

PHYSICIAN CONNECT

Dear Doctor,

Greetings from Micro Labs. We are happy to bring you **"Physician Connect"** which contains latest and interesting news.

This issue contains:

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2. Determination of the causes of High Mortality among Diabetic Patients Without Coronary Artery Disease
3. Assessment of Hematologic Parameters as inflammatory response indicators in colorectal cancer
4. Case report on pseudonodules in thyroiditis

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Looking forward to your valuable feedback.

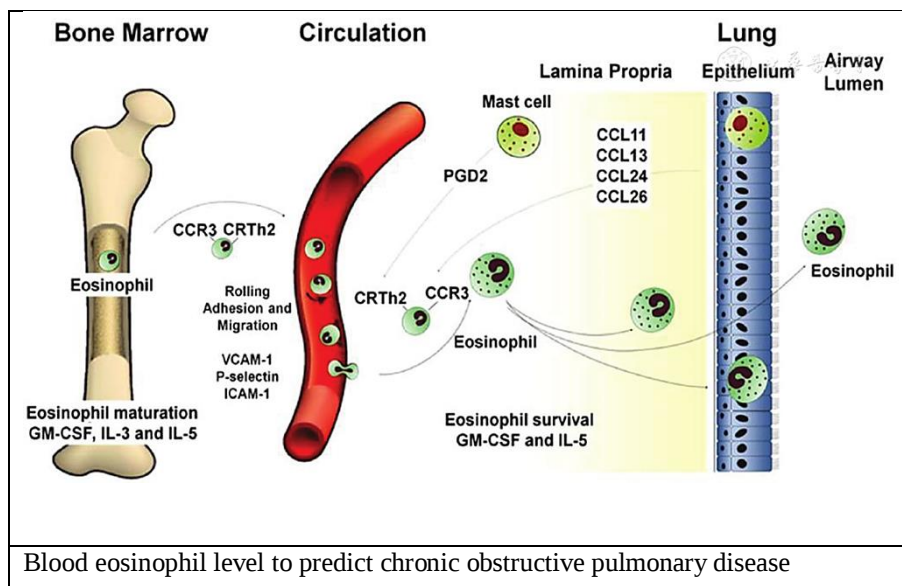
Best Regards,

Medical Team, Micro Labs Limited.

1. Association between blood eosinophil stability, exacerbation rates, and other clinical outcomes in patients With Chronic Obstructive Pulmonary Disease

Introduction:

Chronic obstructive pulmonary disease (COPD) is a prevalent respiratory condition that causes high morbidity and mortality.¹ COPD is currently the third major cause of death worldwide. In 2019, there were more than 384 million COPD patients globally.² Despite its prevalence, COPD is underdiagnosed, with many patients receiving a diagnosis only after the disease has progressed clinically.¹ The blood eosinophil count (BEC) accurately predicts COPD patients' response to inhaled corticosteroids (ICS). ICS-based treatment is recommended for individuals with eosinophilic COPD who have a BEC level of ≥ 300 cells/ μ L. The BEC is a major predictor for COPD exacerbation. Previous studies have demonstrated the reproducibility of blood eosinophil results in COPD patients at both high and low levels. However, the stability of blood eosinophils remains uncertain and may be influenced by exacerbation, corticosteroid use, and comorbidities.² So, this study aimed to explore the stability of BECs in predicting clinical outcomes in areas with high parasite infection rates.



Methods:

This was a prospective observational study that included patients with COPD. The Global Initiative for Asthma (GINA) and Global initiative for chronic Obstructive Lung Disease (GOLD) 2021 guidelines were used to evaluate the asthma and asthma-COPD overlap. BEC

was assessed at enrollment and in 6 and 12 months. Patients were divided into three groups based on their baseline BEC levels: <100, 100-299, and ≥300 cells/μL. This study analyzed blood eosinophil stability in stable COPD patients and compared exacerbation rates and clinical outcomes across 6 and 12 months.

