

Synchronous Malignancies - Unveiling the Genetic Overlap: A Rare Case

Saxena Ayush^{1*}, Gupta Anshu², Mittal Salony³

^{1*}Post Graduate Resident, Pathology, School of Medical Sciences and Research, Sharda University, Greater Noida.

²Professor and Head of Department and Corresponding Author, Pathology, School of Medical Sciences and Research, Sharda University, Greater Noida.

³Professor, Pathology, School of Medical Sciences and Research, Sharda University, Greater Noida.

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Abstract:

Synchronous thyroid and breast malignancies are infrequently reported in literature. Their coexistence do indicate some common genetic and/or hormonal link between the two. We encountered a similar case at our institute and intended it to contribute to the existing literature. As, ongoing research and case reporting will provide more insights into the complexities of these simultaneous cancers and will also help in creating more effective management strategies.

Keywords: Synchronous Malignancy, Papillary Thyroid Carcinoma, Ductal Carcinoma Breast, Invasive Ductal Carcinoma, Dual Malignancy.

Introduction:

Synchronous malignancies, where two primary cancers occur simultaneously in the same patient, are rare but present significant diagnostic and therapeutic challenges. Among these, the concurrent presence of Papillary Thyroid Carcinoma and Ductal Carcinoma of the Breast is an uncommon clinical scenario. Recent studies have suggested potential genetic and environmental links between these malignancies, particularly in the context of radiation exposure and genetic predispositions, such as mutations in PTEN and TP53 genes. A similar case was encountered at our institution and we intend to add it to the literature emphasizing on a potential molecular common link and henceforth common molecular target, if any.

Case Report:

A 62 year old lady presented with breast lump left side in the upper outer quadrant since 6 months. It was painless and rapidly progressive in size. Also, on thorough clinical examination she was found to have left side axillary lump and also a midline neck swelling that moved on deglutition alongwith left cervical lymphadenopathy. Radiology findings from Left Breast lump were suggestive of BIRADS IV lesion and from Thyroid swelling were suggestive of possible TIRADS IV lesion. She had no history of previous surgery or radiotherapy or chemotherapy. And there was no positive family history of breast or thyroid disease.

She was sent to us for Fine Needle aspiration cytology (FNAC) of Breast lump, axillary lump, thyroid swelling and also left cervical lymphnode.

The FNAC smears from Left Breast lump [Figure 1]. revealed many clusters of atypical ductal cells with moderate degree of nuclear pleomorphism and nuclear overlapping. The cells showed eccentrically placed nuclei, vesicular chromatin, prominent nucleoli in a background of blood and its elements. FNAC smears from Left Axillary lump though paucicellular showed atypical cell clusters with similar morphology with that of breast lump [Figure 2]. Subsequently, biopsy was done and histopathological evaluation also confirmed it to be Invasive ductal carcinoma No specific type Nottingham Modified Bloom Richardson Grade II.

FNAC smears from thyroid swelling [Figure 3].were highly cellular and showed atypical cells arranged in cohesive to 3-dimensional clusters with oval nuclei, fine powdery chromatin, nuclear pseudo-inclusions and nuclear grooves at places and marked nuclear pleomorphism. Background showed blood, along with thick colloid at places.

FNAC from Left Cervical Lymph node also revealed atypical cells in cohesive clusters entrapped in blood clot. The morphology of cells resembled with those of thyroid FNAC with prominent nuclear grooves and pseudoinclusions.

Thus, the case was concluded to have dual malignancies-Invasive Ductal carcinoma breast with metastatic left axillary lymph node and Papillary thyroid carcinoma with metastatic left cervical lymph node.

Figure - 1 (Breast) : FNAC smears show atypical cell clusters (shown by arrow)

