

Dear Reviewer:

Thank you for considering our manuscript as potentially acceptable for publication in World Journal of Clinical Cases.

We have revised the manuscript, based on the helpful comments made by the reviewers and editors and are uploading all the revised manuscript files in which all the Inserted text are in red and all the deleted are in blue with deleting lines.

Here are the response to the Review 1 in detail.

Dear Sir:

Thank you for your constructive and meaningful comments for our paper. In this paper, we have reported one rare clinical case of metastatic malignant melanoma of prostate with primary prostate carcinoma. We found differences in the imaging tests of the two tumors. We have putted a high value of the accurate diagnosis.

Here are the response to the Review2 in detail.

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Here are the response to the Review 2 in detail.

Dear Sir:

Thank you for your constructive and meaningful comments for our paper. As you have mentioned “literature review” in this title. We have added discussion as follows:

DISCUSSION

Melanoma is a malignant tumor arising from pigment-containing cells, known as melanocytes, which are mainly located in cutaneous tissue. Prostate malignant melanoma may be primary or secondary[2], and a total of 46 cases have been reported to date including our patient. The median age of the patients was 61 years ranging from 29 to 84 years[1].

The most common presentation consists of obstructive lower urinary tract symptoms. Diagnosis requires histological analysis during transurethral resection of the prostate or core-biopsy material. Pigmented cases should be distinguished from melanosis and blue nevus of the

prostate. After diagnosing prostatic melanoma, the most important clinical distinction to make is between primary and secondary melanoma; therefore, a very careful search for another contiguous or distant melanoma should be performed.

Our patient had primary gastric malignant melanoma with multiple metastases to the prostate and bone. In this case, 18F-FDG PET/CT showed high glucose metabolism on the left side of the prostate. The final pathological findings confirmed that it was prostate carcinoma. Melanoma has the lowest glucose metabolism of all malignant tumors. The lesions in the right prostate, gastric mucosa and ribs were not observed by 18F-FDG PET/CT. **So PET/CT of 18F-FDG may bring in a false negative diagnosis.** Teoh[18] and colleagues found that glutamine metabolism was more specific than deoxyribose metabolism both in melanoma and prostate cancer. **In 2017, US Food and Drug Administration approved 18F-fluciclovine PET/CT for imaging of recurrent prostate cancer. Fluciclovine also has the potential ability to selectively image T-cell modulation in the tumor microenvironment.** Thus, 18F-fluciclovine PET/CT may perform better than 18F-FDG PET/CT in the detection of prostate melanoma.

The MRI manifestations of bone metastases from prostate carcinoma are generally T1 signal hypointensity and T2 hyperintensity. The MRI images in our patient were characterized by T1 enhancement and T2 attenuation, which can be used to differentiate between melanoma and prostate carcinoma of bone metastasis.

Following MRI, PET-CT, and prostate biopsy, our patient underwent gastroenteroscopy, which revealed the primary lesion in the stomach. In the ten cases of primary prostate melanoma reviewed in the present study (Table 1), it was found that there was a lack of thorough examination in most cases: only 3 cases underwent endoscopy of the gastrointestinal tract and 2 received 18F-FDG PET/CT. The prognosis in these patients also varied, ranging from 1 month to 84 months[1-14]. We suggest that some patients diagnosed with primary prostate melanoma may have metastatic lesions at the time of diagnosis.

In the only systematic review presented to date on all cases of prostate melanoma, Caputo[14] and colleagues **summarized 45 cases both in English and non-English literature. The median age of patients was 61 years and only 10 primary prostatic cases have been reported so far.** **Caputo's team** found that patients with prostatic metastases from melanoma had a dismal prognosis with a median survival of 3 months (range 7 days to 6 months). The prognosis of primary prostatic melanoma was not as bad as expected: of the 7 available cases with at least one year of follow-up, two survived longer than five years, while the remaining five died after an average of one year.

It is important to distinguish between primary and secondary melanoma. Radical surgery followed by adjuvant chemo-/immuno-therapy represents the most reasonable therapeutic strategy. For patients with primary disease, a more aggressive approach may provide better benefits.

Here are the response to the Review3 in detail.

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Here are the response to the Review 3 in detail.

Q1: There are grammatical errors in the text. Please control the text in that manner.

Dear Sir:

As a non-native English language author who has published several articles in English journals, I attach great importance to English writing. Thank you for your comments. But we have received editorial certificate by MedE Medical Editing. There may have some errors still, we would appreciate if you could point the grammar errors in detail.

Q2:The keywords should modify. The term of “primary” is not correct/suitable in this part.

Dear Sir:

Thank you for your advice. But for “primary” tumor, we think the word “primary” is correct in this occasion. Since one of the reference has used “primary” in the article.

14.Caputo Alessandro,Addresso Maria,Zeppa Pio et al. Malignant melanoma of the prostate gland: A systematic review.[J] .Pathol Res Pract, 2021, 226: 153594.

Q3:The table is not at high resolution.

Dear Sir:

Here is the table with high DDI.

Table1: Clinicopathological characteristics of the 10 primary prostatic melanomas included in the present review. n/f: full text not found; n/m: not mentioned; no: none; mo: months; LUTS: lower urinary tract symptoms; TURP: trans-urethral resection of the prostate.

