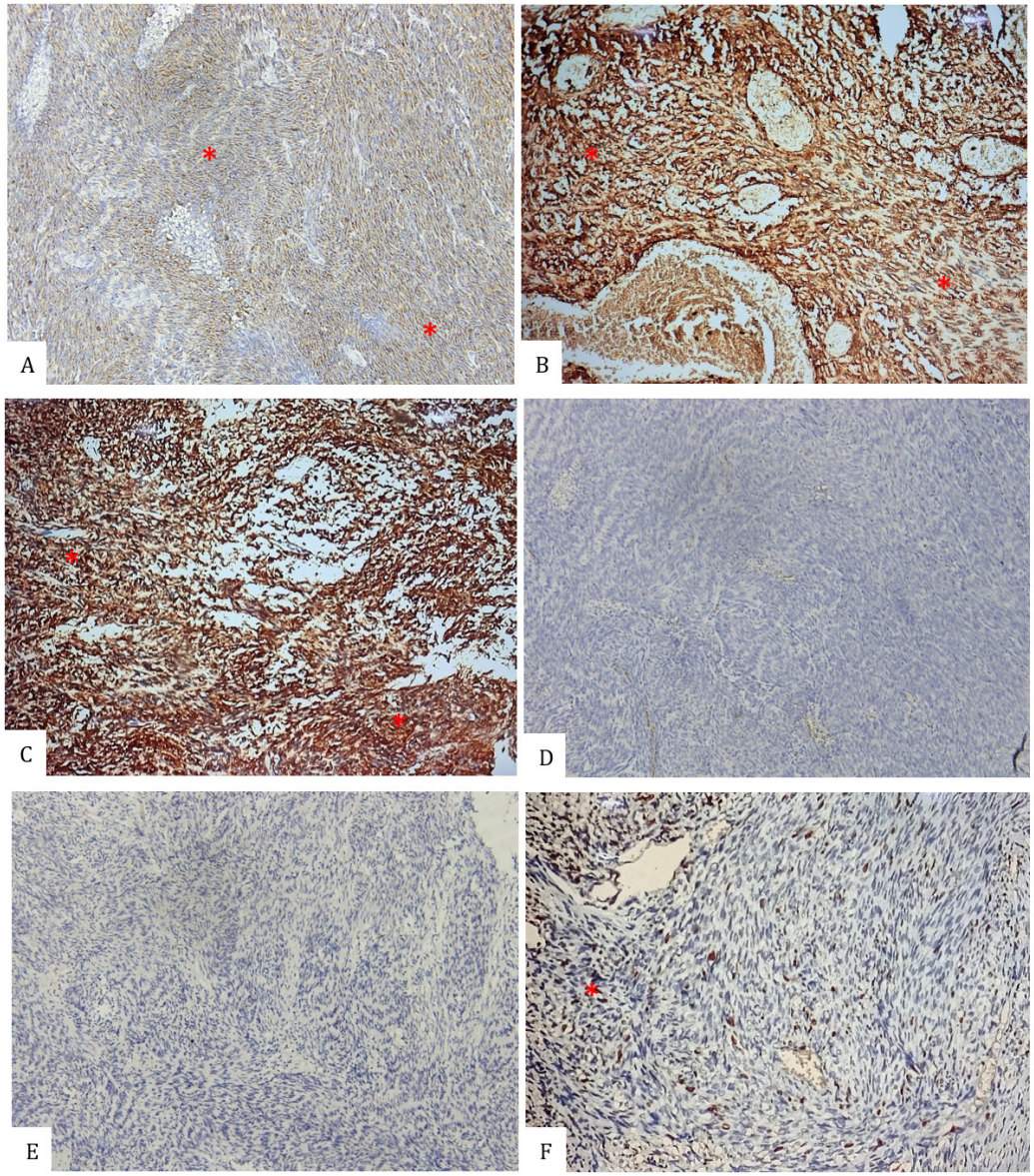

Figure 3. Immunohistochemistry. (A-C) Diffusely positive expression of CD117, CD34, and DOG-1; (D-E) Negative expression of SMA and S-100; (F) The expression of Ki-67 proliferation index in 10%. (x100) (* positive expression); DOG-1: discovered on GIST-1; SMA: smooth muscle actin