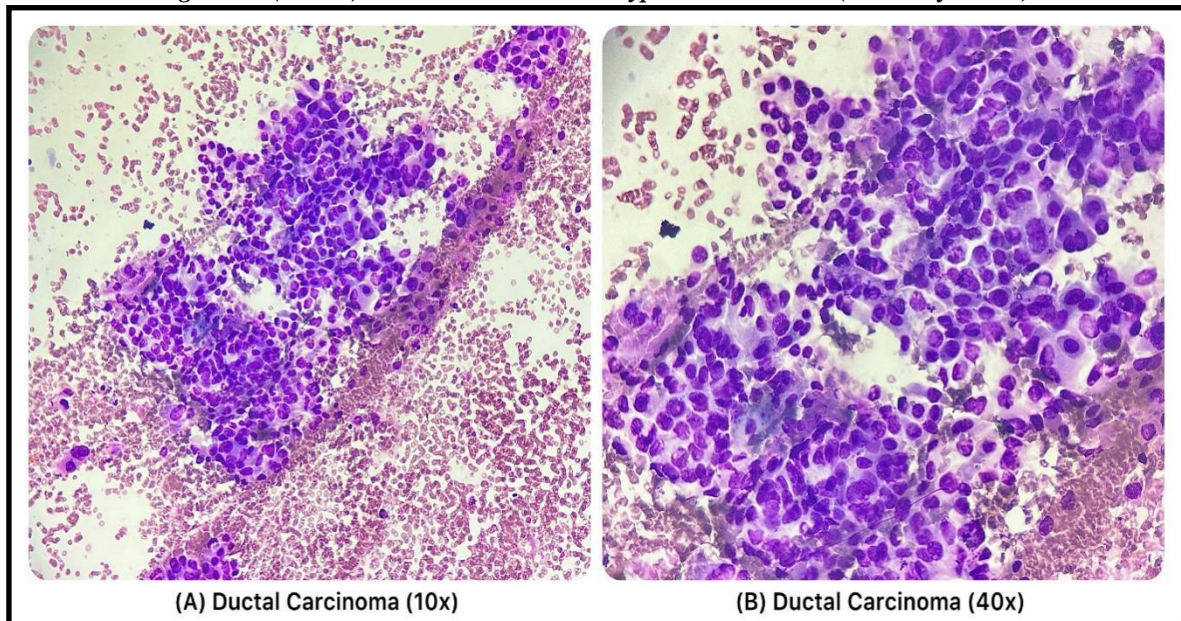
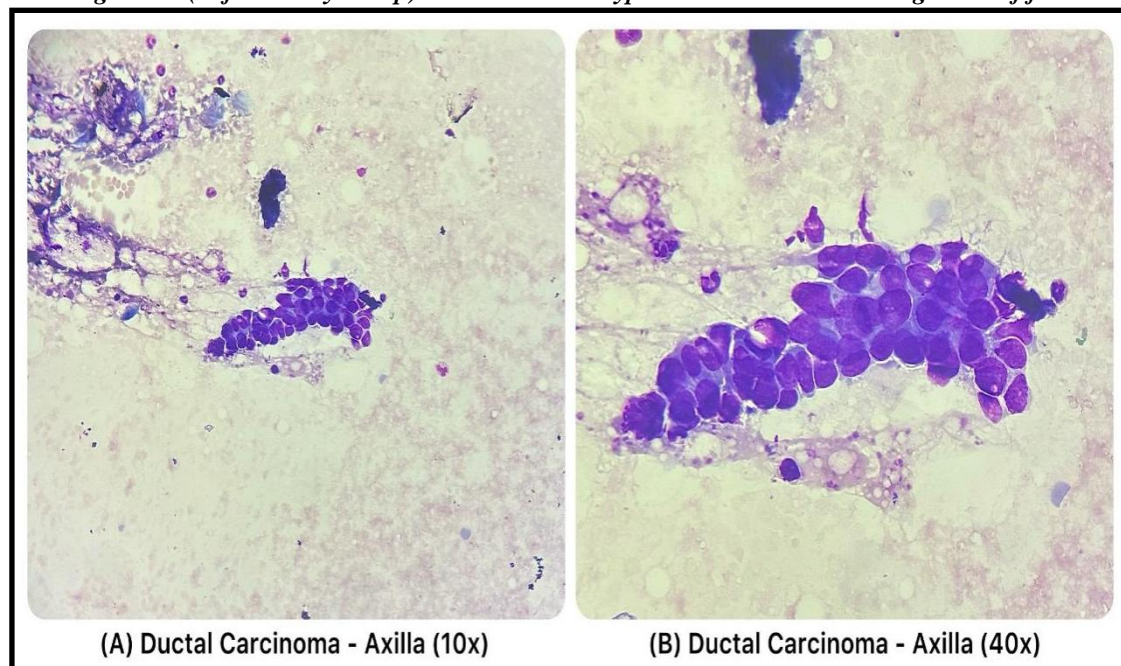


Figure - 2 (Left Axillary Lump) :Smears reveal atypical cell cluster in a background of fat.



