Dramatic clinical response to Lenvatinib in a pediatric patient with advanced metastatic papillary thyroid carcinoma

Thyroid
LB-26

Dujovne Noelia [1], Gazek Natalia [1], Pitoia Fabian [2], Felipe Laura[3], Ayarzabal Victor [4], Lopez Marti Jessica [5],Ciaccio Marta [1] ,Lucero M.Belen[6], Herzovich Viviana[1]

[1] Endocrinology Department, Hospital de Pediatría JP Garrahan - Buenos Aires, Argentina [2] Endocrinology Department, Hospital de Clínicas, Jose de San Martin - Buenos Aires, Argentinna
[3] Imaging Department, Hospital de Pediatría JP Garrahan - Buenos Aires, Argentina.[4] Surgery Department, Hospital de Pediatría JP Garrahan - Buenos Aires, Argentina. [5] Pathology Department, Hospital de Pediatría JP Garrahan, Pulmonology Department, Hospital de Pediatria J.P.Garrahan – Buenos Aires, Argentina. [6] Pulmonology Department, Hospital de Pediatria J.P.Garrahan – Buenos Aires, Argentina.

Introduction

Papillary thyroid cancer (PTC) is the most common thyroid tumor in childhood and adolescence. Most of these patients are referred with locally advanced and/or distant disease at the moment of diagnosis. Whenever possible, these patients should be offered total thyroidectomy and radioiodine remnant ablation; however, this approach is not always possible to perform, rendering these tumors unresectable. These critical cases could benefit from neoadjuvant treatment with multikinase inhibitors (MKI) so the standard treatment can be performed. Lenvatinib is an MKI recently approved in many countries throughout the world for the treatment of radioiodine refractory adult differentiated thyroid cancer. MKI showed relevant and rapid shrinkage of tumoral lesions, probably due to high affinity for VEGF-R2. Only few pediatric cases have been reported.

Case Report

Female patient, 10 y.o. with locally advanced PTC and metastatis to the lungs, who required 3 liters of oxygen due to respiratory failure caused by bilateral miliary lung disease, mistakenly treated as tuberculosis two months previously and referred to our Hospital.

A large thyroid mass adhered to deep tissues was corroborated with a CT scan, which showed a large heterogeneous neck mass with multiple microcalcifications associated with multiple lymph nodes. Both lungs had multiple micro-nodular disease with interstitial involvement.

Total thyroidectomy together with lymph-node dissection was planned, but the extensive local infiltration made the lesion unresectable and surgery was limited to a thyroid biopsy.

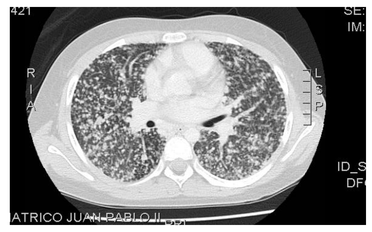
The patient required respiratory assistance. Pathological examination confirmed the presence of a PTC with a rearrangement of the *RET-PTC3* oncogene.

Eight days after surgery, the patient was critical,. and compassionate use Lenvatinib because this MKI showed a relevant and rapid shrinkage of tumoral lesions

The patient was started on oral lenvatinib at a dose of 14 mg daily (14 mg/m/day). Three days later, the patient clinically improved and nine days post-lenvatinib initiation, the patient was discharged from hospital with 10 mg daily of lenvatinib without need for oxygen therapy.

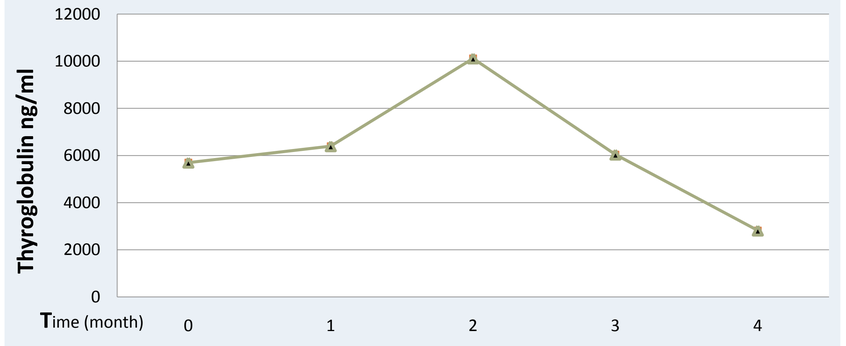
Thyroid ultrasond

CT scan



Evolution parameters under Lenvatinib treatment

Laboratory Tests:



Lenvatinib	Basal	1 month	2 months	3 months	4 months
TSH (0.82-4.74 µUI/ ml)	4.32	0.04	12.4	3.04	11.8
T3 (0.99-2.14 ng/ml)	1.88	0.53	0.75	1.63	1.43
T4 (6.4-11.7 µ /dl)	5.85	9.46	9.03	9.4	9.8
T4L (0.91-1.91 ng/dl)	0.64	1.15	0.94	1.08	0.9
Thyroglobulin (5.6-42 ng/ml)	5700	6396	10120	6041	2818

Lung Function Test:

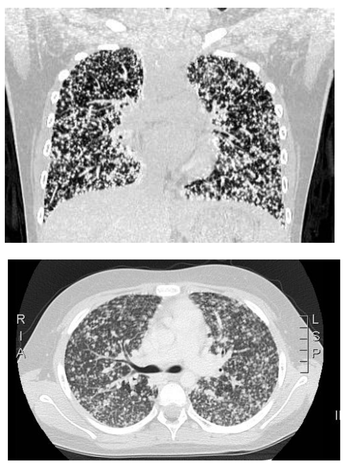
	Spirometry*			DLCO*	6MWT**	
	FVC (L)	FEV_1 (L)	FEV_1/FVC (%)	(ml/min/mmHg)	(m)	SpO_2(%)
Basal	0.93 (43%)	0.84 (44%)	90	-	-	89
2 months	1.22 (55%)	1.18 (61%)	97	10.4 (69%)	360	95-96
4 months	1.19 (53%)	1.08 (51%)	91	10.07 (67%)	390	98-99

*Parameters expressed as percentages (%) of predicted values. (GLI)
DLCO : Diffusing capacity of the lungs for carbon monoxide
** 6MWT : 6-minute walking test. ATS/ERS
SpO_2(%) : Oxygen saturation measured by a pulse oximeter

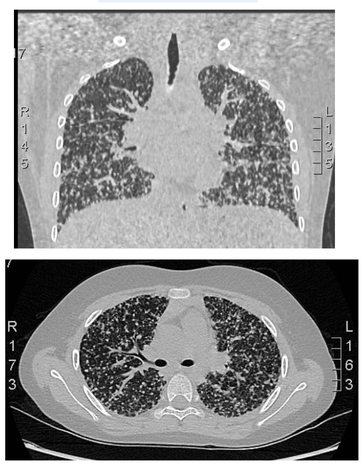
Imaging studies:

After four months on Lenvatinib the thyroid mass appeared stable and pulmonary nodules appeared stable to slightly smaller without evidence of new or progressive disease.

Baseline



4 months



Conclusion

On lenvatinib treatment, our patient showed frank clinical improvement, arrest of disease progression, and stable disease on imaging studies,

This case shows that lenvatinib may be a beneficial option for children with advanced PTC not amenable to surgery/RAI treatment and may be used as a bridge to these first-line therapies.

References :

- *Mahajan P,Dawrant J,Kheradpour A,Quintanilla N,Lopez M,Orth R,Athanassaki I, Venkatramani R.Response to Lenvatinib in Children with Papillary Thyroid Carcinoma.Thyroid Vol 28,Number 11,2018.*
- *Waguespack SG,Sherman SI,Williams MD,Clayman GL,Herzog CE 2009.The successful use of soranefib to treat pediatric papillary thyroid carcinoma.Thyroid 19:407-412.*
- *Iyer P,Mayer JLR,Ewig JM,2014 Response to soranefib in a pediatric atient with papillary thyroid carcinoma with diffuse nodular pulmonary disease requiring mechaical ventilation.Thyroid 24:169-174.*
- *Werner R.A,Luckerath K,Schmid J.S,Higuchi T,Kreissl MC,Grelle C,Reiners C,Buck A,Lapa C.Thyroglobulin fluctuations in patients with iodine-refractory differentiated thyroid carcinoma on lenvatinib treatment-initial experience.Scientific reports 2016 DOI:10.1038.*
- *Valeirio L,Pieruzzi C,Agate V,Bottici L,Lorusso V,Cappagli L,Puleo A,Matrone D,Romei R,Ciampi E,Molinaro R,Elisei.Target Therapy in Thyroid Cancer: State of the Art.Clinical Oncology 29 (2017)316-324.*
- *Capdevila J,Stjepanovic N, Multikinasa inhibitors in the treatmenr of thyroid cancer.Specific role of lenvatinib.Biologics:Target and Therapy 2014:8 129-139*