Results:

A total of 252 patients with COPD were included in this study. Patients were divided into three groups based on their baseline BEC. There were 37 (14.7%), 98 (38.9%), and 117 (46.4%) patients in the <100, 100-299, and ≥300 cells/μL groups, respectively. BEC stability was best (85%) in the ≥300 cells/μL group over both durations. After 6 and 12 months, the group with <100 cells/μL showed the lowest stability of 57% and 46%, respectively. The persistent ≥300 cells/μL group had a greater risk of moderate-to-severe exacerbation (IRR 2.44, 95% CI: 1.13-5.27, p = 0.023) and severe exacerbation (IRR 2.19, 95% CI: 1.39-3.45, p = 0.001). When compared to the variable BEC ≥300 cells/μL group, the persistent BEC ≥300 cells/μL group showed observably greater rates of both moderate-to-severe and severe exacerbation rates. Moderate-to-severe exacerbations occurred 1.16 times per year (95% CI: 0.19-2.13, p = 0.019), while severe exacerbations occurred 0.56 times per year (95% CI: 0.39-0.73, p = <0.001) (Figure 1).

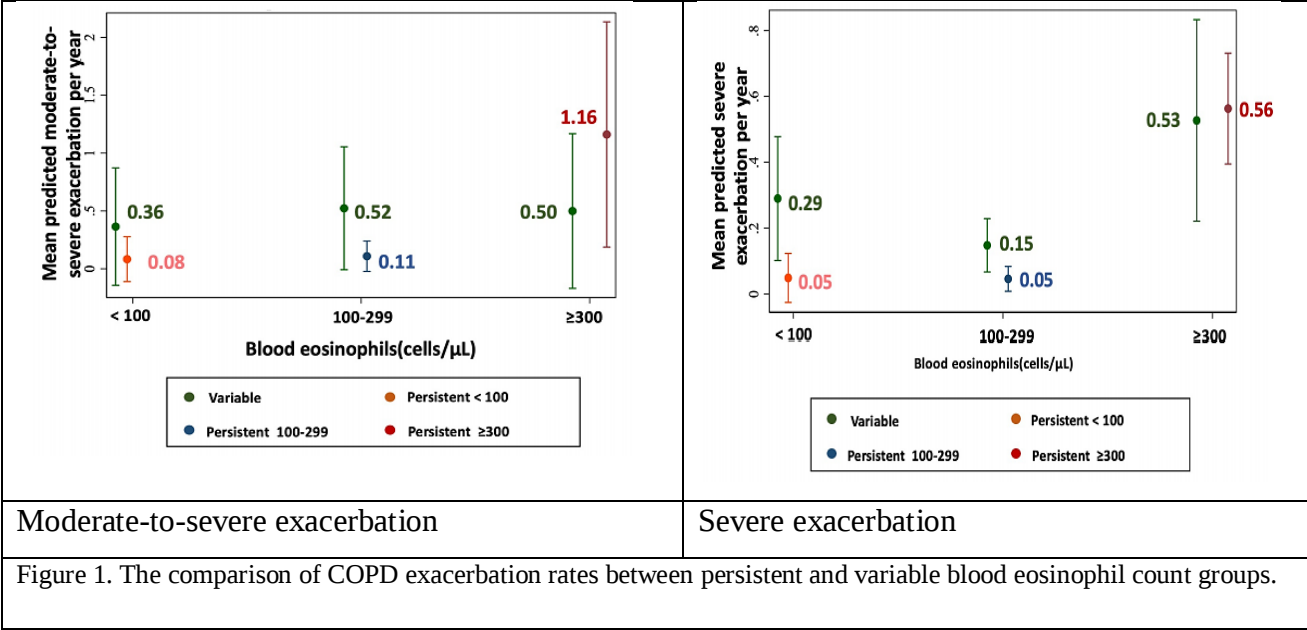


Figure 1. The comparison of COPD exacerbation rates between persistent and variable blood eosinophil count groups.

