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Use of Somatostatin Analogues (STSAs) in the Treatment of Benign Prostatic Hyperplasia (BPH), A Case Report

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ABSTRACT

Prostate overgrowth and urinary symptoms go hand In hand and pose a major threat to the male community of the world. The case study we will discuss is related to benign prostate hyperplasia and effect of somatostatin analogues (STSAs).This report shows a 73 year old male with Gastrointestinal neuroendocrine tumors who concomitantly was diagnosed with BPH and was given Octreotide/somatostatin LAR which led to decrease in both urinary tract symptoms and prostate volume. This report further discuss the underlying mechanism of these drugs and highlight the potential of this drug to be drug of choice or adjunct therapy. Limitations are highlighted as well bit the promising role is to be investigated as well

Keywords:c Benign prostatic hyperplasia; BPH; Case report

INTRODUCTION

Benign hyperplasia of prostate (BPH) is defined as increase in size of prostate gland, being a very prevalent condition in elderly men.[1] Major characteristics seen with BPH is over growth of prostate tissue along with some symptoms of lower urinary tract. Increase in this condition has posed a threat to healthcare setups worldwide.[2]various treatment protocols are used for the treatment of condition, most prevalent ones are through drugs like alpha-blockers or 5-alpha reductase inhibitors and surgical procedures.[1] Most commonly done procedure is transurethral resection of prostate (TURP).[3]issue with the procedure is that it may not be done or may be effective or seemly for patients, therefore indicating the need for other therapeutic interventions.[4]

In previous years keen interest to explore novel treatment approaches for Benign prostate hyperplasia has been prevalent, especially in researchers who are interested in targeting the underlying pathophysiology that leads to the basic over growth.[5]

STSAs, which were initially created to treat neuroendocrine tumors, work by binding to somatostatin receptors (SSTRs) that are present in a variety of tissues, including the prostate gland. Preclinical examinations have exhibited the presence of SSTRs in both typical and hyperplastic prostatic tissue, proposing a likely job for STSAs in regulating prostate cell expansion and tissue development.[6]

Evidence for STSAs in prostate hyperplasia's treatment is under investigation, but evidence has been seen in its efficacy in reducing Lower urinary tract symptoms (LUTS) and the size of prostate cells. Limited volume of evidence is seen regarding safety , dosage and efficiency of these drugs, henceforth more studies are required,[7]

This case report has been reported in line with the SCARE Criteria.[8]

To support this pharmacotherapy this article is going to present a case, reporting the treatment experience of a 73 year old male patient of gastrointestinal neuroendocrine tumors along with BPH. The Patient was administered with Octreotide/Somatostatin LAR and showed improvement in urinary symptoms and reduction of prostate volume, hence showing a probable efficacy of the drug.