case, depends on the tumour size and anatomical location while it was founded . It is crucial to rule out the direct extension of mesenchymal tumors, such as GISTs in the rectum, before diagnosing primary prostatic GIST.[9,10] In this case, the primary of mass was in the prostate infiltrating rectum and bladder, as evidenced from a contrast CT-scan abdomen.

An abdominal CT scan is a gold standard in the initial imaging of the GISTs, as it allows precise detection of the size and location of the primary tumour, its local extension, and metastases.[3,13,14] Large GISTs usually exhibit aggressive behaviour with peritoneal or distant metastases.[4] A study of Ceausu et al. found that the sensitivity of preoperative CT-scan was 84.61% from 39 patients.[12] In diagnosing E-GIST, the origin of tumours in the gastrointestinal tract should be removed. Few GISTs are rectum-related, and some of these cases are mistakenly identified as prostatic E-GIST. A large rectal GIST can give the impression on imaging of a prostatic mass.[13,15]

The anatomic location of the tumour has a significant role in differential diagnoses. Clinical and radiological reports are crucial in determining whether rectal GIST invades the prostate. The tumour's primary origin may not be determined by clinicians and radiologists occasionally. Gastrointestinal stromal tumours may grow up as a small nodule or a large pelvic mass, extended

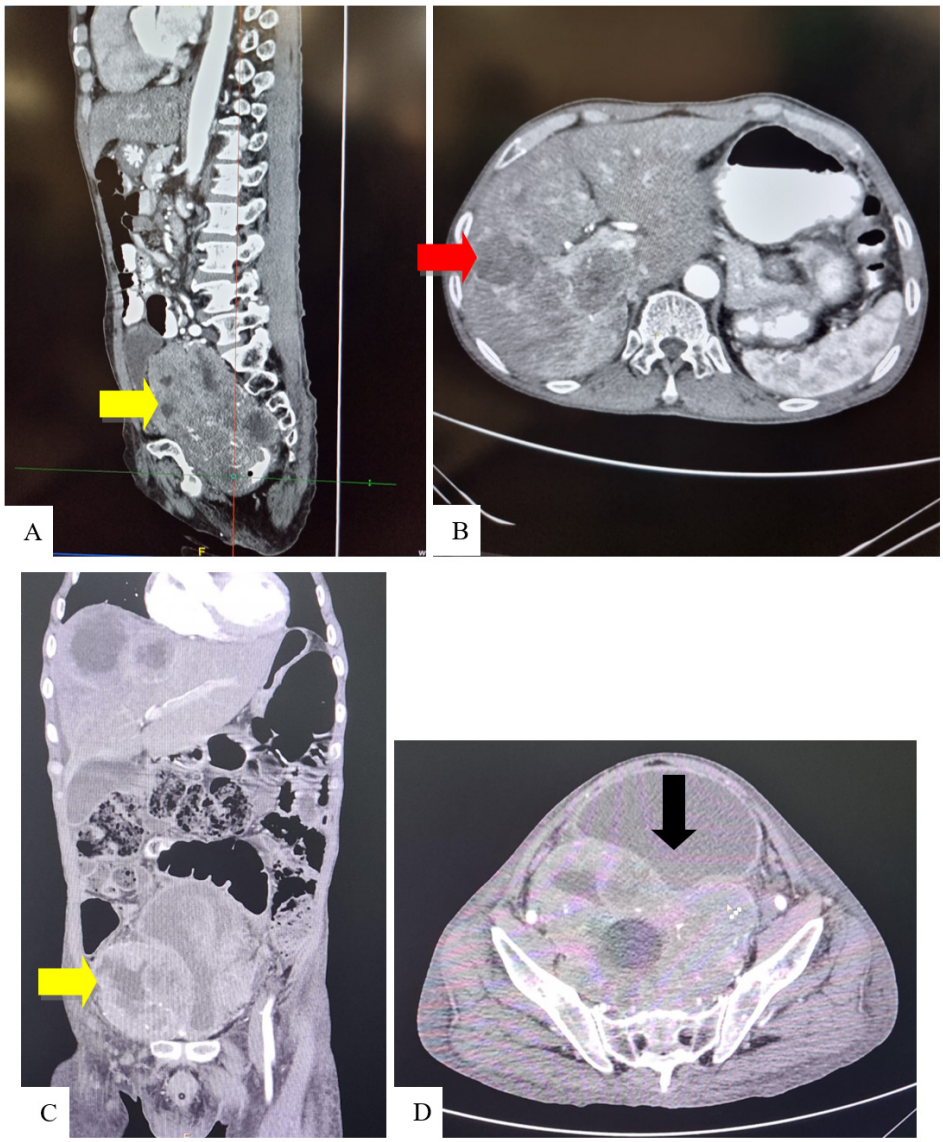

Figure 4. Abdominal contrast computerized tomography (CT) scan. (A) & (C) An isodense and inhomogeneous mass with poorly circumscribed and irregular border (yellow arrow); (B) Multiple hypodense and inhomogeneous nodules in the liver (red arrow); (D) Trilobed sign (black arrow).

to the prostate mimicking primary prostatic GISTs.[10,16] A number studies reported primary E-GIST of prostat.[10,13,17]