Discussion:

This study examined the relationship between blood eosinophil stability, exacerbation rates, and other clinical outcomes, as well as the stability of BEC in COPD patients at the 6- and 12-month follow-ups. This study found that COPD patients have increased blood eosinophil

stability, especially in the ≥ 300 cells/ μ L group.² A previous study reported that the intraclass correlation coefficient (ICC) for 12-month blood eosinophil stability was 0.84. In this investigation, patients with blood eosinophil counts between 100 and 299 cells/ μ L showed the highest stability, while the group with less than 100 cells/ μ L showed the lowest stability.³

Conclusion:

COPD patients with a BEC of ≥ 300 cells/ μ L had stable blood eosinophil levels, while those with a persistent BEC of ≥ 300 cells/ μ L were at a higher risk for exacerbation. COPD patients with BEC levels < 300 cells/ μ L showed increased variability.

Blood eosinophil stability is higher in COPD patients, particularly in the group with BEC ≥ 300 cells/ μ L.

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2. Determination of the causes of High Mortality among Diabetic Patients Without Coronary Artery Disease

Introduction:

Diabetes mellitus (DM) is defined primarily by high blood glucose levels (hyperglycemia), polydipsia, and polyphagia. Diabetes is a prevalent and rapidly growing metabolic condition worldwide. The global incidence of diabetes among individuals over 18 has increased from 4.7% in 1980 to 8.5% in 2014. According to WHO predictions, by 2030, diabetes would rank as the seventh leading cause of death.¹ Patients with diabetes mellitus (DM) are more likely to develop cardiovascular disease (CVD) than those without DM. People with DM are estimated to have 1.7 times higher CVD death rates than people without DM. DM was linked to several risk factors for the development of CVD, such as dyslipidemia, obesity, hypertension,

hyperglycemia, and chronic renal disease. The all-cause mortality rate was higher in patients with diabetes mellitus (DM) without coronary artery disease (CAD) than in patients without either condition. Therefore, it was necessary to investigate particular causes of death among DM patients who do not have CAD in order to identify prospective areas for future research and prevention.² The purpose of this study was to investigate the potential causes of higher mortality in DM patients without CAD.

Methods:

This was a registry-based cohort study included all the patients who underwent CAG. Patients were categorized based on their DM and CAD status and monitored for up to ten years. Outcomes were characterized as both all-cause and cause-specific mortality, such as cancer, cardiovascular, and endocrinological mortality. This study also investigated mortality caused by diabetes-related complications, such as nephropathy and ketoacidosis.

	No DM, no CAD	DM only
Cancer death	1887 (100%)	319 (100%)
Gastro-intestinal cancer	489 (25.9%)	99 (31.0%)
Lung cancer	502 (26.6%)	81 (25.3%)
Female reproductive organ cancer	193 (10.2%)	39 (12.2%)
Urinary cancer incl. prostate	215 (11.4%)	33 (10.3%)
Endocrinologic death	98 (100%)	175 (100%)
Diabetes-related	26 (26.5%)	155 (88.6%)
Obesity	11 (11.2%)	9 (5.1%)
Cystic fibrosis	50 (11.2%)	11 (6.2%)
Circulatory death	2,472 (100%)	444 (100%)
Ischemic heart disease	561 (22.7%)	112 (25.2%)
Non-ischemic cardiomyopathy	437 (17.7%)	86 (19.4%)
Valve disease	479 (19.4%)	81 (18.2%)
Stroke	334 (13.5%)	55 (12.4%)

Notes: CAD indicates coronary artery disease; DM: diabetes mellitus.

Table 1: Most Common Causes of Death: Circulatory, Endocrinologic, and Cancer-Related

Results:

This study included 132,432 patients in total (28,524 fatalities, median follow-up of 6.2 years). Patients with diabetes mellitus without CAD had increased 10-year risks of circulatory death (9.1% versus 6.9%, aHR 1.35 [95% CI 1.22–1.49]), cancer death (7.2% versus 5.4%, aHR 1.29 [95% CI 1.15–1.46]), endocrinologic death (3.9% versus 0.3%, aHR 14.02 [95% CI 10.95–17.95]) and all-cause death (27.9% versus 19.7%, aHR 1.43 [95% CI 1.35–1.52]) in comparison to patients with neither DM nor CAD. Eighty-seven percent of endocrinologic deaths were attributed to traditional diabetes complications, such as ketoacidosis and diabetic nephropathy, in DM individuals without coronary artery disease. Among DM patients without CAD, endocrinologic death accounted for 13.6% of all deaths (Table 1).