USG-Guided FNAC from Left Breast lump was reported as Invasive Ductal Carcinoma And the Left Axillary Lump was reported as Metastatic Invasive Ductal Carcinoma.

Figure - 3 (Thyroid Swelling) :FNAC smears from thyroid swelling show hypercellular smears with cells showing marked nuclear enlargement and overlapping with prominent nuclear grooves(shown by arrow) and pseudoinclusions.

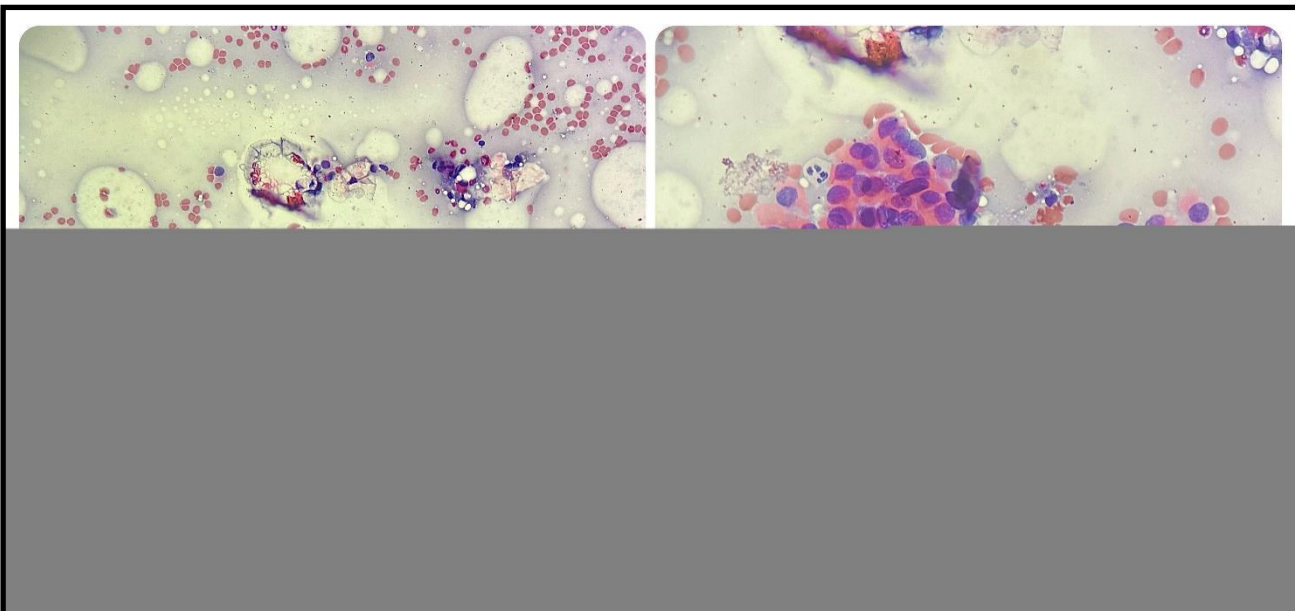
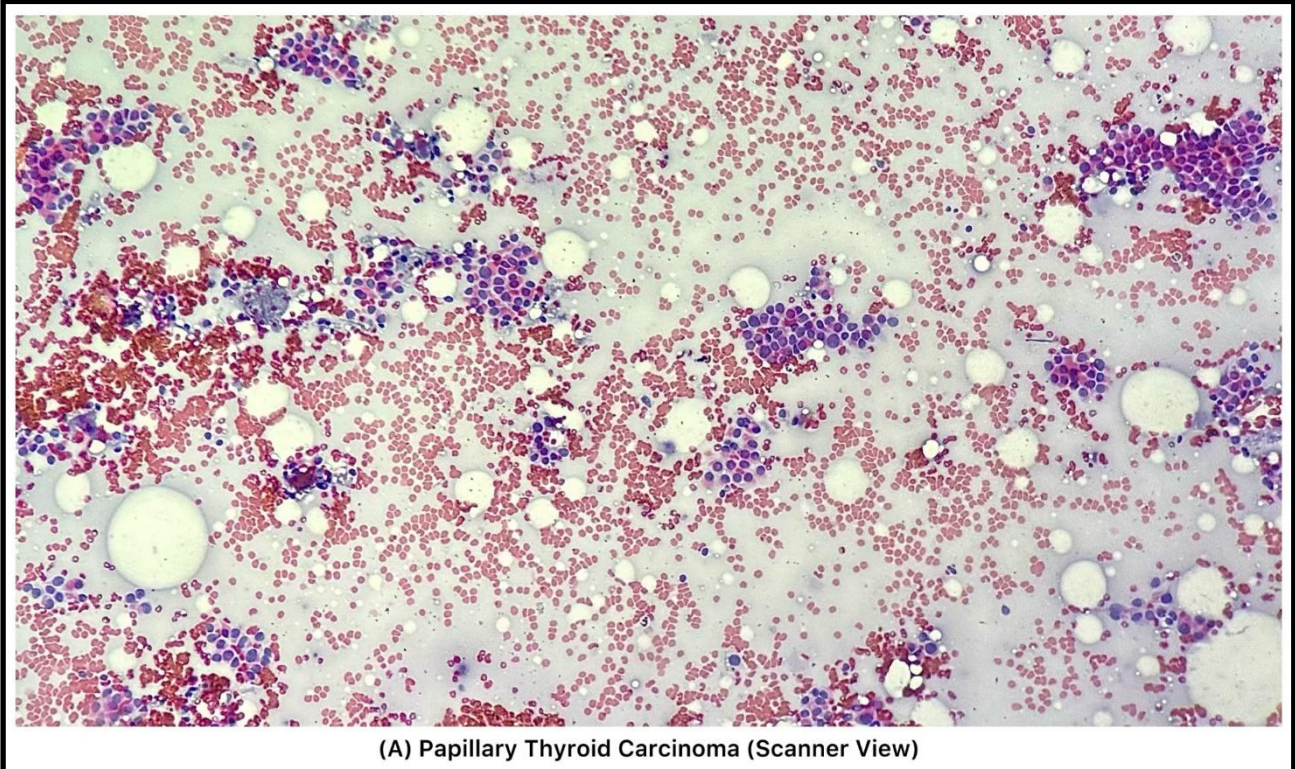
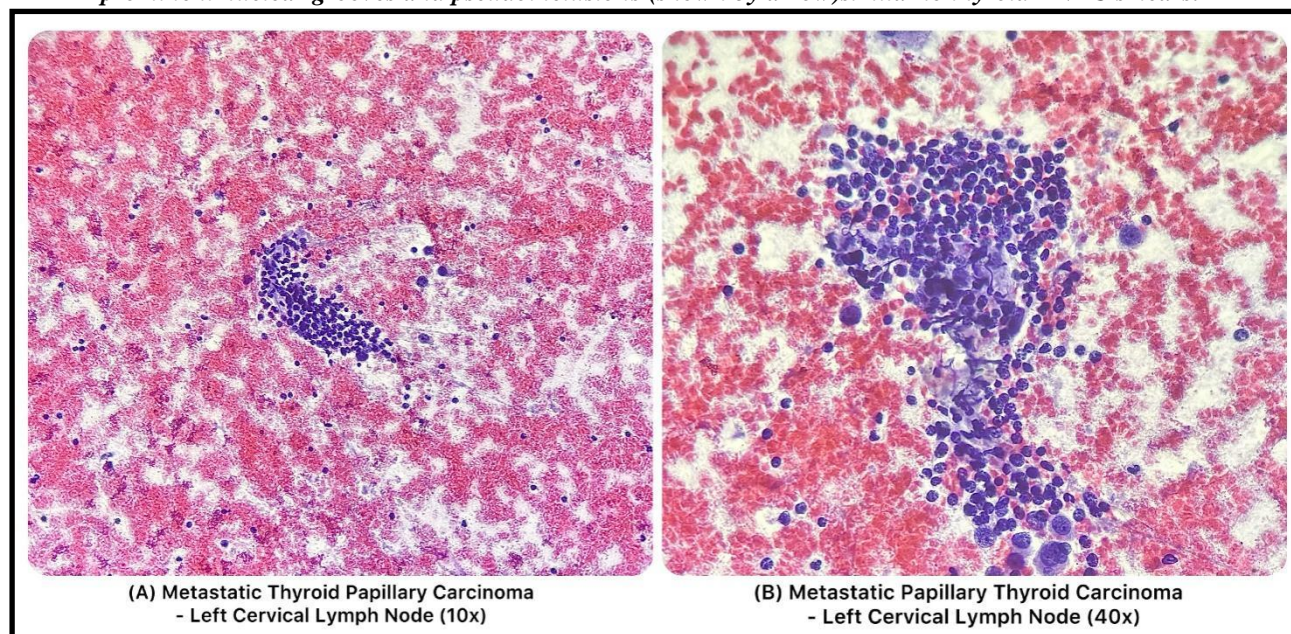


Figure - 4 (Left Cervical Lymph Node) : FNAC smears from left cervical lymphnodes show atypical cell clusters with prominent nuclear grooves and pseudoinclusions (shown by arrow) similar to thyroid FNAC smears.