Pathology examination has a main role in diagnosing GISTs. The diagnosis of GISTs depends on histopathology and immunohistochemistry. The molecular analysis is used as a complementary diagnosis in certain cases.[12,18] The morphologic variants of GISTs are spindle (70%), epithelioid (20%), and mixed (10%) from histopathological examination. Spindle variants are the most common morphology in a syncytial pattern. They consist of bland spindle cells with pale eosinophilic cytoplasm, elongated nuclei, and inconspicuous nucleoli. The spindle cells have perinuclear vacuoles in a fascicular and storiform pattern. The tumours may have sclerotic background, palisaded cells, hypercellularity, or sarcomatoid features. Epithelioid variants are composed of round cells with clear to eosinophilic cytoplasm in sheets or nests. The combined spindle and epithelioid morphology are termed mixed variants.[2,4,12,19] In this case, the pathology examination demonstrated cellular spindle cells with a fascicular growth pattern of GISTs.

Immunohistochemical examination is crucial for the definitive diagnosis of GISTs. Expression of CD117 (c-KIT) was found in most Cajal cells. It becomes a highly sensitive and is a specific marker for GIST diagnosis. In prostate spindle cell

tumours, more than 95% of GISTs stained with CD117 are expressed diffusely in the cytoplasm (75%) and membrane of cells occasionally.[5,10,20] It has recently been discovered that the chloride channel protein DOG-1 is even more sensitive and specific for GISTs than CD117. An examination of DOG-1 is generally recommended for an accurate diagnosis. Expression of DOG-1 in membranous and cytoplasmic patterns usually highlights E-GISTs.[4,5,12,21] The 11-kDa glycosylated transmembrane protein CD34 is positively expressed in up to 70%, and SMA is in 30-40%. Desmin and S-100 are only expressed in 5% of cases. Cytokeratin is focally and weakly positive in 1-2% of cases.[10,12]

This current observed case revealed diffuse immunoreactivity for CD117, CD34, and DOG-1. Ceausu et al. also reported the positive expression for CD117, CD34, and DOG-1 of tumour cells.[12] Distinguishing GISTs from other mesenchymal spindle cell lesions is critical due to their therapeutic impact. They respond to targeted therapies with imatinib mesylate and sunitinib malate. Immunostaining of CD117 should always be part of the diagnostic panel.[10,20]

