

# Pandemics and thyroid neoplasia

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## ABSTRACT

Poorly differentiated/undifferentiated thyroid carcinoma represents a very severe type of malignancy with limited therapeutically resources. Fortunately, the diagnosis is very rare in general population; however, delayed presentation to a health care system might aggravate the evolution and during COVID-19 pandemic it was suggested an exacerbation of this phenomenon. This is a case report of a 56-year old lady diagnosed with poorly differentiated – undifferentiated thyroid carcinoma according to fine needle aspiration – based cytological exam. Despite having progressive large, neck mass with bone pain, asthenia, weight loss, and dysphagia since last months, she delayed the medical examination because of social anxiety amid COVID-19 pandemics. Poorly differentiated carcinoma still represents a sector of endocrinology with poor survival. Controversies around endocrine practice amid pandemic are still ongoing topics.

**Keywords:** poorly differentiated thyroid cancer, well differentiated thyroid cancer, follicular thyroid cancer, follicular cell, prognostic, COVID-19 pandemic

## INTRODUCTION

Poorly differentiated/undifferentiated thyroid carcinoma represents a very severe type of malignancy with limited therapeutically resources (1,2). Fortunately, the diagnosis is very rare in general population; however, delayed presentation to a health care system might aggravate the evolution and during COVID-19 pandemic it was suggested an exacerbation of this phenomenon (3,4).

## AIM

Our purpose is to introduce a post-menopausal female with late recognition of a severe thyroid neoplasia amid pandemic era.

## METHOD

This paper is a case report.

## CASE PRESENTATION

### Admission

This is a 56-year old, non-smoking female, with prior occupational exposure to toxins for several years. The lady is admitted for thyroid evaluation as an emergency. She has a recently developed, large goiter without previous medical history. She accused persistent cervical pain, diffuse bone pain, weight loss, asthenia, and dysphagia since last months. She delayed the medical presentation because of social anxiety amid COVID-19 pandemics. The medical history includes: chronic bronchitis, chronic ischemic cardiomyopathy, type 2 diabetes mellitus under oral anti-diabetics, and mild obesity. Her family medical history is irrelevant. She was not evaluated for a thyroid condition before current admission, neither had she had any particular medication targeting thyroid function. Clinical examina-

tion confirmed the large, firm thyroid mass with block lymph nodes at later-cervical area and apparently no anomaly of thyroid function.

### Blood assays

The biochemistry panel showed a mild increase of ALT (alanin aminotransferase) and a higher above normal limit of HgA1c (glycated hemoglobin A1c) (Table 1). An inflammatory syndrome was confirmed based on increased ESR (erythrocyte sedimentation rate) as well as fibrinogen and C-reactive protein (Table 1).

**TABLE 1.** Blood assessments on a 56-year old female who was admitted for poorly differentiated thyroid carcinoma with compressive symptoms

Parameter	Value	Normal ranges	Units
Uric acid	3.3	2.6-6	mg/dl
<b>ALT (alanin aminotransferase)</b>	<b>35</b>	<b>0-31</b>	<b>U/l</b>
AST (aspartat aminotransferase)	19	0-32	U/l
Ionic serum calcium	4.11	3.9-4.9	mg/dl
Total serum calcium	9.5	8.4-10.2	mg/dl
Total cholesterol	178	0-200	mg/dl
Serum phosphorus	4.2	2.3-4.7	mg/dl
<b>Fasting glycaemia</b>	<b>109</b>	<b>70-105</b>	<b>mg/dl</b>
<b>Glycated hemoglobin A1c (HgA1c)</b>	<b>7.1</b>	<b>4.8-5.9</b>	<b>%</b>
HDL-cholesterol	36	40-60	mg/dl
Potassium	4.8	3.5-5.1	mmol/l
Magnesium	2.1	1.6-2.55	mg/dl
Sodium	141	136-145	mmol/l
Total proteins	7.3	6.4-8.3	g/dl
Triglycerides	125	0-149	mg/dl
Urea	33	15-50	mg/dl
Creatinine	0.62	0.5-1.2	mg/dl
<b>Erythrocyte sedimentation rate (ESR)</b>	<b>110</b>	<b>1-25</b>	<b>mm/1-hour</b>
Serum iron	46.52	37-145	µd/dl
<b>C-reactive protein</b>	<b>1.82</b>	<b>0-0.5</b>	<b>mg/dl</b>
<b>Fibrinogen</b>	<b>742.658</b>	<b>200-500</b>	<b>mg/dl</b>

PCR SARS CoV-2 test was negative. Endocrine assays confirmed a normal thyroid function and mild thyroid autoimmunity on terms of increased TPOAb (Anti thyroperoxidase antibodies) (Table 2). Normal calcitonin excluded a medullary thyroid cancer. A low level of 25-hydroxyvitamin D was consistent with vitamin D deficiency (Table 2).

