Case Report
Persistence of Elevated Procalcitonin in a Patient with Coronavirus Disease 2019 Uncovered a Diagnosis of Medullary Thyroid Carcinoma

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Abstract

Objective: During the ongoing coronavirus disease 2019 pandemic, procalcitonin (PCT) levels have proven useful in assisting clinicians to diagnose bacterial superinfection. However, in the absence of signs of infection or at the resolution thereof, inappropriately and persistently high PCT levels may suggest and reveal the presence of other pathologies. We report a patient with severe acute respiratory syndrome coronavirus 2 pneumonia with initially elevated PCT levels that persisted during recovery, prompting the diagnosis of medullary thyroid carcinoma (MTC).

Methods: A 43-year-old man presented with a 2-day history of fever, sneezing, sore throat, and dry cough. His PCT was 94 ng/mL (normal value, 0.00-0.10 ng/mL), and he was positive for severe acute respiratory syndrome coronavirus 2 RNA.

Results: Empirical antibiotic therapy was administered for 7 days, but despite a clinical improvement, serum PCT remained high (84 ng/mL). Serum calcitonin (CTN) was 2120 pg/mL (normal, <12 pg/mL). Cytologic examination of thyroid nodules and CTN measurement of the aspiration needle washout confirmed MTC. The patient underwent total thyroidectomy with bilateral cervical lymph node dissection. Lowered CTN (986 pg/mL) and PCT (16 ng/mL) levels were observed 48 hours after surgery. A close follow-up was planned following the results of RET gene analysis.

Conclusion: PCT can be a useful biochemical marker of MTC suspicion in patients with inflammatory conditions and persistently elevated PCT, even after resolution. In our case, high levels of PCT in a patient with coronavirus disease 2019 pneumonia without signs of bacterial infection led to MTC diagnosis.

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Introduction

Medullary thyroid carcinoma (MTC) is a neuroendocrine neoplasm derived from thyroid parafollicular or C-cells, accounting for about 5% of all thyroid cancers. Its peak incidence is during early adulthood.1,2 Calcitonin (CTN), a peptide that results from the cleavage and posttranslational processing of procalcitonin (PCT), is the main product of the C-cells of the thyroid gland and acts to reduce blood calcium, thereby opposing the effects of parathyroid hormone. CTN measurement is, to date, the most sensitive diagnostic test for identifying patients with MTC and C-cell hyperplasia, and it is a marker for residual or recurrent disease in MTC.2 PCT, the CTN precursor, is found in low concentrations in the serum of healthy individuals, whereas the production and release into circulation from extrathyroidal sources, such as immune cells or the liver, increases during severe systemic inflammation, bacteremia, and sepsis, as do concentrations of proinflammatory cytokines (Table).3 PCT was first described as a marker of bacterial infection in 1993 when high concentrations of CTN-like

Abbreviations: CTN, calcitonin; MTC, medullary thyroid carcinoma; PCT, procalcitonin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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immunoreactivity were detected in the blood of patients with extrathyroid diseases, and it is now commonly used in clinical practice as a biochemical marker of sepsis. Thus, it is potentially useful in raising suspicion of bacterial infection and guiding the duration of antibiotic therapy in both sepsis and lower respiratory tract infections. PCT has been also proposed by some authors as a suitable marker, together with CTN, in the MTC diagnostic workup. Here, we report the case of a man affected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia with persistently high PCT levels, despite his recovery from the infectious disease, who was subsequently diagnosed with MTC.

Case Report

A 43-year-old man of Caucasian origin was admitted to the Emergency Department of a hub hospital in Piedmont, Italy, in March 2020 because of a 2-day history of fever, sneezing, fatigue, sore throat, and dry cough with no dyspnea. He had a medical history of mild cognitive impairment since birth and arterial hypertension. Systemic lupus erythematosus with lupus nephritis was diagnosed at the age of 27, and he was receiving mycophenolate and prednisone. His family history was negative for cancer, endocrinopathy, and inflammatory diseases. His parents were dead, and neither he nor his sister had children.

Physical examination on admission showed fever (38°C) and oxygen saturation of 94% in room air, with a respiratory rate of 18 breaths/min. Chest auscultation revealed decreased breath sounds and coarse crackles in both lung bases. Laboratory evaluations revealed a white blood cell count of 7110/mm³ and coarse crackles in both lung bases. Oxygen saturation of 94% in room air, with a respiratory rate of 18 breaths/min. Laboratory examinations and a nonhomogeneous thyroid with multiple nodules, the largest of which had a diameter of nearly 30 mm. Cytologic examinations and a nonhomogeneous thyroid with multiple nodules, the largest of which had a diameter of nearly 30 mm. Cytologic examination of the surgical specimen confirmed the diagnosis of MTC. In particular, neoplastic cells from both thyroid lobes and the draining lymph nodes showed positive immunohistochemical staining for CTN, carcinoembryonic antigen, synaptophysin, chromogranin A, and thyroglobulin, leading to the diagnosis of MTC. MTC metastases were shown in 3 of 12 lymph nodes, of which the largest was 30 mm. The patient’s MTC was classified as pathologic T1b-N1a, stage III, according to the TNM classification of the American Joint Committee on Cancer Staging Manual, 7th Edition.