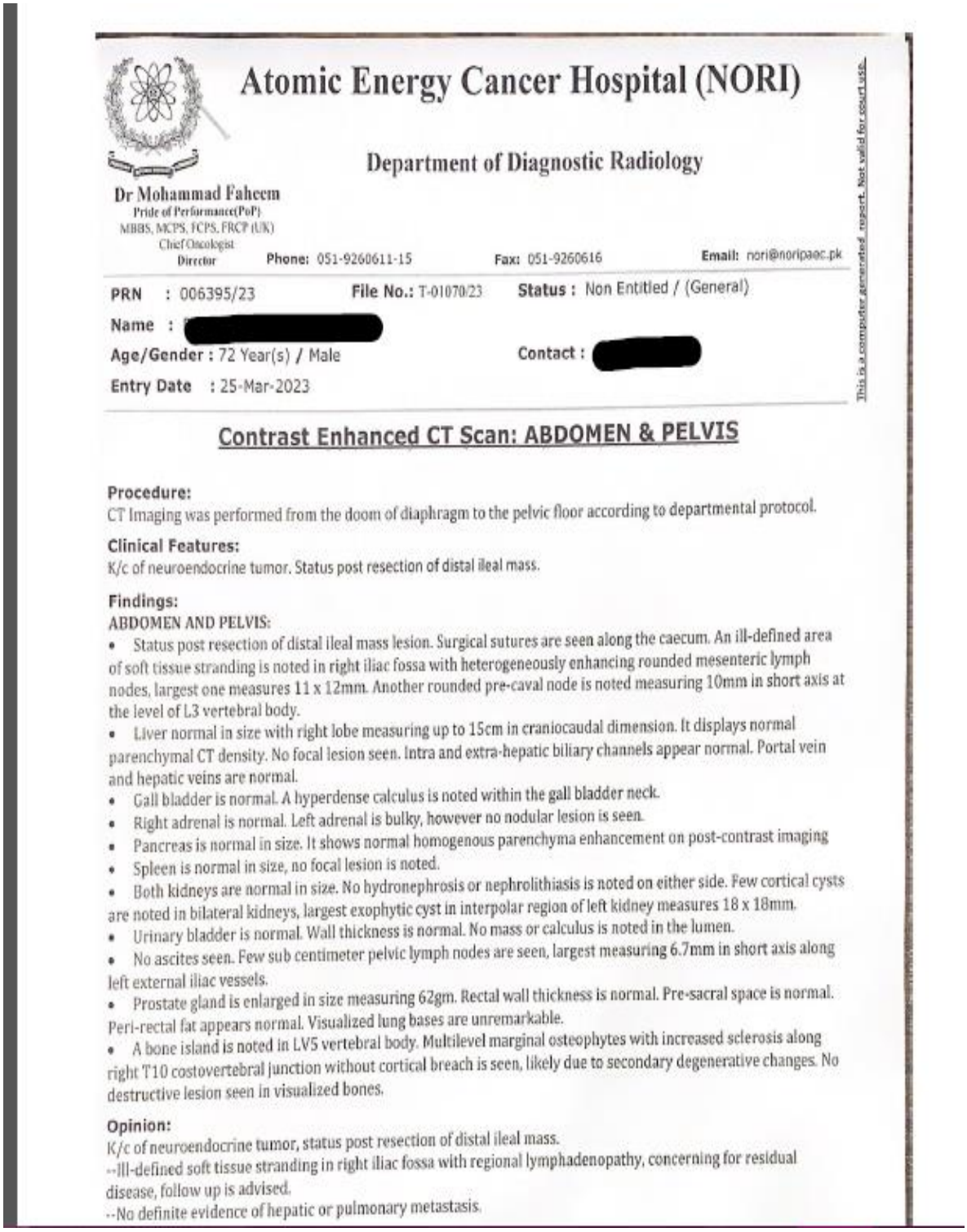
By clarifying the molecular processes and clinical results linked to STSA therapy, we hope to open the door to better treatment approaches and better outcomes for BPH patients. With this case report and discussion that follows, we hope to further the understanding of STSAs as a viable therapeutic option for BPH and encourage additional research into their clinical utility.

CASE REPORT

Consent was taken in written form from the patient to disclose and display the course of his treatment in order to strengthen the treatment protocols and research paradigms. A suspicious growth on the small intestine was discovered during a follow-up CT scan of a 73-year-old man patient who was initially being watched for an aortic aneurysm. Figure 1 represents the first CT the patient underwent. After that, he went to Shifa International Hospital for treatment. There, a CTAP scan was performed, and an excisional biopsy revealed gastrointestinal neuroendocrine tumors (NETs).A PET scan was done before and after the treatment protocol Additional examination verified Grade 1 stage 4 metastatic illness (pT4 N2 M1b), with a Ki67 - 1%. Notably, no metastases to the liver were seen. The first dosage of Octreotide (30 mg) was administered intramuscularly once a month. The patient reported a history of nocturia and urine hesitancy, which he attributed to a prior diagnosis of benign prostatic hyperplasia (BPH) at the age of 50, even though he did not show any overt symptoms associated with his illness.

Despite exhibiting no overt symptoms related to his condition, the patient disclosed a history of nocturia and urinary hesitancy, which he attributed to previously diagnosed benign prostatic hyperplasia (BPH) at the age of 50. Initial medical therapy for BPH was unsuccessful, prompting two transurethral resection of the prostate (TURP) procedures, providing temporary relief for a decade. However, the symptoms recurred, albeit milder, prompting further investigation coinciding with the diagnosis of the neuroendocrine tumor. A PET CT DOTATE scan in September 2023 revealed a prostate weighing 62g Figure 2 depicts this. Following five months of Octreotide/Somatostatin LAR 30mg IM therapy, a subsequent PET CT DOTATE scan in April 2024

demonstrated a normalization in prostate size, accompanied by reported symptom improvement Figure 3 depicts this.