Thyroid ultrasound showed: hypoechoic, inhomogeneous, nodularized pattern, with normal Doppler signal, a left thyroid lobe with a nodule of 2.77 by 2.4 by 3.1 cm, right later-cervical block of lymph nodes of 5.37 by 1.7 by 2 cm with hypoechoic,

**TABLE 2.** Endocrine assays on a menopausal lady with advanced thyroid cancer

Parameter	Value	Normal ranges	Units
TSH (thyroid stimulating hormone)	2.13	0.5-4.5	µU/ml
FT4 (free levothyroxine)	13.77	9-19	pmol/l
T3 (triiodothyronine)	109.3	80-200	ng/dl
Calcitonin	1	5.17-9.82	pg/ml
<b>TPOAb (anti-thyroperoxidase antibodies)</b>	<b>15.86</b>	<b>0-5.61</b>	<b>UI/ml</b>
<b>25OHD (25-hydroxyvitamin D)</b>	<b>9.74</b>	<b>30-100</b>	<b>ng/ml</b>
PTH (parathormone)	42.93	15-65	pg/ml
Plasma metanephrines	29.4	10-90	pg/ml
Plasma normetanephrines	152.8	15-180	pg/ml

highly vascularized pattern, and a left later-cervical block of maximum 2 cm diameter (TIRADS 5). Computed tomography scan at the level of neck and thorax confirmed the extra-capsular extension of thyroid process with invasion of surrounding fat tissue in association with bilateral block of lymph nodes (Figure 1). Thrombosis was detected at the level of upper cave vein, in addition to pulmonary micronodules (probable secondary spreading) with right pleural effusion.



**FIGURE 1.** Computed tomography scan with intravenous contrast showing a large thyroid mass which is a primary thyroid malignancy with bilateral lymph nodes blocks at later-cervical level (neck section – coronal plan)

### Management

Cytological exam was provided based on fine needle aspiration at thyroid level. A poorly differentiated malignant proliferation of undifferentiated thyroid carcinoma (Bethesda 5 scoring). Surgical evaluation noted that adherent right thyroid lobe forms a tumor block with lymph nodes, also bilateral jugular-carotid lymphadenopathy. Based on fine needle aspiration result pointing the undifferentiated pattern of thyroid carcinoma with pulmonary metastases and vascular thrombosis, thyroidectomy is not feasible and a recommendation of oncological follow-up for external radiotherapy is needed.

## DISCUSSIONS

Poorly differentiated or undifferentiated carcinoma of the thyroid might be the result of late anaplastic shift from a prior differentiated thyroid cancer (1,2). Terminology surrounding this particularly extremely severe subtype is still a controversy (3,4). Limited options are available like radiotherapy, probably tyrosine kinase inhibitors, some chemotherapy protocols with poor outcome (5,6). In this case, at the moment of admission, thyroidectomy was not optional due to locally invasive aspects and bilateral block lymph nodes involvement. The patient also associated high ESR which requires a differential diagnostic with acute thyroiditis and some hematological malignancies like primary thyroid

lymphoma (7,8). Probably, pandemic should be regarded as an issue considering the late diagnostic and, of course, the differential diagnostic of acute inflammation with active coronavirus infection is required (9,10). The patient also had some vitamin D deficiency which is not unusual, especially in menopausal population; whether this is a trigger of malignant transformation regarding thyroid, it is controversial (11-20).

## CONCLUSIONS

Poorly differentiated carcinoma still represents a sector of endocrinology with poor survival. Controversies around endocrine practice amid pandemic are still ongoing topics.