Discussion:

Diabetes-related microvascular disease contributes to higher mortality rates in people without CAD. In this study, 69% of DM patients without CAD redeemed their statin prescriptions within 180 days of CAG, compared to 39% of individuals without DM or CAD.² A previous study found that increased primary preventive medication, such as statins, had significantly reduced cardiovascular morbidity and mortality.³ DM patients who continue statin medication after CAG have a lower risk of CVD, even without having CAD.⁴

Conclusion:

Diabetes patients without CAD have a higher risk of all-cause mortality due to increased rates of cancer, cardiovascular, and endocrinologic deaths, mostly from diabetic microvascular complications.

Patients without CAD who have diabetes have an increased chance of mortality from all causes, mostly from cancer, cardiovascular disease, and endocrinology—particularly from complications associated with diabetes microvascular disease.

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3. Assessment of Hematologic Parameters as inflammatory response indicators in colorectal cancer

Introduction:

Colorectal cancer is the third most frequent malignant tumor globally, characterised by abnormal cells growing in the colon or rectum of the large intestine. The International Agency for Research on Cancer (IARC) released global cancer data for 2020, which showed that there were 940,000 cancer deaths and about 1.9 million new cases of colorectal cancer (CRC) worldwide in 2020.¹ Preoperative markers are becoming more and more necessary to classify patients for further treatment and predict prognosis. Studies on the relationship between inflammation and cancer have been ongoing for a long time. Malignant tumors are strongly influenced by inflammation and the local immune response. Markers like the

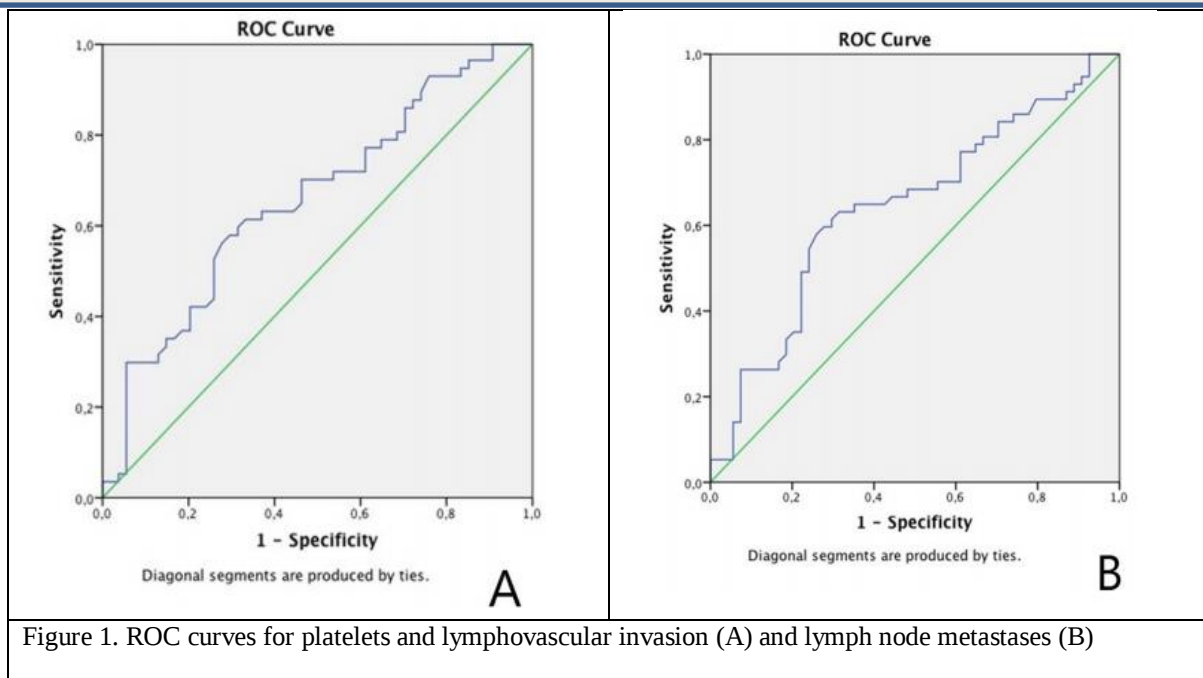
neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are nonspecific indicators of inflammation. Lymphocyte-to-CRP ratio (LCR), a novel marker has gained attention. These biomarkers have been studied globally for the prediction of tumor due to their affordability, ease of use, and accessibility. Prognostic variables NLR and PLR have been linked to poor overall survival (OS) and disease-specific survival in a number of solid tumors, such as gynecological, lung, gastric, and renal cancers.² So, the purpose of this study was to assess the relationship between neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-CRP ratio (LCR), which are readily available markers of inflammatory response.

