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Case Presentation
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Unexplained Elevation of Carcinoembryonic Antigen: Focus on the Thyroid

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Abstract

Carcinoembryonic antigen (CEA), recognized as one of the most widely utilized tumor markers in clinical practice, had limitations as an independent diagnostic tool due to its relatively low specificity. Its principal clinical value lay in aiding diagnosis and tracking therapeutic responses.

The present case report described the clinical course of a 34-year-old female patient who presented with elevated serum CEA levels during a routine health examination. Subsequent follow-up and comprehensive assessment led to the identification of a suspicious lesion in the right thyroid lobe. Further evaluation revealed a markedly elevated serum calcitonin level. The patient consequently underwent total thyroidectomy and right central lymph node dissection. Postoperative histopathological examination confirmed the diagnosis of medullary thyroid carcinoma. This case highlighted the importance of adopting an integrated diagnostic approach in instances of unexplained isolated elevation of carcinoembryonic antigen. Such an approach involved serum-specific markers (e.g., calcitonin), imaging modalities, and histopathological evaluation, while systematically ruling out nonspecific confounding factors to establish an accurate diagnosis.

Keywords: Carcinoembryonic antigen; Calcitonin; Procalcitonin; Medullary thyroid cancer

Introduction

Carcinoembryonic antigen (CEA), recognized as one of the most frequently utilized broad-spectrum tumor markers in clinical practice [1,2], played a critical role in the comprehensive management of colorectal cancer diagnosis and treatment [3-6]. However, its specificity proved to be notably inadequate, as it exhibited non-specific increases in various other malignant tumors [7-10] and benign conditions [11,12]. Due to limitations in both sensitivity and specificity, CEA could not serve as a standalone diagnostic marker. Consequently, its clinical significance resided in aiding diagnosis and monitoring treatment, while definitive diagnostic and therapeutic decisions necessitated a multidimensional integration and systematic analysis of clinical signs and symptoms, imaging results, and pathological findings. When confronted with elevated CEA levels, the primary challenge involved accurately interpreting the underlying pathophysiological implications and effectively mitigating the influence of non-specific factors.

Case Presentation

A 34-year-old female patient with persistent elevation of CEA. The elevated CEA was initially discovered in 2019 during a routine physical examination, with a serum CEA level of 14.4 ug/L (reference <5ug/L) in other hospital. Subsequent follow-up showed a gradual increase in CEA levels without corresponding clinical manifestations or abnormalities in other biochemical markers. In 2021, despite reaching 33.8ug/L measured by the CEA Reagent Kit in our hospital, initial gastroscopy and colonoscopy examinations did not reveal any typical malignant lesions. Enhanced computed tomography (CT) scans of the thorax, abdomen, and pelvis indicated retrograde abdominal organs, hepatic cysts, poly-splenic syndrome, and cysts in the left adnexal area, but no definitive neoplastic lesions were observed. In the absence of pathological or imaging evidence, the persistent CEA elevation was attributed to the physiological variations. In 2022, a follow-up examination showed a significant rise in serum CEA levels to 87.4 ug/L, confirmed at 84.8ug/L (Figure 1A). Colonoscopy did not detect any conclusive lesions, while gastroscopy revealed chronic protuberant erosive antral gastritis with atrophy and intestinal metaplasia, which was deemed insufficient to explain

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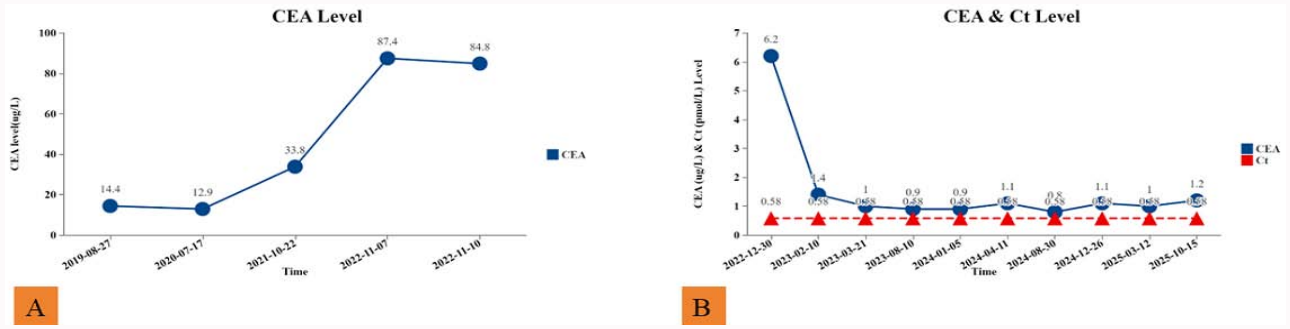

Figure 1: The serum levels of CEA or Ct. A: The serum CEA levels during the preoperative follow-up. B: The serum CEA & Ct levels during the postoperative follow-up (Note: As the Ct level was below 2.00pg/mL, it was recorded as 1.99pg/mL and converted into 0.58pmol/L).