## REFERENCES

- Hsu YC, Hsueh C, Lin WN, Tsai TY, Hung SY, Lu YA. Carcinoma Showing Thymus-like Differentiation (CASTLE) with Synchronous Papillary Thyroid Carcinoma: A Case Report and Review. *Ear Nose Throat J*. 2021 Dec 6;1455613211060167.
- Bellini MI, Biffoni M, Patrone R, Borcea MC, Costanzo ML, Garritano T, et al. Poorly Differentiated Thyroid Carcinoma: Single Centre Experience and Review of the Literature. *J Clin Med*. 2021 Nov 12;10(22):5258.
- Singh A, Ham J, Po JW, Niles N, Roberts T, Lee CS. The Genomic Landscape of Thyroid Cancer Tumorigenesis and Implications for Immunotherapy. *Cells*. 2021 May 1;10(5):1082.
- Romei C, Elisei R. A Narrative Review of Genetic Alterations in Primary Thyroid Epithelial Cancer. *Int J Mol Sci*. 2021 Feb 9;22(4):1726.
- Volante M, Lam AK, Papotti M, Tallini G. Molecular Pathology of Poorly Differentiated and Anaplastic Thyroid Cancer: What Do Pathologists Need to Know? *Endocr Pathol*. 2021 Mar;32(1):63-76.
- Xu B, Ghossein R. Poorly differentiated thyroid carcinoma. *Semin Diagn Pathol*. 2020 Sep;37(5):243-247.
- Weetman AP. Thyroid abnormalities. *Endocrinol Metab Clin North Am*. 2014 Sep;43(3):781-90.
- Gheorghisan-Galateanu AA, Terzea D, Ioachim D, Carsote M. Not just Hashimoto's thyroiditis. *Acta Endocrinologica (Buc)*. 2019;15(4):537-8.
- Murugan AK, Alzahrani AS. SARS-CoV-2: Emerging Role in the Pathogenesis of Various Thyroid Diseases. *J Inflamm Res*. 2021 Nov 24;14:6191-6221.
- Sandru F, Carsote M, Petca RC, Gheorghisan-Galateanu AA, Petca A, Valea A, Dumitrascu MC. COVID-19-related thyroid conditions (Review). *Experimental and Therapeutic Medicine* 2021;22(756):1-5.
- Vassalle C, Parlanti A, Pingitore A, Berti S, Iervasi G, Sabatino L. Vitamin D, Thyroid Hormones and Cardiovascular Risk: Exploring the Components of This Novel Disease Triangle. *Front Physiol*. 2021 Sep 16;12:722912.
- Abuduwaili M, Xing Z, Xia B, Fei Y, Zhu J, Su A. Correlation between Pre-Operative 25-Hydroxyvitamin D Levels and Poor Prognostic Factors for Papillary Thyroid Cancer. *J Invest Surg*. 2021 Dec 5:1-7.
- Bains A, Mur T, Wallace N, Noordzij JP. The Role of Vitamin D as a Prognostic Marker in Papillary Thyroid Cancer. *Cancers (Basel)*. 2021 Jul 14;13(14):3516.
- Barrea L, Pugliese G, Frias-Toral E, Laudisio D, Rodriguez D, Vitale G, Colombo C, Colao A, Savastano S, Muscogiuri G. Diet as a possible influencing factor in thyroid cancer incidence: the point of view of the nutritionist. *Panminerva Med*. 2021 Sep;63(3):349-360.
- Mull B, Davis R, Munir I, Perez MC, Simental AA, Khan S. Differential expression of Vitamin D binding protein in thyroid cancer health disparities. *Oncotarget*. 2021 Mar 30;12(7):596-607.
- Rozmus D, Ciesielska A, Płomiński J, Grzybowski R, Fiedorowicz E, Kordulewska N, Savelkoul H, Kostyra E, Cieślińska A. Vitamin D Binding Protein (VDBP) and Its Gene Polymorphisms-The Risk of Malignant Tumors and Other Diseases. *Int J Mol Sci*. 2020 Oct 22;21(21):7822.
- Pang R, Xu Y, Hu X, Liu B, Yu J. Vitamin D receptor knockdown attenuates the antiproliferative, pro-apoptotic and anti-invasive effect of vitamin D by activating the Wnt/beta-catenin signaling pathway in papillary thyroid cancer. *Mol Med Rep*. 2020 Nov;22(5):4135-4142.
- Gnagnarella P, Raimondi S, Aristarco V, Johansson HA, Bellerba F, Corso F, Gandini S. Vitamin D Receptor Polymorphisms and Cancer. *Adv Exp Med Biol*. 2020;1268:53-114.
- Gunes A, Yazicioglu MB, Tiryaki C, Uren N, Ergul E, Simsek T, Cubukcu A. Evaluation of vitamin D receptor gene polymorphisms in patients with differentiated thyroid carcinomas and nodular goiter. *Minerva Endocrinol (Torino)*. 2021 Sep;46(3):317-324.
- Abdellateif MS, Shaarawy S, Elesawy YF, Mansour M, Tharwat E, Ibrahim NH, Eissa MS. The Role of Vitamin D, Platelet-Derived Growth Factor and Insulin-Like Growth Factor 1 in the Progression of Thyroid Diseases. *Asian Pac J Cancer Prev*. 2020 Jul 1;21(7):2083-2089.