The role of tyrosin kinase inhibitors in a MEN2B patient with metastatic medullary thyroid carcinoma

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Introduction:
Medullary thyroid carcinoma (MTC) is present in up to 100% of patients with multiple endocrine neoplasia syndrome type 2 (MEN2). Traditional chemotherapy or external beam radiation have shown limited effects. Development of tyrosine kinase inhibitors open a new era in the management of the disease.

Case report:
A 23-year-old man with marfanoid phenotype was admitted to emergency room with pneumothorax. Surgery was performed and anamopatologic diagnosis of lung samples was metastatic MTC. The patient underwent total thyroidectomy and cervical lymphadenectomy. Genetic test was positive for protooncogene RET Met138Tr mutation. The extension study included a whole body scan with 111In-octreotide, PET-CT scan with 18F-FDG, whole body scintigraphy with 99mTc-DMSA and cervical ultrasound. The results confirmed extension of local and distant metastases in the right lung, the liver, mesenteric and retroperitoneal lymph nodes and vertebral spine. Biochemical study presented an elevation in CEA 59ng/ml (NV<5ng/ml), calcitonin (CT) 2000pg/ml (NV<18pg/ml), and an increase in urinary free catecholamines. Pheochromocytoma was excluded by imaging methods and repeated catecholamines. Clinically the patient had malnutrition, diarrhea, dyspnea and cervical nodules and calcitonin was increasing rapidly (CT 10,128pg/ml). Dual treatment with octreotide LAR 20mg/28d and sorafenib 400mg/12h was started with clinical relief and a decrease in CT levels (2,000pg/ml). Seven months later tumor progression was observed with an increase in calcitonin (26,753pg/ml) and everolimus was used instead of sorafenib. No decrease in CEA or CT was observed with everolimus and moreover, the patient experienced limited clinical tolerance. Some months later compassionate treatment with sunitinib 37.5 mg/d was started in addition to the octreotide LAR 20mg/28d. Four months later after the 3rd sunitinib cycle, a reduction in CEA and CT levels was seen (CEA 72ng/ml, CT 19.249pg/ml). Again, four months later, clinical and biochemical tumor progression prompted a change to vandetanib 200mg/24h with a significant reduction in CT (2000pg/ml). Seven months later, vandetanib is still ongoing with maintained reduction in CEA and CT and an improvement in clinical condition.

Conclusion:
Tyrosine kinase inhibitors are promising drugs for the treatment of metastatic MTC. A possible mechanism of tolerance causing loss of efficacy has led to sequential treatment being proposed. The effective chronic use of these drugs enhances the need for personalized treatment to weigh the risk/benefit ratio.