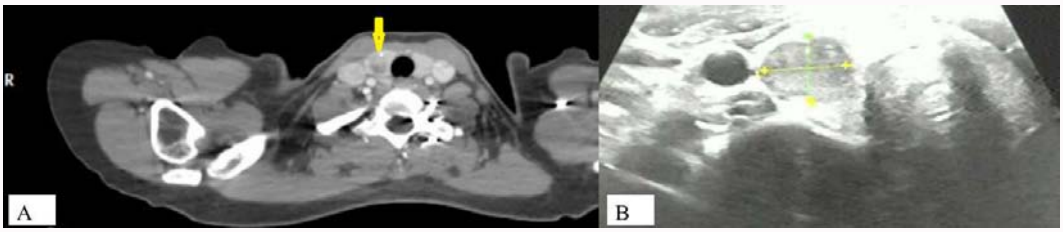

Figure 2: A suspicious nodule in the right thyroid lobe. A: Enhanced CT of thorax, a low-density shadow with calcification. B: Thyroid ultrasound, medullary thyroid cancer presenting as a hypoechoic appearance, an aspect ratio >1, irregular margins, and punctate hyperechoic areas.

the substantial CEA elevation. Enhanced CT of the thorax revealed a low-density shadow with calcification in the right thyroid lobe (Figure 2A). Enhanced CT of the abdomen and pelvis demonstrated no significant changes from previous observations. Consequently, further investigation concentrated on thyroid lesions. A thyroid ultrasound, performed by a junior physician at our hospital, identified a suspicious malignant nodule in the right lobe (Figure 2B), characterized by a hypoechoic appearance, an aspect ratio >1, irregular margins, and punctate hyperechoic areas. According to the Thyroid Imaging Reporting and Data System (TI-RADS) scoring system published by the American College of Radiology (ACR), the nodule was classified as Class V.

Ultrasound-guided fine needle aspiration cytology suggested a likely malignant tumor, indicating medullary thyroid cancer (MTC; Figure 3A). The subsequent serum calcitonin level significantly increased to 87.9 pmol/L (reference <1.5 pmol/L) by the Calcitonin Kit chemiluminescent assay, confirming the diagnosis of MTC. The patient underwent a total thyroidectomy and right central lymph node dissection. The postoperative pathological examination, along with immunohistochemical analysis showing positive staining for both CEA and calcitonin (Figure 3C and 3D), confirmed the diagnosis of MTC (TNM stage: pT1b pN0 cM0; Figure 3B). During one-month after the operation, serum levels of calcitonin (<0.6pmol/L) and CEA (6.2ug/L) decreased significantly. In November 2025, after more than 36 months of follow-up, the patient remained in complete remission with no evidence of tumor recurrence or metastasis, and serum CEA and calcitonin all stayed within normal ranges (Figure 1B).

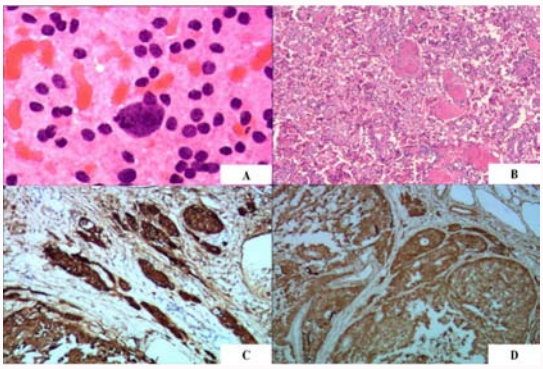

Figure 3: Pathological examination: A: Fine needle aspiration cytology (HE×100). B: Postoperative paraffin sections (HE×100). C: Immunohistochemistry CEA (+). D: Immunohistochemistry Ct (+).

Discussion

This case underscored the clinical challenges associated with reliance on a single tumor marker, specifically CEA, for the screening and diagnosis of malignant tumors. Although CEA primarily served to monitor patients with colorectal cancer, clinicians needed to adopt a comprehensive differential diagnosis approach when faced with consistently elevated CEA levels [13]. In this instance, the differential diagnosis initially focused on common gastrointestinal and pulmonary tumors, while timely consideration of MTC was overlooked due to the limited clinical reasoning influenced by the nonspecific characteristics of CEA. Non-malignant conditions could have been associated with elevated CEA levels, but value >15μg/L, particularly when displaying a consistent upward trend, warranted increased vigilance for potential malignancies and prompted the implementation of systematic tumor screening [11]. Due to its non-specific nature, gastrointestinal malignancies were ruled out, necessitating the consideration of rare malignant neoplasms such as MTC, an aggressive thyroid cancer that represented 5% to 10% of all thyroid cancers and contributed to 8% to 13% of thyroid cancer-related mortalities [14]. Derived from parafollicular C cells that secrete calcitonin, MTC, despite its infrequency in clinical practice, should not be disregarded during routine screenings. Calcitonin played a

pivotal role as a diagnostic biomarker for MTC, boasting diagnostic sensitivity and specificity exceeding 95%, thus offering practicality and cost-effectiveness [15]. Guidelines recommended that individuals suspected of having malignant thyroid tumors should undergo serum calcitonin evaluation to distinguish MTC [15]. In cases where MTC was suspected, the detection of CEA was deemed essential. Recent research has shown that serum procalcitonin, commonly used as an infection marker, was a valuable addition to calcitonin, offering crucial guidance for diagnosing and treating MTC [16]. In retrospect, detecting calcitonin or procalcitonin simultaneously, along with early CEA elevation, could have led to a definitive diagnosis years earlier. This approach might have greatly decreased healthcare resource utilization and relieved patients of the physical and psychological strain of prolonged monitoring and repeated screenings. This case highlighted the significant advantages of combining marker detection to optimize clinical pathways.

Conclusion

CEA, a crucial serum tumor marker, significantly contributed to the detection of potential pathological conditions and the surveillance of colorectal cancer[5]. Nevertheless, its restricted specificity posed challenges in interpreting isolated elevated CEA levels in asymptomatic individuals. Clinicians undertook comprehensive differential diagnoses in such scenarios, methodically ruling out confounding variables (i.e. smoke, physiology …) and meticulously evaluating rare conditions (i.e. calcitonin detect in this case). Finally, to sum up, in instances of unexplained elevation CEA level, please focus on the thyroid.

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