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PRN : 006395/23 File No.: T-01070/23 Status : Non Entitled / (General)
Name : [redacted]
Age/Gender : 72 Year(s) / Male Contact : [redacted]
Entry Date : 25-Mar-2023

Contrast Enhanced CT Scan: ABDOMEN & PELVIS

Procedure:
CT Imaging was performed from the doom of diaphragm to the pelvic floor according to departmental protocol.

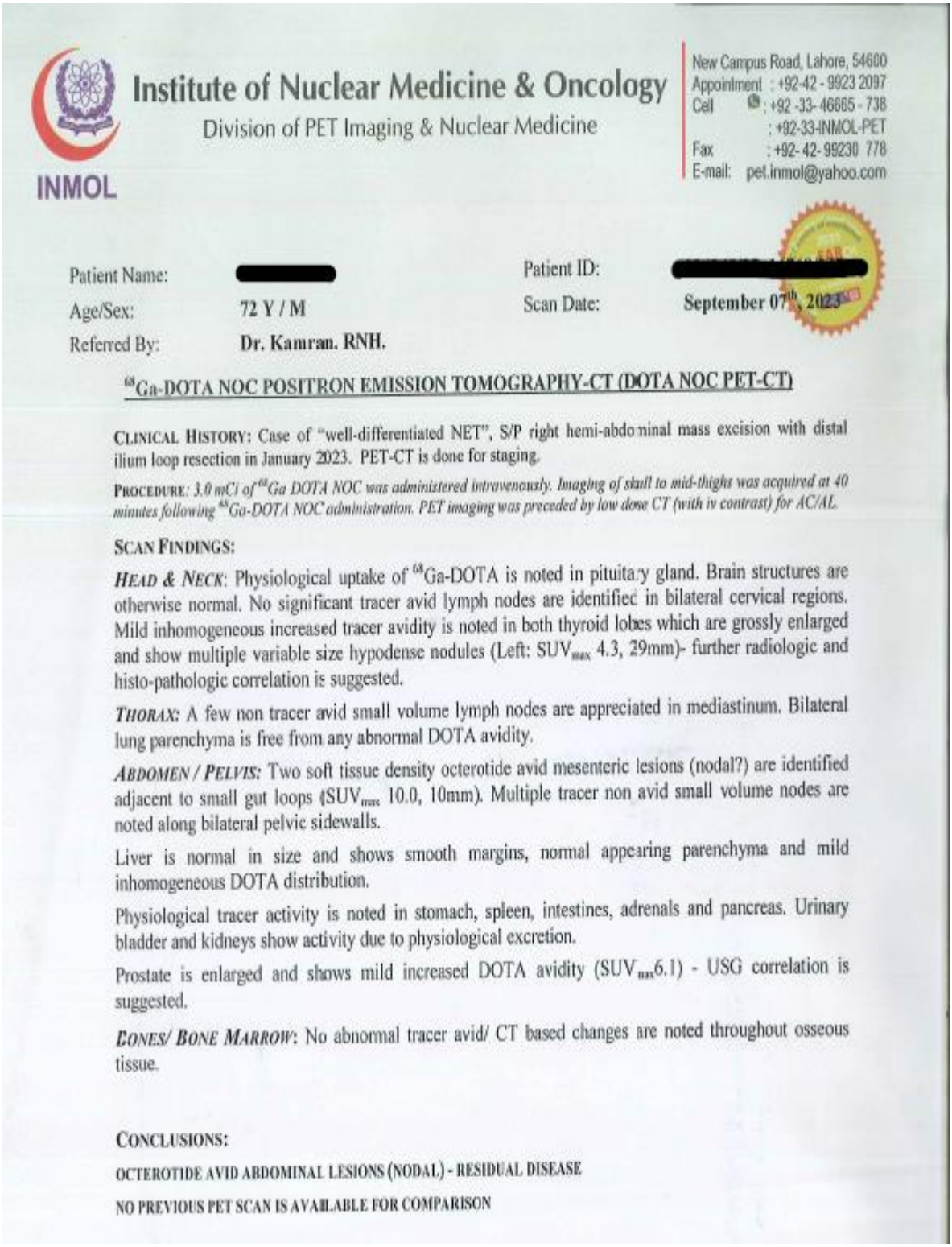
Clinical Features:
K/c of neuroendocrine tumor. Status post resection of distal ileal mass.

