Response to Lenvatinib in Progressive Metastatic Paraganglioma

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Abstract

Background: Paragangliomas are rare vascular endocrine tumors that highly express vascular endothelial growth factor (VEGF). Anti-angiogenic agents may play a role in the treatment of these tumors. We herein report a dramatic clinical response to the oral VEGFR 1-3 and multi-kinase inhibitor lenvatinib.

Clinical Case: A 49-year-old female with longstanding metastatic pelvic paraganglioma who presented during pregnancy with SDHB (p.V140F - c.418G>T) mutation was treated with multiple surgical resections. She also underwent systemic and localized therapeutic approaches including multiple chemotherapeutic regimens as well as an array of local therapies at metastatic sites. Given osteoid osteitis, progressing bony metastasis, and pelvic fistulae after multiple pelvic surgeries, she was initiated on octreotide therapy and RANK-Ligand-directed bone therapy. She also benefited from pazopanib therapy.

Upon disease progression, she developed hypertension. Laboratory values showed metanephrine level >0.20 mmol/L (>0.50 mmol/L), normetanephrines 5.7 mmol/L (<0.90 mmol/L), norepinephrine 3542 pg/ml (200-1700 pg/ml), dopamine 3919 pg/ml (< 30 pg/ml). CT scans of chest, abdomen and pelvis showed new and increasing pulmonary nodules and progression of hilar, pelvic and peritoneal metastatic lymphadenopathy. After focal radiotherapy to a right hilar PR, Laboratory evaluation were consistent with Oct-15. She developed disease progression and hypertension through pazopanib therapy. Laboratory values showed metanephrine level <0.20 mmol/L (<0.50 mmol/L), normetanephrines 5.7 mmol/L (<0.90 mmol/L), norepinephrine 3542 pg/ml (200-1700 pg/ml), dopamine 3919 pg/ml (< 30 pg/ml).

Results

• Within 48 hours of lenvatinib initiation, she had dramatic nodal clinical tumor regression associated with fever. Work up revealed no infectious source for fever.

• Laboratory evaluation were consistent with mild tumor lysis syndrome.

• Biochemical response (Figure 1)

• Follow up imaging showed interval decreases in hilar and retroperitoneal adenopathy and a confirmed RECIST response (Figure 2)

• Side effects prominently included fatigue.

Case Description

• A 49-year-old female with longstanding metastatic pelvic PGL1 with SDHB (p.V140F - c.418G>T) mutation.

• Multiple surgical resections, chemotherapeutic regimens, local therapies at metastatic sites, octreotide therapy and RANK-Ligand-directed bone therapy. Pazopanib therapy was trailed for about 2 years with good initial response.

• She developed disease progression and hypertension through pazopanib therapy.

• Laboratory values showed metanephrine level <0.20 mmol/L (<0.50 mmol/L), normetanephrines 5.7 mmol/L (<0.90 mmol/L), norepinephrine 3542 pg/ml (200-1700 pg/ml), dopamine 3919 pg/ml (< 30 pg/ml).

Discussion/Conclusions

We describe a promising clinical response to lenvatinib therapy in a patient with widely metastatic malignant paraganglioma.

Systemic therapies, like multi-kinase inhibitors, can induce hypertensive episodes, which require close monitoring, as well as have potential to induce tumor lysis like phenomena.

Special care must be taken to respond emergently to minimize patient risks in the event of rapid tumor regression.

References

5. Joshua J Clin Endocrinol Metab 94: 5–9, 2009

Figure 1A: Chromogranin A

Figure 1B: Normetanephrine (nmol/L)

Figure 2: CT chest before and after therapy

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Study Type N Response Ki
Jimez et al. 2009 Case report 1 PR Sunlentib
Gross et al. 2006 Non-randomized, open label, Phase II study 2 NR Imatinib-mesylate
Park et al. 2009 Case report 1 PR Sunlentib
Joshua et al. 2009 Case studies 3 PR, 1 year Sunlentib
Montserrat et al. 2012 Retrospecti ve cohort 1 PR, 3 PR, 3 Stable=5 DC=3 Sunlentib

Ki’s in Pheo/PGL