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Bilateral orbital soft tissue metastases from Renal Neuroendocrine Tumor: successful Theranostic application of $^{68}Ga/^{177}Lu$-DOTATATE with improvement of vision

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Abstract:

Gratifying clinical response obtained in the clinical setting of bilateral orbital metastases from renal neuroendocrine tumor (NET) is reported. **Methods:** A 53 year-old male, diagnosed case of renal NET (MIB1 index-4%), with symptoms of skeletal and abdominal pain, proptosis and decrease in vision of left eye, was found to harbor bilateral orbital soft tissue lesions on ^{68}Ga-DOTATATE PET-CT and MRI in addition to widespread metastatic skeletal lesions, and metastatic lymph nodal disease. His symptoms worsened despite radiotherapy to left eye (20Gy) and long-acting octreotide therapy for 18 months, with increase in serum chromogranin A (CgA) level and was considered for ^{177}lutetium(Lu)-DOTATATE peptide receptor radionuclide therapy (PRRT). **Results**: There was significant improvement in skeletal pain, proptosis and vision after 4 cycles of PRRT (cumulative dose of 22.2GBq), stable disease on scan and decrease in serum CgA (from 150 to 36.39 ng/ml) with progression free survival at 18 months. **Conclusion**: PRRT through theranostic application of ^{68}Ga/^{177}Lu-DOTATATE was thus helpful in this uncommon clinical setting.

Keywords: Renal Neuroendocrine Tumor; orbital metastases; ^{68}Ga-DOTATATE;^{177}Lu-DOTATATE;PRRT.

Introduction

NETs are heterogeneous group of neoplasms with differing biological behavior and response to treatment. NE cells are usually not found within normal renal parenchyma resulting in relatively rare incidence of primary renal NET with debatable pathogenesis. Different theories have been put forth to support the origin: [a] from primitive totipotential stem cells that subsequently differentiate in neuroendocrine direction,[b] metastasis from an occult primary tumor site to the kidney, [c] activation of aberrant gene sequences in a totipotential stem cell line that differentiates into aberrant neuroendocrine tumor cells *(1, 2).*

Methods

A 53 year-old male, diagnosed case of renal NET (MIB1 index-4%), presented with skeletal pain all over body, abdominal pain, proptosis and decrease in the vision of left eye, one year after right nephrectomy. The ^{68}Ga-DOTATATE PET-CT demonstrated enhanced tracer uptake in widespread metastatic skeletal lesions, cervical, mediastinal, abdomino-pelvic metastatic lymph nodal disease and bilateral orbital soft tissue lesions. MRI of head showed oval to rounded T2-hyperintense and T1-hypointense lesions with moderate homogenous enhancement involving left lateral rectus, left inferior oblique, right lateral rectus and right inferior oblique in intraconal location with compression of left optic nerve. He received local radiotherapy to left eye (20 Gy) and systemic octreotide (for 18 months duration), however the symptoms worsened even on these therapies alongwith increase in serum chromogranin A level. Thus, he was considered for ^{177}lutetium(Lu)-DOTATATE-PRRT in view of high uptake on ^{68}Ga-DOTATATE-PET-CT. There was significant improvement in skeletal pain, proptosis and vision of eyes (resulting in better QoL) following 4 cycles of PRRT with cumulative dose of 22.2GBq, stabilization of disease on scan and decrease in serum CgA level (from 150 to 36.39 ng/ml) and progression free survival at 18 months.

Discussion

The clinical course of renal NET is unpredictable: largely believed to have an indolent course (well-differentiated type), the current recommended management includes radical nephrectomy with surveillance. For any metastatic disease, medical management with or without surgical approach is considered (*1*). Because of its asymptomatic nature, renal NET can present with metastatic disease (around 45.6% of reported cases), the common sites being lymph nodes and liver(*2*).

Orbital metastases from NET are rare and typically occur through hematogenous spread by carotid and ophthalmic artery. The management options includes excision, orbital exenteration, radiotherapy, hormonal therapy, and chemotherapy. However, there is no definitive consensus approach in management with loss of vision after exenteration, high chance of recurrence after surgical excision, and mixed response after radiotherapy(*3*). The overall reported survival for metastatic orbital NET is 72% at 5 years and 38% at 10 years(*4*); preserving vision and maintaining good QoL are fundamentally important in management of these cases. In such cases, PRRT is a potential treatment option for treating patients with disseminated lesions which is well-tolerated, safe, and can be an effective treatment modality resulting in improvement of vision alongwith better QoL.

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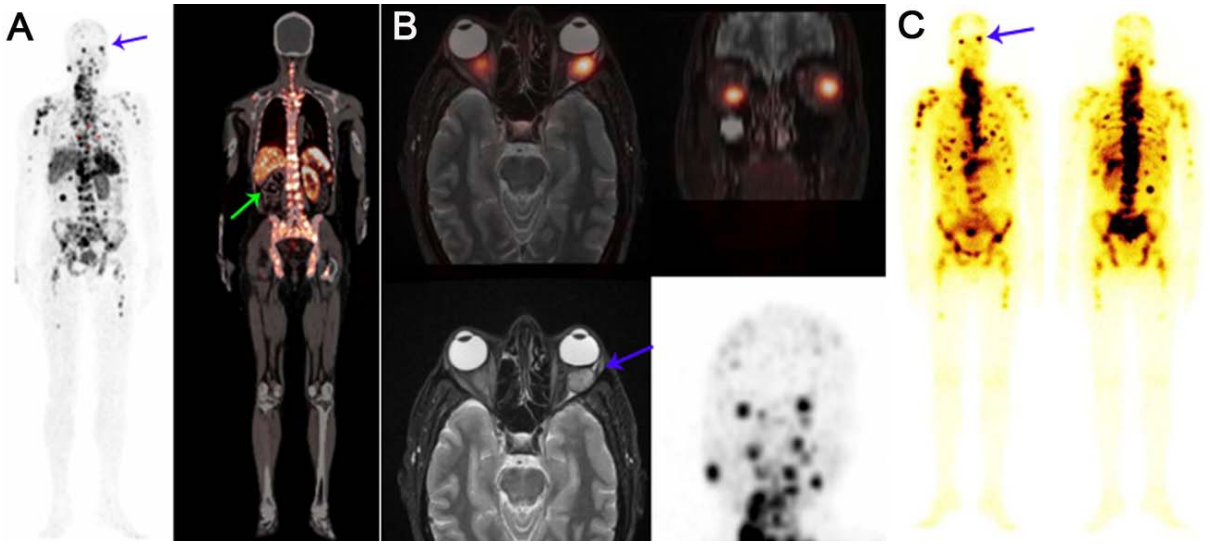

Fig 1- ^{68}Ga-DOTATATE PET/CT (A) showing increased tracer uptake in widespread metastatic skeletal lesions, cervical, mediastinal, abdomino-pelvic lymph nodes and bilateral orbital soft tissue lesions. MRI of head (B) showed oval to rounded T2-hyperintense and T1-hypointense lesions with moderate homogenous enhancement involving left lateral rectus, left inferior oblique, right lateral rectus and right inferior oblique in intra-conal locations with compression of left optic nerve alongwith abnormal tracer uptake on fused PET/MRI. Post-PRRT scan (C) at 24 hrs after PRRT demonstrate adequate tracer uptake in multiple metastatic lesions.