Findings:
ABDOMEN AND PELVIS:

- Status post resection of distal ileal mass lesion. Surgical sutures are seen along the caecum. An ill-defined area of soft tissue stranding is noted in right iliac fossa with heterogeneously enhancing rounded mesenteric lymph nodes, largest one measures 11 x 12mm. Another rounded pre-caval node is noted measuring 10mm in short axis at the level of L3 vertebral body.
- Liver normal in size with right lobe measuring up to 15cm in craniocaudal dimension. It displays normal parenchymal CT density. No focal lesion seen. Intra and extra-hepatic biliary channels appear normal. Portal vein and hepatic veins are normal.
- Gall bladder is normal. A hyperdense calculus is noted within the gall bladder neck.
- Right adrenal is normal. Left adrenal is bulky, however no nodular lesion is seen.
- Pancreas is normal in size. It shows normal homogenous parenchyma enhancement on post-contrast imaging
- Spleen is normal in size, no focal lesion is noted.
- Both kidneys are normal in size. No hydronephrosis or nephrolithiasis is noted on either side. Few cortical cysts are noted in bilateral kidneys, largest exophytic cyst in interpolar region of left kidney measures 18 x 18mm.
- Urinary bladder is normal. Wall thickness is normal. No mass or calculus is noted in the lumen.
- No ascites seen. Few sub centimeter pelvic lymph nodes are seen, largest measuring 6.7mm in short axis along left external iliac vessels.
- Prostate gland is enlarged in size measuring 62gm. Rectal wall thickness is normal. Pre-sacral space is normal. Peri-rectal fat appears normal. Visualized lung bases are unremarkable.
- A bone island is noted in LV5 vertebral body. Multilevel marginal osteophytes with increased sclerosis along right T10 costovertebral junction without cortical breach is seen, likely due to secondary degenerative changes. No destructive lesion seen in visualized bones.

Opinion:
K/c of neuroendocrine tumor, status post resection of distal ileal mass.
--Ill-defined soft tissue stranding in right iliac fossa with regional lymphadenopathy, concerning for residual disease, follow up is advised.
--No definite evidence of hepatic or pulmonary metastasis.

Figure 1: This document represents the initial Contrast CT (abdominal-pelvic) of the patient when he was diagnosed with tumors



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Patient Name: [redacted]
Patient ID: [redacted]
Age/Sex: 72 Y / M
Scan Date: September 07th, 2023
Referred By: Dr. Kamran. RNH.

^{68}Ga-DOTA NOC POSITRON EMISSION TOMOGRAPHY-CT (DOTA NOC PET-CT)

CLINICAL HISTORY: Case of "well-differentiated NET", S/P right hemi-abdominal mass excision with distal ilium loop resection in January 2023. PET-CT is done for staging.

PROCEDURE: *3.0 mCi of ^{68}Ga DOTA NOC was administered intravenously. Imaging of skull to mid-thighs was acquired at 40 minutes following ^{68}Ga-DOTA NOC administration. PET imaging was preceded by low dose CT (with iv contrast) for AC/AL*

SCAN FINDINGS:

HEAD & NECK: Physiological uptake of ^{68}Ga-DOTA is noted in pituitary gland. Brain structures are otherwise normal. No significant tracer avid lymph nodes are identified in bilateral cervical regions. Mild inhomogeneous increased tracer avidity is noted in both thyroid lobes which are grossly enlarged and show multiple variable size hypodense nodules (Left: SUV_{max} 4.3, 29mm)- further radiologic and histo-pathologic correlation is suggested.

THORAX: A few non tracer avid small volume lymph nodes are appreciated in mediastinum. Bilateral lung parenchyma is free from any abnormal DOTA avidity.

