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TOPIC:
Clinical Case Reports

SECONDARY ADRENAL INSUFFICIENCY AND HYPOGONADOTROPIC HYPOGONADISM IN A PATIENT WITH ADVANCED MEDULLARY THYROID CARCINOMA ON TREATMENT WITH VANDETANIB. MAY IT HAVE A PATHOGENIC ROLE?

Hospital Universitario La Paz
SaludMadrid
Comunidad de Madrid

IdiPAZ
Instituto de Investigación Hospital Universitario La Paz

Álvarez Escola Cristina[1], Moreno Domínguez Óscar[1], Cárdenas Salas Jersy Jair[1], Castelo Fernández Beatriz[2], Lecumberri Santamaría Beatriz[1], Elviro Peña Rosa[3]

1. *Endocrinology and nutrition. Hospital Universitario La Paz, Madrid (Spain)*
2. *Medical Oncology. Hospital Universitario La Paz, Madrid (Spain)*
3. *Endocrinology and nutrition. Hospital Universitario de Getafe, Getafe(Spain)*

CLINICAL CASE

We report the case of a 40-year-old woman, diagnosed when she was 27, with sporadic medullary thyroid carcinoma (MTC). After diagnosis, she was treated with total thyroidectomy, cervical lymph node dissection and adriamicyn as chemotherapy.

While following, cervical lymph node, lung, breast, bone and sub-centimeter cerebellous affectation was observed. Because disease progression, the patient was enrolled in a phase III clinical trial with XL-184. Pulmonary metastases increased, so the patient withdrew consent to continue in the study.

Treatment with sunitinib was started, whithdrawn after 6 weeks due to the appearance of severe inguinal inverse psoriasis. In august of 2011 treatment with vandetanib (300 mg/day) was started, with good biochemical and morphological responses.

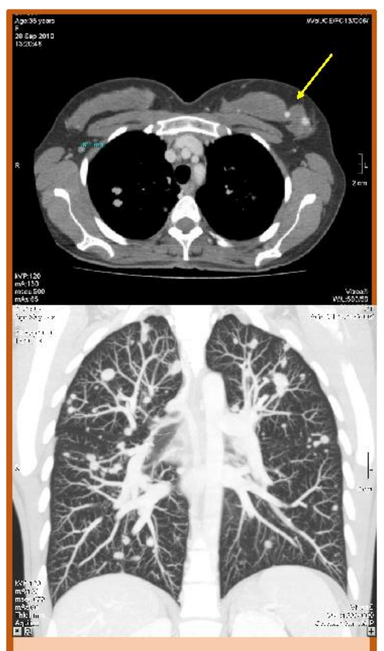
Tumor markers levels at baseline of treatment with tyrosine kinase inhibitors (TKIs) were calcitonin: 19504 pg/mL and carcinoembryonic antigen (CEA): 202.1 ng/mL. In the last review on august of 2015, tumor markers levels were calcitonin: 273 pg/mL and CEA: 23.4 ng/mL. In a computerized tomography (CT) of neck, chest and abdomen; laterocervical, supraclavicular, axillary, mediastinal and hilar lymph nodes had dissapeared, as well as breast metastasis. Lung and bone lesions remained stables.

During follow-up, secondary adrenal insufficiency (AI) appeared with ACTH <5 pg/mL and plasma cortisol 0.3 µg/dL and hypogonadotropic hypogonadism with secondary amenorrhea. Rest of hypophysis function, pitituary MRI and anti-hypophysis antibodies were normal.