The potential assessment of biological GISTs that are evaluated in tumour risk stratification criteria include tumour size and mitosis per 5 mm2 or 50 HPF. Diameter tumours <5 cm is typically at low-risk, while > 5 cm are intermediate/high-risk. Mitotic rates <5/50 HPFs usually characterize GISTs as low risk, and >5/50 HPFs is as intermediate/high-risk. The National Institutes of Health (NIH) stated in April 2008 that tumour size and mitotic activities were reported as significant prognostic factors. It should be considered a consensus risk stratification for GISTs.[4,7,19,22] All GISTs are potentially malignant as Khan et al. found that tumour size > 5 cm and high-grade histologic features had the strongest influence on survival.[3] A higher risk of malignancy is linked to GISTs discovered in addition to the stomach.[4] Metastases in the liver are commonly present in advanced cases of GISTs, while it is rare to find metastases in lymph nodes.[4,21] Puckett et al. reported a rectal GIST with diffuse liver metastases.[23] The case revealed multiple lesions in the liver.

CONCLUSION

The GIST has become a diagnostic challenge, notably manifesting as pelvic mass that extended to the prostate and the rectum. It is considered one of the prostatic mesenchymal tumor differential diagnoses. If the case is a GIST on TURP, it is necessary to ascertain whether the primary prostatic lesion or extension from other organs. This is due to different clinical impacts on treatment and patient outcomes. The behavior of an extra-gastrointestinal stromal tumor is more aggressive. The imaging, histopathology, and immunohistochemistry combination are critical in substantially diagnosing a GIST in an unusual location. Immunostaining of CD117, CD34, and DOG-1 must be included in the diagnostic panel. The immunohistochemistry expressions will confirm the diagnose of GIST from in mesenchymal tumors.

CONFLICT OF INTEREST

There is no conflict of interest, and the authors obtained the patient's informed consent.

ACKNOWLEDGEMENT

We thank for the patient for allowing us to share the details of the case.

AUTHOR CONTRIBUTIONS

AP had major contribution in writing the manuscript; YZ had contribution in clinical examination and surgical treatment; AP and SS performed the histopathological examination and IHC; YZ and LI analysed and interpreted the patient data. All authors read and approved the final manuscript.

LIST OF ABBREVIATIONS

DOG-1: Discovered on GIST-1; E-GIST: Extra-Gastrointestinal Stromal Tumour; GIST: Gastrointestinal Stromal Tumour; HE: Haematoxylin Eosin; HPF: High-Power Field; NIH: National Institutes of Health; PDGFRA: Platelet-Derived Growth Factor Receptor-Alpha; SFT: Solitary Fibrous Tumour; SMA: Smooth Muscle Actin; STUMP: Stromal Tumours of Uncertain Malignant Potential; TURP: Trans-Urethral Resection of the Prostate

REFERENCES

1. Öznur M. Mesenchymal tumors of the prostate. J Urol Surg. 2018;5(1):59–62.
2. McKenney JK. Mesenchymal tumors of the prostate. Mod Pathol. 2018;31(September 2017):133–42.