Methods:

This retrospective cross-sectional study included 111 patients with colorectal cancer who underwent radical surgery. Age, gender, and histopathologic parameters were recorded, along with preoperative blood sample analysis, CRP levels, serosal inflammation, lymphovascular invasion (LVI), perineural invasion (PNI), lymph node metastasis (LNM), distant metastasis, tumor size, and surgical margin status (proximal, distal, and radial). Statistical analysis was conducted to determine the relationship between histopathological characteristics and the hematologic indices platelet (PLT) levels, neutrophil-to-lymphocyte ratio (NLR), platelet (PLT)-to-lymphocyte ratio (PLR), and lymphocyte-to-CRP ratio (LCR).

Results:

The average tumor size was 5.41 cm (± 2.54), and the subjects' mean age was 65.37 (± 11.16) years. Most of the tumors had a T3 stage ($n=51$), were moderately differentiated ($n=77$), and were found in the left colon ($n=78$). There was a statistically significant correlation between the number of platelets and lymphovascular invasion, perineural invasion, radial surgical margin positivity, lymph node metastases, localization, and stage. PNI ($p=0.001$), LNM ($p=0.048$), and stage (beginning/advanced) ($p=0.045$) showed significant relationships with NLR. There was no correlation between the parameters and PLR/LCR. ROC analysis demonstrated that PLT levels were discriminative for LVI and LNM. The PLT cutoff values for LVI and LNM were determined to be 280.5 (sensitivity 63.2% and specificity 63%) and 278 (sensitivity 64.9% and specificity 63%), respectively (Figure 1A and B).



Discussion:

Hematological parameters have been thoroughly examined for their potential as prognostic indicators in a variety of cancers due to their affordability and ease of use. This study shows a strong correlation between NLR and adverse prognostic factors such as advanced stage, PNI, and LNM. Among these hematological markers, NLR has received substantial attention.² A previous study showed that NLR with recurrence and lower survival following recurrence in individuals receiving neoadjuvant treatment.³ Several studies have examined the appropriate cutoff value for NLR with respect to other prognostic indicators. The two cutoff values of $\text{NLR} \leq 3$ and $\text{NLR} > 3$ did not lead to a significant association between NLR and other prognostic factors.² A previous investigation demonstrated that the NLR cut-off of 5 had the highest sensitivity and specificity.⁴

Conclusion:

Histopathological characteristics such as perineural invasion, lymph node metastases, and tumor stage may be associated with hematologic parameters, but further research is needed to determine their potential as prognostic indicators.

Hematologic markers are easily accessible and cost-effective, making them a valuable tool for studying the effects of inflammation on carcinogenesis.

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4. Case report on pseudonodules in thyroiditis

Introduction:

Thyroid nodules are frequent in the general population, with a higher incidence in women and with age. Approximately 5% of thyroid nodules are malignant; the majority of this subset comprises papillary thyroid carcinoma. The prevalence of thyroid nodules may be as low as 4-5% of individuals, while ultrasonography and autopsy studies indicate an incidence of 50-67%. Female sex, aging, iodine shortage, history of radiation to the head and neck, and ionizing radiation before the age of eighteen are risk factors for the development of nodules.¹ Patients with thyroid nodules frequently seek clinical attention. A normal evaluation includes a history, neck examination, thyroid function test, laryngoscopy, ultrasound of the thyroid gland, and fine-needle aspiration cytology (FNAC) for nodules suspected of cancer. This case report focuses on pseudonodules caused by thyroiditis, which can appear suspicious on sonography with just discomfort and subclinical hyperthyroidism as diagnostic clues. Diagnosing pseudonodules can prevent invasive operations and allow for preventative therapy.²