Source	Age	History disease	Symptoms	Other test	Treatment	Stage	Time to recurrence	Metastases	Secondly Treatment	OS
Berry 1953	38	no	Luts	n/m	cystoprostatectomy	n/m	7mo	n/m	n/m	36mo
Hubler 1980	n/f	n/f	n/f	n/f	n/f	n/f	n/f	n/f	n/f	n/f
Wang 2001	61	n/m	BPH	1.physical examination of the whole body skin surface, oralcavity, and mucosa and optic fundus. 2.CT and MRI of the brain, abdo men and pelvic cavity.3.endoscopy of gastrointestinal tract	TURP	T1N0Mo	n/m	n/m	no	84mo
Wong 2006	71	n/f	Urinary rentention	n/f	TURP	n/f	n/f	n/f	n/f	5mo
Wong 2008	n/f	n/f	n/f	n/f	n/f	n/f	n/f	n/f	n/f	n/f
Doublali 2010	75	n/m	Urinary tract obstruction Urethroscopy had revealed a black discoloration of the prostate	1.physical examination of body skin surface, mucosa, 2.CT of brain, abdomen and pelvic 3.Colonoscopy and gastroscopy,	TURP	n/m	n/m	n/m	no	1mo
Ma 2010	29	n/m	Disuria Digital rectal examination and Transrectal Ultrasound of a mass	1.Pelvic CT scan with contrast	radical prostatec tomy	T2N0M0	n/m	n/m	n/m	3mo
Tosec 2015	37	Hodgkin's disease	Hematuria and urinary retention. in-house cystoscopy showed an asymmetric prostate enlargement with purple discoloration Prostate biopsy	1.Skin of the body 2.Colonoscopy and gastroscopy, 3(CT of chest and abdomen 4.pelvic MRI	open retropubic radical prostatectomy with extended lymph-node dissection	n/m	4mo	Lung	dacarbazine, ipilimumab, nivolumab	16mo
Rogerli 2018	42	no	Hematuria Accepy Photoselective Vaporization of the Prostate (PVP). Intraoperatively, a dark lesion was noted in the patient's prostatic urethra	1.CT of the chest, abdomen, and pelvis, MRI 3.Bone scan. 4.18F-FDG PET/CT scan	2.Brain radical retropubic prostatectomy (RRP) and pelvic lymph node dissection (PLND)	T2N1M0	3mo	Lesion along the right iliac artery, pulmonary nodule	Biochemotherapy for 6 cycles dacarbazine, vinblastine, cisplatin, IL2	84mo
Parmar 2019	65	no	Acute urinary retention	1.physical examination of whole body skin surface, oral cavity and anal mucosa 2. PET-CT	TURP, Dacarbazine, Chemotherapy	n/m	3mo	n/m	n/m	n/m

Q4: Figures 4 and 5 need error bars.

Dear Sir:

Thank you for your advice. You are very observant. Here is new one.

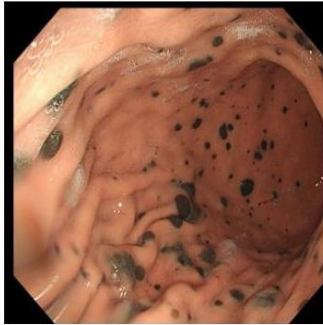


Figure5a

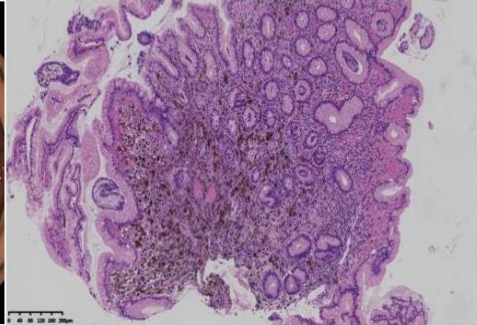


Figure5b

Figure5a: Gastroscope: multiple mucosal black spots in the body and floor of the stomach

Figure5b: Microscopically: small foci of melanocytes in gastric mucosa (hematoxylin-eosin, original magnifications $\times 25$)

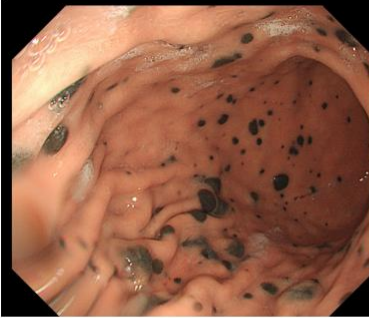


Figure5a

5a: Gastroscope: multiple mucosal black spots in the body and floor of the stomach.

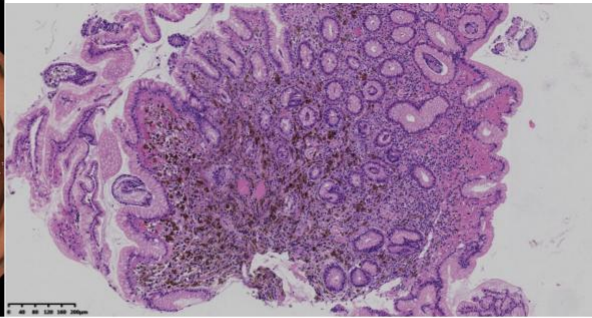


Figure5b

5b: Microscopically: small foci of melanocytes in gastric mucosa (hematoxylin-eosin, original magnifications $\times 25$)