

Case Report

Papillary Thyroid Cancer Presenting with Splenic Infarction

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Abstract

Introduction: The association between malignancy and hypercoagulability state is long known. Thyroid malignant neoplasms, however, have been rarely associated with pro-thrombotic paraneoplastic syndromes.

Case Presentation: We present the case of a 39-year-old man who was admitted with splenic infarction. The extensive diagnostic workup of this occurrence revealed a thyroid papillary carcinoma.

Conclusion: To our knowledge, this is the first reported case of paraneoplastic organ infarction due to thyroid papillary carcinoma. This case reinforces the need to search for occult tumors in patients presenting with thrombotic events with no other obvious cause, including with thyroid ultrasound especially if other exams are inconclusive.

Keywords: Papillary thyroid carcinoma; Paraneoplastic syndrome; Thyroid cancer; Organ infarction

Introduction

The close relationship between cancer and thrombotic phenomena has been widely recognized. It is a well-established fact that cancer is associated with a hypercoagulability state [1] and paraneoplastic organ infarctions may occur as a consequence of this condition. Although uncommon, spleen infarctions due to malignant neoplastic disease have been reported [2]. These typically present with pain referred to the left upper quadrant of the abdomen, fever, nausea or vomiting and splenomegaly [3].

Thyroid cancers have seldom been associated with paraneoplastic syndromes. Reports of papillary thyroid cancer leading to paraneoplastic phenomena are particularly scarce. However, some associations have been reported, namely with neurological manifestations [4-7], dermatomyositis and polymyositis [8-10], mixed connective tissue disease [11], polyarthritis [12], Raynaud's phenomenon [13] and syndrome of inappropriate antidiuresis [14].

Case Report

We present the case of a 39-year-old man with no prior medical history who presented to the emergency department with acute onset of fever, malaise and mild pain referred to his left hypochondrium.

He reported no other focalizing symptoms, including respiratory, gastrointestinal, or genitourinary. Except for the fever, the patient had no abnormal findings described on physical examination. Analytically, he had no alterations on the complete blood count, with an elevation of serum C-reactive protein (75.4 mg/L, reference range 0.0-5.0 mg/L) and normal urinalysis. The chest X-ray showed no consolidations or other signs of ongoing pulmonary infection. However, his abdominal echography revealed a triangle-shaped hypoechoic area on the spleen suggestive of splenic infarction.

Despite reporting no history of intravenous drug use nor having

any other obvious entrance point, due to the patient's young age, fever, and splenic infarction, the main initial diagnostic suspicion was infective endocarditis. As so, blood cultures were collected and the patient underwent a transthoracic echocardiogram. This exam, however, did not show any images compatible with vegetations or other signs of ongoing endocarditis. Notwithstanding the above mentioned, he was admitted to the ward, under antibiotic treatment with intravenous ceftriaxone and gentamycin, to complete diagnostic workup.

Repeated transthoracic echocardiogram 48 hours after admission and transesophageal echocardiogram were both negative for signs of endocarditis. In total, four pairs of blood cultures were collected during the first days of hospitalization (one of them was even subjected to a prolonged culture time) and all were sterile. Therefore, no criteria for infective endocarditis according to Duke's criteria were found [15]. Virus serologies for human immunodeficiency virus, Epstein-Barr virus, cytomegalovirus, hepatitis C virus and hepatitis B virus were all negative. Serology for *Coxiella burnetii*, to exclude the unlikely diagnosis of Q fever, was also negative. The patient underwent a pro-thrombotic study, which included partial thromboplastin time, thrombin time, dilute Russell viper venom time, dosing of anticardiolipin and beta-2 glycoprotein 1 antibodies and lupus anticoagulant test. All of them were normal.

Thoraco-abdominopelvic computed tomography scan confirmed the splenic infarction with no other abnormal findings except for a contrast-enhanced nodular lesion measuring 2.0x2.0cm on the right lobe of the thyroid gland (Figure 1A). His thyroid function tests and calcitonin levels were within normal range [TSH 2.51 μ UI/mL (reference range 0.30-3.18 μ UI/mL); free-T4 1.40 ng/dL (reference range 1.01-1.65 ng/dL); serum calcitonin 8.80 pg/mL (reference range 0.00-20.00 pg/mL)].