Case presentation:

A 58-year-old female presented to hospital with acute left anterior neck pain, soreness, and edema that lasted a month. This was related with palpitations, but no fever, heat intolerance, sleeplessness, diarrhea, weight loss, dysphagia, dyspnea, or hoarseness. Hypertension was her only comorbidity. Her mother had earlier been diagnosed with unidentified cancer in the neck. After a week, the pain subsided, but the swelling in the neck continued. Examination revealed a palpable and sensitive mass in the left lower central neck that moved after swallowing. No cervical lymphadenopathy was clear. There were no signs of thyrotoxicosis. Flexible laryngoscopy demonstrated normal vocal cord mobility.

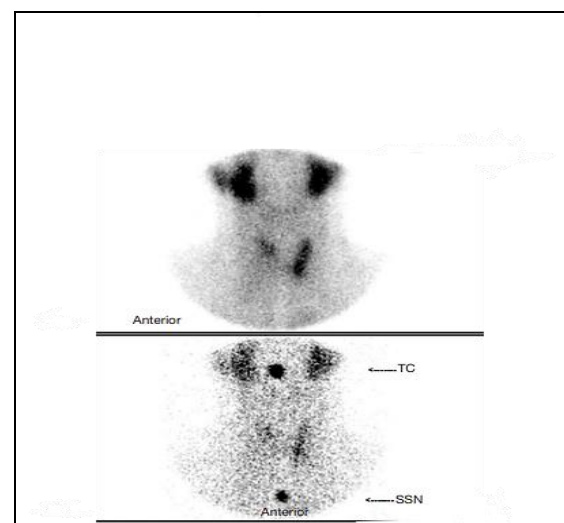
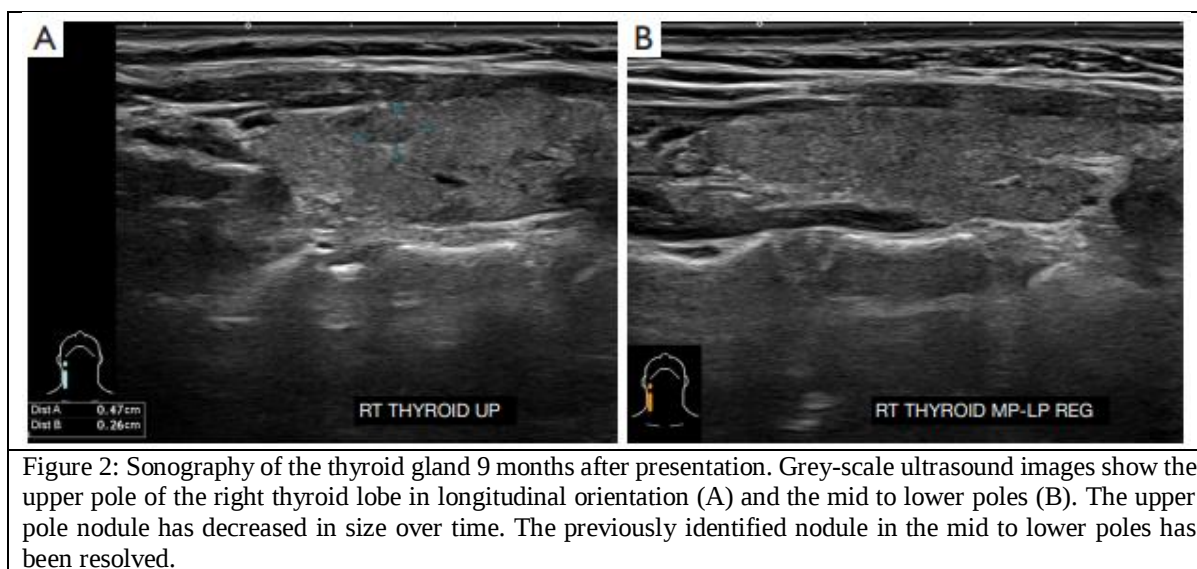


Figure 1: Technetium-99m pertechnetate thyroid scintigraphy reveals decreased tracer uptake in the thyroid gland, with a photopenic region in the right mid-to-lower pole. TC, thyroid cartilage; SSN, suprasternal notch.