ABDOMEN / PELVIS: Two soft tissue density octerotide avid mesenteric lesions (nodal?) are identified adjacent to small gut loops (SUV_{max} 10.0, 10mm). Multiple tracer non avid small volume nodes are noted along bilateral pelvic sidewalls.

Liver is normal in size and shows smooth margins, normal appearing parenchyma and mild inhomogeneous DOTA distribution.

Physiological tracer activity is noted in stomach, spleen, intestines, adrenals and pancreas. Urinary bladder and kidneys show activity due to physiological excretion.

Prostate is enlarged and shows mild increased DOTA avidity (SUV_{max}6.1) - USG correlation is suggested.

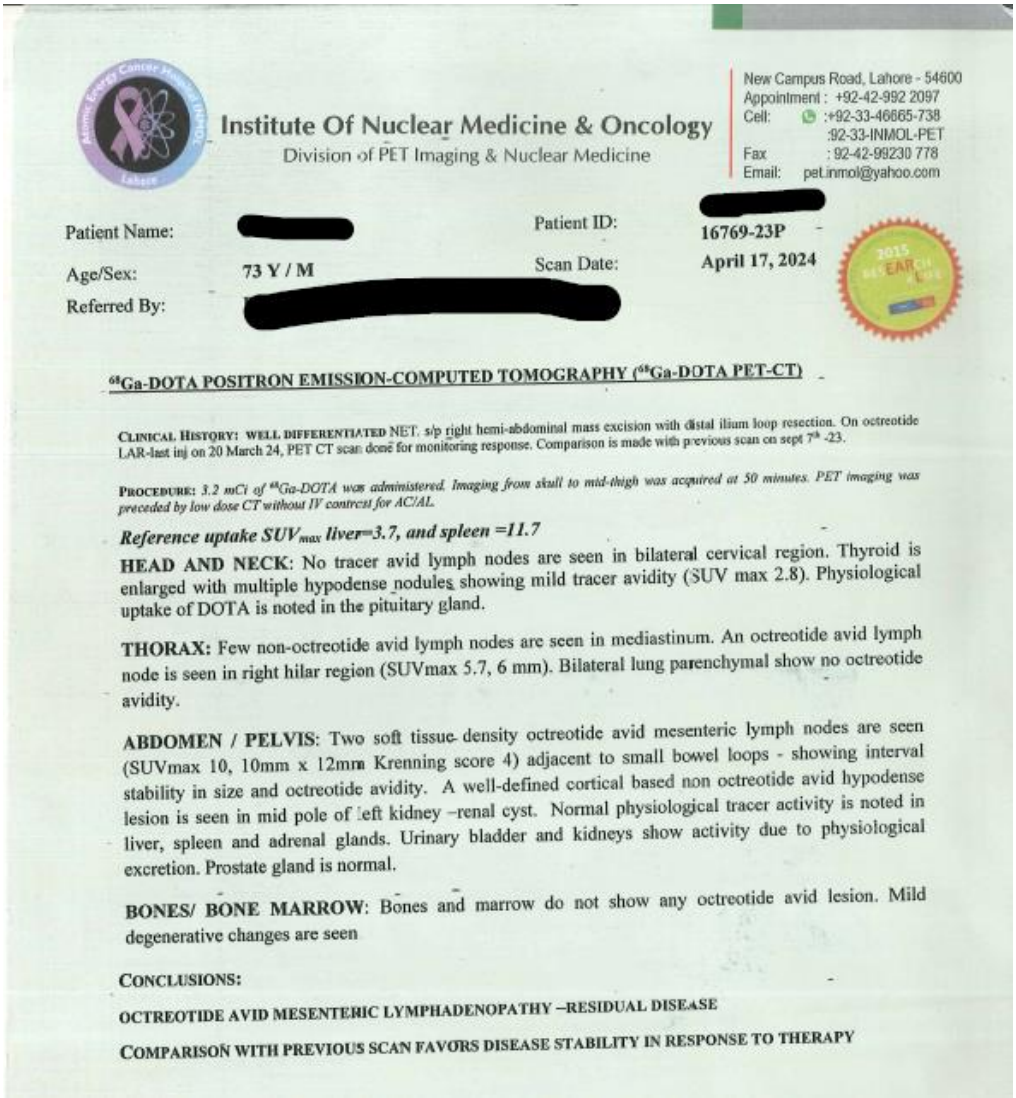
BONES/ BONE MARROW: No abnormal tracer avid/ CT based changes are noted throughout osseous tissue.