Ultrasound thyroid evaluation revealed a predominantly iso-

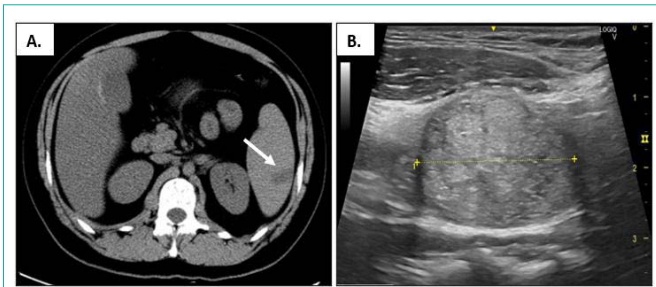


Figure 1: A. Splenic infarction (white arrow), conformed by computerized tomography scan. B. Ultrasound evaluation of the thyroid nodule showing some suspicious features (microcalcifications, irregular borders).

echogenic thyroid nodule with microcalcifications measuring 19x21x28mm [European Thyroid Association Thyroid Imaging Reporting and Data System (EU-TIRADS) category 5] (Figure 1B) with no suspicious cervical lymph nodes. Fine needle aspiration cytology revealed a pattern suggestive of papillary carcinoma (Bethesda category VI [16]). A total thyroidectomy was performed uneventfully and confirmed the presence of a classical variant of papillary carcinoma with 3.5cm of maximal diameter. Vascular invasion was not identified but foci of papillary microcarcinoma were found within the thyroid parenchyma, suggesting intrathyroidal dissemination. Lymph node metastasis in the central compartment were documented in 8 out of 10 excised lymph nodes (TNM cancer staging, T2N1Mx; American Thyroid Association risk of recurrence, *intermediate* [17]). The patient underwent radioiodine ablation (100 mCi) with post-therapy whole-body scanning showing signs of residual thyroid tissue in the cervical region but with no evidence of macroscopic local or distant functional metastasis. At last follow-up evaluation (nine months after total thyroidectomy and six months after radioiodine ablation) thyroglobulin levels were 0.7 ng/mL (reference range 1.4-78 ng/mL) and anti-thyroglobulin antibody levels were 13.8 UI/mL (*positive* if greater than 115 ng/mL) with TSH levels of 0.09 μ UI/mL (reference range 0.30-3.18 μ UI/mL), revealing an *indeterminate* biochemical response [17].

Discussion

Papillary thyroid cancer is usually a slow-growing tumor that is often diagnosed after cervical imaging [18]. It is also a known fact that paraneoplastic syndromes may precede, follow or be concurrent with a malignancy [19]. This is due to multiple mechanisms, including the release of procoagulant and fibrinolytic proteins, as well as inflammatory cytokines, by the cancer cells and the host cell inflammatory response to the tumor [1]. Splenic infarctions with no obvious cause are frequently attributed to endocarditis but a paraneoplastic etiology must be always sought when this diagnosis is uncertain [20]. The symptoms of our patient were nonspecific, but retrospectively compatible with an acute splenic infarction. During his extensive diagnostic workup, the only “positive” finding was a thyroid nodule with high-risk ultrasound features that turned out to be a papillary carcinoma with regional lymph node involvement.

To our knowledge, this case represents the first report of organ infarction potentially caused by a hypercoagulability state due to a differentiated thyroid cancer. When evaluating patients with thrombotic events with no other recognizable cause, our case

reinforces the need for searching occult tumors that should include the thyroid gland.

Conflict of Interest Statement

Miguel Saraiva declares that he has no conflict of interest. Magda Garça declares that she has no conflict of interest. Ana Rita Costa declares that she has no conflict of interest. Guiomar Pinheiro declares that she has no conflict of interest. Ana Rita Cruz declares that she has no conflict of interest. Sofia Ribeiro declares that she has no conflict of interest. Cláudia Freitas declares that she has no conflict of interest. André Couto de Carvalho declares that he has no conflict of interest.

Author Contributions Statement

Miguel Saraiva, Magda Garça, Ana Rita Costa and Guiomar Pinheiro actively participated in the patient’s diagnostic workup during the patient’s hospitalization. Ana Rita Cruz and Sofia Ribeiro took responsibility for any decision that was made and led the main clinical decisions during the patient’s hospitalization. Cláudia Freitas and André Couto de Carvalho performed the thyroid ultrasound and the diagnostic fine needle aspiration. Cláudia Freitas became the patient’s physician and was responsible for the main treatment and follow-up decisions. Miguel Saraiva wrote the case report. André Couto de Carvalho reviewed and supervised the case report writing. All authors approved the final version submitted and are accountable for all aspects of the work. All authors read and approved the final manuscript.

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