Blood tests performed 48 hours after surgery showed a lowering of CTN (986 pg/mL) and PCT (16 ng/mL). On hospital day 22, nasopharyngeal and oropharyngeal swabs were repeated and were reported as negative. The patient was discharged with oral therapy of prednisone (5 mg/die), ramipril (10 mg/die), levothyroxine (50 µg/die), cholecalciferol (800 IU/die), and calcium carbonate (1 g/die). A 6-month follow-up was scheduled, and (18)F-fluorodeoxyglucose positron emission tomography/computed tomography scan showed an increased tracer uptake in the right lobarcervical lymph nodes (SUVmax: 3.8), while only a slight tracer uptake was present in both the thyroid and the dorsal vertebral bodies (Fig. 2). The patient underwent total thyroidectomy with bilateral cervical lymph node dissection. The histologic examination of the surgical specimen confirmed the diagnosis of MTC. In particular, neoplastic cells from both thyroid lobes and the draining lymph nodes showed positive immunohistochemical staining for CTN, carcinoembryonic antigen, synaptophysin, chromogranin A, and thyroglobulin, leading to the diagnosis of MTC. MTC metastases were shown in 3 of 12 lymph nodes, of which the largest was 30 mm. The patient’s MTC was classified as pathologic T1b-N1a, stage III, according to the TNM classification of the American Joint Committee on Cancer Staging Manual, 7th Edition.

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Discussion

We report the case of a patient in whom the persistence of elevated PCT levels after resolution of SARS-CoV-2 infection, together with the presence of a painless right lobarcervical
Fig. 1. Computed tomography scan of the chest. A, Bilateral ground-glass opacities in the basilar lung zones. B, Hyperdense and irregular foci in the thoracic vertebral bodies suspected as metastatic lesions were also reported.

Fig. 2. Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography scan showed an increased tracer uptake in the right laterocervical lymph nodes (SUVmax: 3.8) with no significant tracer uptake either in the thyroid or in the dorsal vertebral bodies.

Fig. 3. Blood tests performed 48 hours after total thyroidectomy showed a reduction of calcitonin (986 pg/mL) and PCT (16 ng/mL). At 6-month follow-up, calcitonin was 921 pg/mL, and PCT was 16 ng/mL. CTN = calcitonin; PCT = procalcitonin.
swelling, uncovered a diagnosis of MTC. Sporadic MTC typically occurs between the fourth to sixth decades of life, and the most common presentation is a painless solitary thyroid nodule, whereas patients with hereditary disease present earlier multifocal and bilateral lesions. MTC prognosis depends on early detection and treatment, and elevated CTN levels are mandatory for the diagnostic workup. However, diagnosing MTC is still a challenge in clinical practice, and over the past few decades, there has been no significant trend toward detecting the disease at an earlier stage, with no significant increase in patient survival.6,7

Among the available diagnostic tests are thyroid ultrasound, cytologic examination by fine-needle aspiration, and serum CTN, which represents a highly sensitive method for the diagnosis of MTC. It has been shown that the positive predictive values for basal CTN levels in the preoperative diagnosis of MTC ranges from 8% to 25% for values >20 pg/mL and <100 pg/mL and 100% for values >100 pg/mL, while 3% to 10% of subjects without thyroid disease have CTN levels >10 pg/mL. In fact, CTN is also affected or influenced by physiologic and other pathologic conditions (Table). Furthermore, there is still no agreement is also affected or in

Remarkably, in contrast to the short half-life of CTN (10 minutes), produced by extrathyroid tissues in large amounts (Table). Additionally, there is a lack of comparability of results obtained in the diagnosis of MTC, being close to 100% for both markers. Nonetheless, the specificity of CTN in the diagnosis of MTC is reduced in cases of a bacterial infection or systemic inflammation. As a result, since the use of CTN is very common in clinical practice as a marker in bacterial infections, neuroendocrine neoplasia should be suspected and investigated (eg, by measuring CTN) if PCT levels remain high despite the resolution of the infection.

Conclusion

This case report describes the diagnosis of advanced MTC in a patient affected by SARS-CoV-2 pneumonia in which levels of PCT continued to be high despite clinical and laboratory pneumonia recovery. A complete anamnestic investigation and clinical workup, including neck palpation, CTN measurement, and thyroid ultrasound, should be performed if elevated PCT levels persist in the absence of clinical signs of infection. This case suggests that MTC should be ruled out in patients with inflammatory conditions if PCT remains elevated after resolution.

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Disclosure

The authors have no multiplicity of interest to disclose.

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