USG Guided FNAC from Left Thyroid lobe was reported as Papillary Thyroid Carcinoma - Bethesda Category VI, Left cervical lymph node FNAC was reported as Positive for Malignant Cells (Morphology of cells resembling with those of Thyroid FNA).

Discussion:

Synchronous malignancy is defined as 2 or more histologically distinct malignancies detected within duration of 6 months of diagnosis of first primary malignancy. But, both the tumours should be malignant and the 2nd malignancy detected should not be metastatic from the first one and they should have different histomorphology. These malignancies were first reported in 1889 by Billroth.

Zhang et al. observed that following breast cancer, the most frequently occurring double primary cancers were thyroid cancer, endometrial cancer, cervical cancer, stomach cancer, and lung cancer.

On reviewing the literature, very few case series and case reports of co existing papillary thyroid carcinoma and ductal carcinoma breast were found. Other less common co existence of malignancies noted with papillary carcinoma thyroid were squamous cell carcinoma, melanomas and also the bone tumours.

Besides papillary thyroid carcinoma, few case reports on medullary and anaplastic thyroid carcinoma have also been reported by few authors^[1].

Papillary thyroid carcinoma the most common thyroid cancer, and Invasive ductal carcinoma, the predominant form of breast cancer, are both often hormone-sensitive, which might explain their co-occurrence in hormonally active patients, particularly women. Breast as well as thyroid malignancies are common in women. And several studies^[2,3] do suggest a common occurrence of thyroid diseases like autoimmune thyroid disease and also Thyroglobulin gene polymorphism in females with breast cancer^[4], thus, indicating some hormonal or genetic link between the two. There are two genes-TR α and TR β that encode thyroid receptors. Out of these two, TR β 1 was found to be associated with breast carcinoma. Furthermore, estrogen hormone has effect on thyroid as well and estrogen receptors are positive in thyroid tissue contemplating potential role of Tamoxifen on thyroid malignancies as well.

There may be a potential link between increased iodine uptake and the development of thyroid carcinoma. Both dietary iodine deficiency and intracellular iodine deficiency could contribute to carcinogenesis in these two organs. Thus, the radioiodine therapy, used in the treatment of thyroid cancer, works on the basis of sodium iodide symporter (NIS) also present in breast tissue. It facilitates transfer of iodine in milk.

Liu et al in his review of literature proposed that (NIS) could be a potential co passageway for breast and thyroid malignancy indicating role of radioiodine therapy in treatment of both the tumours. They also proposed potential role of tyrosine kinase inhibitors that enhance NIS activity, facilitating radioiodine therapy in breast carcinoma. Another common link between the two malignancies identified recently is RET/PTC.

RET/PTC kinase, an oncogene in PTC is estrogen dependent and its expression may be enhanced in breast carcinoma cases, thus laying a fertile soil for thyroid carcinoma as well.

Cowden syndrome, a known genetic disorder caused by mutation of antioncogene PTEN shows the same dual coexistence-breast and thyroid malignancies. However, due to financial constraints, the genetic testing was not done in our case. But at the same time, there was no positive family history in the present case.

The recent literature^[5,6,7] underscores the clinical complexity of managing synchronous breast invasive ductal carcinoma and papillary thyroid carcinoma. These studies reveal that while synchronous cases are uncommon, they present unique challenges in diagnosis, treatment, and management. Comprehensive genetic and molecular analyses are crucial for understanding potential shared risk factors and optimizing treatment strategies^[8,9]. Multidisciplinary approaches and personalized care plans are essential for improving patient outcomes in synchronous malignancies.

Conclusion

This case highlights the rare co-existence of the two common malignancies. However, further research is needed to better understand the biological interactions between them and to optimise treatment protocols for affected patients. Continued research and case reporting will further elucidate the nuances of these synchronous malignancies and aid in developing more effective management strategies.

Conflict of interest: None

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