CONCLUSIONS:

OCTEROTIDE AVID ABDOMINAL LESIONS (NODAL) - RESIDUAL DISEASE

NO PREVIOUS PET SCAN IS AVAILABLE FOR COMPARISON

Figure 2: This is an initial PET scan .This PET CT DOTATE scan in September 2023 revealed a prostate weighing 62g.



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Email: pet.inmol@yahoo.com

Patient Name: [redacted]
Patient ID: 16769-23P
Age/Sex: 73 Y / M
Scan Date: April 17, 2024
Referred By: [redacted]

^{68}Ga-DOTA POSITRON EMISSION-COMPUTED TOMOGRAPHY (^{68}Ga-DOTA PET-CT)

CLINICAL HISTORY: WELL DIFFERENTIATED NET. s/p right hemi-abdominal mass excision with distal ilium loop resection. On octreotide LAR-last inj on 20 March 24, PET CT scan done for monitoring response. Comparison is made with previous scan on sept 7th -23.

PROCEDURE: *3.2 mCi of ^{68}Ga-DOTA was administered. Imaging from skull to mid-thigh was acquired at 50 minutes. PET imaging was preceded by low dose CT without IV contrast for AC/AL.*

Reference uptake SUV$_{max}$ liver=3.7, and spleen =11.7

HEAD AND NECK: No tracer avid lymph nodes are seen in bilateral cervical region. Thyroid is enlarged with multiple hypodense nodules showing mild tracer avidity (SUV max 2.8). Physiological uptake of DOTA is noted in the pituitary gland.

THORAX: Few non-octreotide avid lymph nodes are seen in mediastinum. An octreotide avid lymph node is seen in right hilar region (SUVmax 5.7, 6 mm). Bilateral lung parenchymal show no octreotide avidity.

ABDOMEN / PELVIS: Two soft tissue density octreotide avid mesenteric lymph nodes are seen (SUVmax 10, 10mm x 12mm Krenning score 4) adjacent to small bowel loops - showing interval stability in size and octreotide avidity. A well-defined cortical based non octreotide avid hypodense lesion is seen in mid pole of left kidney –renal cyst. Normal physiological tracer activity is noted in liver, spleen and adrenal glands. Urinary bladder and kidneys show activity due to physiological excretion. Prostate gland is normal.

BONES/ BONE MARROW: Bones and marrow do not show any octreotide avid lesion. Mild degenerative changes are seen

CONCLUSIONS:

OCTREOTIDE AVID MESENTERIC LYMPHADENOPATHY –RESIDUAL DISEASE

COMPARISON WITH PREVIOUS SCAN FAVORS DISEASE STABILITY IN RESPONSE TO THERAPY

Figure 3: Later a PET scan was done. This figures shows PET CT DOTATE scan of April 2024 and a normalization in prostate size was seen.

DISCUSSION

A non-cancerous situation where there's an excessive growth of tissue in the prostate, causing it to enlarge. Consequently, the gland puts pressure on and narrows the urethra causing symptoms.[6]

The prostatic tissue has high affinity (Kd = 0.4 nmol/L) and high specificity receptors for physiologically active SRIH analogues; the presence of the SSTR2 receptor subtype is suggested by the high affinity for SRIH-14, SRIH-28, and octreotide that was found.[4] SRIH-R were found in the stroma's smooth muscle of both hyperplastic and normal prostates. It has been shown that somatostatin inhibits the proliferation of both normal and altered cells in vitro through the action of SRIF receptors (SSRs). Additionally, similar to other neuroendocrine compounds.[9]

Only one original study has been conducted and published in a Turkish journal called Medeniyet Medical Journal in 2019. It consisted of 15 patient diagnosed with Gastrointestinal NET's being treated with 30MG.Long-acting somatostatin analog every 4 weeks only one patient was given 120MG dose. CT scans both

prior to and following somatostatin analogue therapy. Each patient also had liver metastases and neuroendocrine tumors of Grade 1 or 2, as confirmed by histopathology. After using STS analogues, the prostate volume decreased in thirteen (86.6%) of the patients.[9]