3. Khan J, Ullah A, Waheed A, Karki NR, Adhikari N, Vemavarapu L, et al. Gastrointestinal stromal tumors (GIST): A population-based study using the SEER database, including management and recent advances in targeted therapy. Cancers (Basel). 2022;14(15).
4. Parab TM, DeRogatis MJ, Boaz AM, Grasso SA, Issack PS, Duarte DA, et al. Gastrointestinal stromal tumors: A comprehensive review. J Gastrointest Oncol. 2019;10(1):144–54.
5. Wu CE, Tzen CY, Wang SY, Yeh CN. Clinical diagnosis of gastrointestinal stromal tumor (GIST): From the molecular genetic point of view. Cancers (Basel). 2019;11(5):1–15.
6. Lu LJ, Xu XP, Dong F, Min J. Diffuse primary extra-gastrointestinal stromal tumor of the peritoneum: A rare case report. Medicine (Baltimore). 2020;99(40):e22493.
7. Shen H, Wang Z, Feng M, Liu J, Li J, Wang X, et al. Primary prostatic extra-gastrointestinal stromal tumor treated with imatinib mesylate as neoadjuvant and adjuvant therapy: A case report and literature review. Onco Targets Ther. 2019;12:11549–53.
8. Naiken S, Craig A, Guedj N, Peixoto N, Zufferey G. Rectal gastrointestinal stromal tumour: What do we know in 2017? A systematic review protocol. Int J Surg Protoc [Internet]. 2018;7:5–7.
9. AlAhmadi HH, AlEssa A, Shawarby M, AlOtaibi K, alhamam A, Al Dandan OS. Primary prostatic GIST vs rectal GIST: A case report of a 62 years old male with a pelvic mass. Hum Pathol Case Reports. 2020;22:200422.
10. Al-Maghrabi H, Alahmadi S, Falemban AH. Primary gastrointestinal stromal tumor of the prostate: Unexpected guest. Cureus. 2020;12(9).
11. Khan SI, O'Sullivan NJ, Temperley HC, Rausa E, Mehigan BJ, McCormick P, et al. Gastrointestinal stromal tumours (GIST) of the rectum: A systematic review and meta-analysis. Curr Oncol. 2023;30(1):416–29.
12. Ceausu M, Socea B, Ciobotaru V, Constantin V, Enache S, Enache V, et al. A multidisciplinary approach in the diagnostic challenge of GIST. Exp Ther Med. 2021;22(4):1–8.
13. You YH, Zhang Y. Primary prostatic extra-gastrointestinal stromal tumor: A case report and literature review. J Int Med Res. 2018;46(10):4343–9.
14. Kim JS, Kim HJ, Park SH, Lee JS, Kim AY, Ha HK. Computed tomography features and predictive findings of ruptured gastrointestinal stromal tumours. Eur Radiol. 2017;27(6):2583–90.
15. Huh J-S, Park KK, Kim YJ, Kim SD. Diagnosis of a gastrointestinal stromal tumor presenting as a prostatic mass: A case report. World J Mens Health. 2014;32(3):184.
16. Reinke DA, Deisch JK, Reinke DD. Gastrointestinal stromal tumor with an unusual presentation as an enlarged prostate gland: A case report and review of the literature. J Gastrointest Oncol. 2016;7(Suppl 1):S71–4.
17. Etit D, Kar H, Ekinci N, Yenipazar AE, Çakalağaoğlu F. Extra-gastrointestinal stromal tumor of prostate. Balkan Med J. 2017;34(2):168–71.
18. Landi B, Blay JY, Bonvalot S, Brasseur M, Coindre JM, Emile JF, et al. Gastrointestinal stromal tumours (GISTs): French intergroup clinical practice guidelines for diagnosis, treatments and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO). Dig Liver Dis. 2019;51(9):1223–31.
19. Martin-Broto J, Martinez-Marín V, Serrano C, Hindi N, López-Guerrero JA, Ramos-Asensio R, et al. Gastrointestinal stromal tumors (GISTs): SEAP–SEOM consensus on pathologic and molecular diagnosis. Clin Transl Oncol. 2017;19(5):536–45.
20. Poveda A, García del Muro X, López-Guerrero JA, Cubedo R, Martínez V, Romero I, et al. GEIS guidelines for gastrointestinal sarcomas (GIST). Cancer Treat Rev. 2017;55:107–19.
21. Valdes-Peregrina EN, Hernández-González M, de León-Pacheco O, Mendoza-Ramírez S. Extra-gastrointestinal stromal tumour. Report of primary tumour in the omentum. Rev Médica del Hosp Gen México. 2018;81(4):221–5.
22. Nishida T. Asian consensus guidelines for gastrointestinal stromal tumor: What is the same and what is different from global guidelines. Transl Gastroenterol Hepatol. 2018;2018.
23. Puckett Y, Aryaie A. Case report of diffusely metastatic rectal GIST. Int J Surg Case Rep. 2017;37:4–9.