Thyroid function tests revealed TSH levels of 0.16 mIU/mL (normal range: 0.45-4.5 mIU/mL), free thyroxine (T4) of 16 pmol/L, anti-thyroid peroxidase (TPO) of <5 IU/mL (normal range: 0-50 IU/mL), anti-thyroglobulin (TG) of <10 IU/mL (normal range: 0-100 IU/mL), and TSH receptor antibody (TRAB) was 1.0 IU/L (range of normality 0–1.0 IU/L). Thyroid gland sonography 16 days post-presentation showed two right-sided thyroid nodules as a solid, circumscribed, heterogeneous, hypoechoic nodule measuring 2.5 cm in size and located in the right mid-to-lower pole without peripheral vascularity, and a solid, 1.1 cm nodule without calcifications in the right upper pole. The American College of Radiologist Thyroid Imaging Reporting and Data System (ACR-TIRADS) indicated that both were TR4. The left lobe was heterogeneous, with dimensions of 4.0 cm × 1.0 cm × 1.6 cm and nodules that were easily identifiable. For subclinical hyperthyroidism, she was referred to endocrinology and given a prescription for etoricoxib. Repeated thyroid function tests were performed at the follow-up. During a two-month period, TSH dropped from 0.16 to <0.0001 mIU/mL, while free triiodothyronine (T3) was 5.1 pmol/L (normality range: 3.5–6.0). Meanwhile, free T4 stayed within the normal range. When using technetium-99m pertechnetate thyroid scintigraphy, the thyroid gland's overall tracer uptake was reduced. Additionally, a photopenic region in the right mid-to-lower pole suggested that the patient may have localized thyroiditis (Figure 1). After 9 months, the patient's neck swelling disappeared TSH levels returned to normal, and a repeat thyroid sonography revealed only one 0.5 cm nodule in the right lobe with no concerning signs (Figure 2). A year later, sonography revealed no change in the nodule's appearance, and the patient remained euthyroid.



Discussion:

Most patients with thyroid nodules are euthyroid, and the primary goal of the evaluation was to rule out malignancy. Sonographic evaluation and FNAC of sonographically suspicious nodules were typically required for this. The clinical history, radiological, and laboratory results for the patient in this case support the diagnosis of De Quervain's thyroiditis. This

syndrome was associated with inflammatory pseudonodules, which were known to resolve on their own. Except for hypoechogenicity, the pseudonodules show no other concerning signs on ultrasonography.² In a study of 899 patients revealed 28 cases of pseudonodules. The pseudonodules were hypoechogenic, with a smooth edge, oval shape, similar vascularity to the neighboring parenchyma, and no calcification. FNAC scans typically reveal only benign lymphocyte infiltration in pseudonodules. Except for hypoechogenicity, the pseudonodules do not have any other concerning signs.³

Conclusion:

The clinical history, radiological, and laboratory results for the patient in this case support the diagnosis of De Quervain's thyroiditis. This syndrome was associated with inflammatory pseudonodules, which were known to resolve on their own. Except for hypoechogenicity, the pseudonodules showed no other concerning signs on ultrasonography. With the rising number of thyroid nodules being detected, it's important to keep in mind that inflammatory pseudonodules can disappear on their own. Physicians should be aware of this diagnosis in order to prevent giving patients needless fine-needle aspiration cytology (FNAC) or creating unwarranted anxiety about cancer.

Thyroid nodules are typically evaluated with a thorough history and physical examination, followed by laryngoscopy, ultrasonography, and fine-needle aspiration cytology (FNAC) if malignancy is suspected.

References:

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