In contrast, the bispecific sst2/sst5-preferential ligand BIM-23244 decreased cell proliferation after 24 hours at a dose of 10−9 M. This was demonstrated in another investigation where lanreotide suppressed cell proliferation after both 24 and 48 hours with a maximum effect at 10−11 M. After 48 hours of treatment, the bi-specific sst1/sst2-preferential ligand BIM-23704 (dose range: 10−10 M to 10−11 M) reduced the proliferation of LNCaP. Further proving the point that Somatostatin analogue do have a role to play in inhibiting prostatic cell proliferation.

Our study highlighted the effect of somatostatin analogue on benign proliferation of prostate as we know that the effect of STR2 receptors has been reported in the treatment of prostatic cancer but the focus on benign prostate has not been undertaken. This case report further adds to the data showing that somatostatin indeed has an effect on prostatic volume and can potentially be considered for the treatment of BPH.[10]

While looking at other options for treatment BPH we see that those treatment plans are not always successful and may not be suitable for everyone. According to one study by Fourcade et al. (2012),[11]52.8% of patients receiving medical treatment reported disappointing results. Approximately 15 to 20 percent of patients who have their prostate removed via transurethral resection for benign prostatic hyperplasia have persistent or recurrent problems urinating, necessitating additional treatment. In these cases,[12] 80% of patients had involuntary bladder contractions, 27% had blockage, 27% had decreased contractility, and 20% had sphincter incontinence. It should be emphasized that less than half of patients who do not react favorably to transurethral resection of the prostate have residual or recurrent blockage.[13]the data shows the failure rate of TURP and repeated need to undergo the procedure and with each attempt the chance for involuntary bladder contractions.

In certain cases TURP has absolute contraindications would be if a patient couldn't tolerate anesthesia or potential surgical complications. Another absolute contraindication would be having an untreated urinary tract infection. A history of post-radiation therapy for prostate cancer, myasthenia gravis, multiple sclerosis, and Parkinson's disease are examples of relative contraindications, as these conditions may lead to postoperative incontinence due to sphincter dysfunction.[14] Furthermore, typical TURP procedures are somewhat contraindicated by active anticoagulant medication, although laser TURP or temporary discontinuation of blood thinners can be considered. Prostate sizes exceeding 100 grams may require alternative procedures such as simple prostatectomy or HoLEP due to safety concerns with TURP. Severe hyperactive bladder not easily managed is also a relative contraindication.[15]which shows that In the event that medical therapy using 5-alpha reductase inhibitors and alpha blockers is ineffective, some patients will be left without treatment choices. So the treatment with LAR injections can be very promising in such cases.0020[1]

The limitations of this study are that not many similar studies have been done and comparison was done with only one other study. More research needs to be done to be. Also both studies had NET patients receiving octreotide and on general population there are no results available. Long term follow up is not available to determine how long the patient will be symptoms free and if more doses will need to be repeated in the future. If it is cost effective treatment choice. Regardless of the limitations the results were promising so far and

indicating a potential for an alternative treatment option for patients with BPH-related symptom such as compression-related disorders or lower urinary tract symptoms.

CONCLUSION

The case study that is being given here provides insight into the possible therapeutic use of somatostatin analogues (STSAs) in the treatment of benign prostatic hyperplasia (BPH), a condition that is common in older men. Through the documented case and subsequent discussion, it becomes evident that STSAs, such as Octreotide/Somatostatin LAR, hold promise in alleviating BPH symptoms and reducing prostate volume. This finding aligns with existing knowledge of STSAs' inhibitory effects on prostate cell proliferation, offering a novel avenue for BPH treatment. While the observed results are promising, further research is warranted to validate these findings on a larger scale and elucidate the long-term efficacy and safety of STSAs in BPH management. For BPH, prospective studies should investigate the best possible dose schedules, patient selection standards, and any side effects before recommending STSAs as a treatment. In conclusion, the insights gleaned from this case report underscore the need for continued investigation into the therapeutic potential of STSAs in BPH. By expanding our understanding of their mechanisms of action and clinical outcomes, we can improve the quality of life and treatment options for people who suffer from this common urological illness.

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