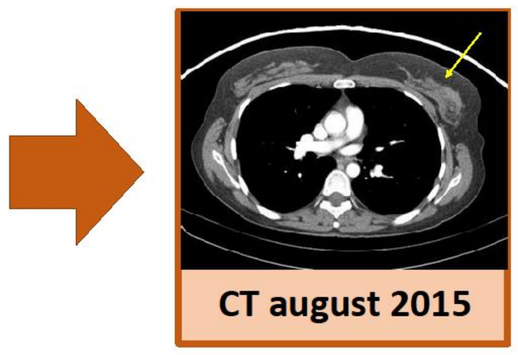
DISCUSSION

AI has been reported as consequence of hypophysitis secondary to anti-tumor agents as Ipilimumab (1). In our case, there were not data of hypophysitis. As etiology, we suggest that this effect of vandetanib may due cause its anti-angiogenic effect inhibiting epidermal growth factor receptor (EGFR). EFG is a mitogen related to neoplasms. It is expressed in a lower form in nontumoral cells, as hypophysis cells, where EGFR has been detected in 5-10% of them, mainly in gonadotrope and thyrotrope cells. Likewise, EGFR sobreexpression has been described in metastatic MTC (2), associated with RET mutation M918T in metastatic cells with a specific well response to vandetanib. In the same way, ACTH-producing pituitary macroadenomas has been identifed as good responders to TKIs, as gefitinib, due to the sobreexpression of EGF in tumoral corticotrope cells, that could be present in nontumoral corticotrope cells (3).

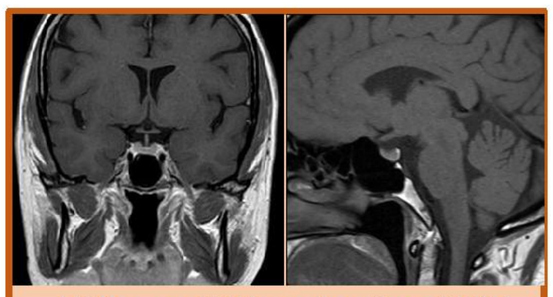
IMAGING TESTS



CT april 2010

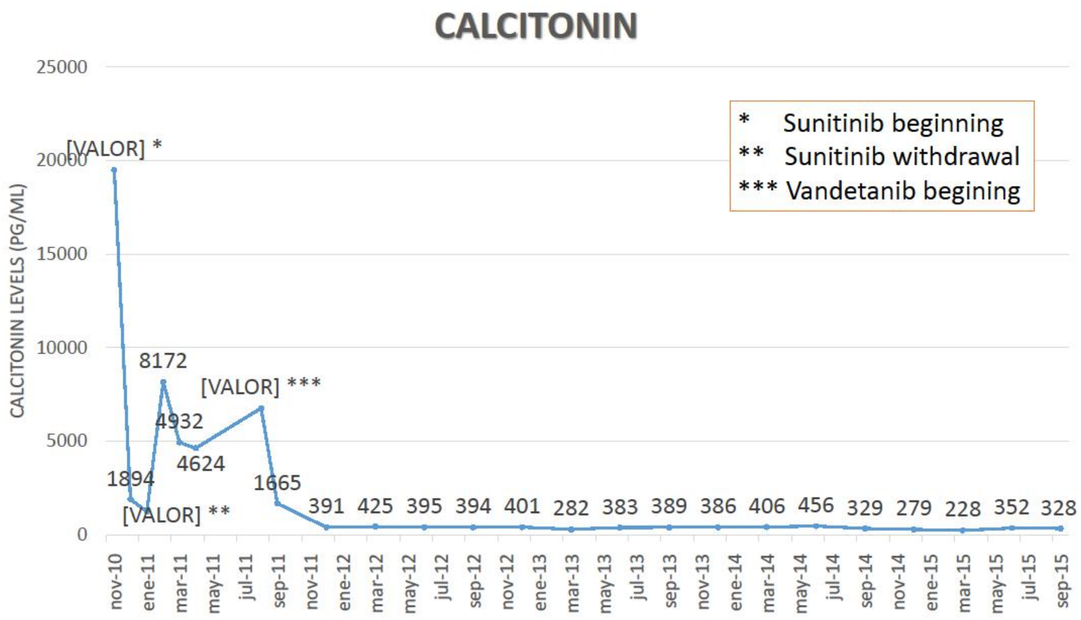


CT august 2015



Pitituary MRI september 2015

TUMOR MARKERS



CONCLUSION

In patients on treatment with TKIs, specially those with effect on EGFR, may be interesting to rule out the presence of pituitary abnormalities if it is clinically suspected.

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