



Hyaline Globules (Thanatosomes) in Invasive Breast Carcinoma: An Uncommon Histological Finding

Sanjiban Patra ¹, Sunitha Shankaralingappa ^{*1}

1. Assistant Professor, Department of OncoPathology, The Gujarat Cancer Research Institute, Ahmedabad, Gujarat 380016.

***Correspondence to:** Sunitha Shankaralingappa. Assistant Professor, Department of OncoPathology, The Gujarat Cancer Research Institute, Ahmedabad, Gujarat 380016.

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Introduction

Hyaline globules or ‘thanatosomes’ are eosinophilic globular structures found in several non-neoplastic and neoplastic conditions and independent of the tumour type. ‘Thanatosomes’, a term derived from the Greek words “Thanatos” meaning death and “soma” meaning body, representing a consequence of apoptotic cell death.[1] They are large (3- 30 micrometre) proteinous, and can be intracellular or extracellular. They are presumed to originate as a result of high membrane permeability of the apoptotic bodies, formed by plasma proteins with the globular shape.[2] They are most often found in renal cell carcinomas, oncocytomas, and hepatocellular carcinomas, and less frequently in gastrointestinal adenomatous polyps and adenocarcinomas, ovarian tumors, Kaposi sarcoma, cartilaginous tumors, gallbladder carcinosarcoma and testicular cancer. [3–10] They are rare in breast carcinoma. [1, 2, 11-13] Here we report a case of invasive duct carcinoma of no special type (IDC-NST) with both intra and extracellular hyaline globules (Thanatosomes).

Case Description

A 50-year-old woman presented with palpable nodular mass in the inferior portion of the left breast. Physical examination of the adjacent breast and right breast was within normal limits. She had no family history of breast cancer. On Ultrasonography a space occupying lesion (SOL) was detected measuring 2.2 cm in diameter with heterogeneous echotexture, spiculated margins and microcalcifications [BIRADS 5]. A Breast core biopsy was done for histopathology and hormone receptor immunohistochemistry (IHC). On histopathology, a diagnosis of Invasive ductal carcinoma, grade 2 was rendered. On IHC, tumor cells were positive for hormonal receptors (Estrogen and Progesterone), and negative for HER-2, with a Ki-67 (Mib-1) proliferation index of 40%. Subsequently breast conservative surgery (BCS) with sentinel lymph node biopsy was done. On gross examination, an infiltrative gray-white solid tumor was identified, measuring 2.5x2x1.5 cm. The tissue was fixed in 10% neutral buffered formalin (NBF), embedded in paraffin and sections were stained with Hematoxylin and eosin (H&E) histological examination. Microscopy showed an invasive ductal carcinoma of NST composed of infiltrative cords, sheets and clusters of malignant epithelial cells which was classified as grade 2 according to the Elston-Ellis histological grading system (Fig.1.A-B). Part of the tumor contained numerous homogenous, eosinophilic hyaline globules of various size both

intracytoplasmic and extracellular (Fig.2. A-D). These findings were consistent with an invasive breast carcinoma with hyaline globules (thanatosomes). Sentinel lymph node was free of tumor metastasis. Pathological staging was given as pT2N0. The patient had an uneventful post-operative recovery.

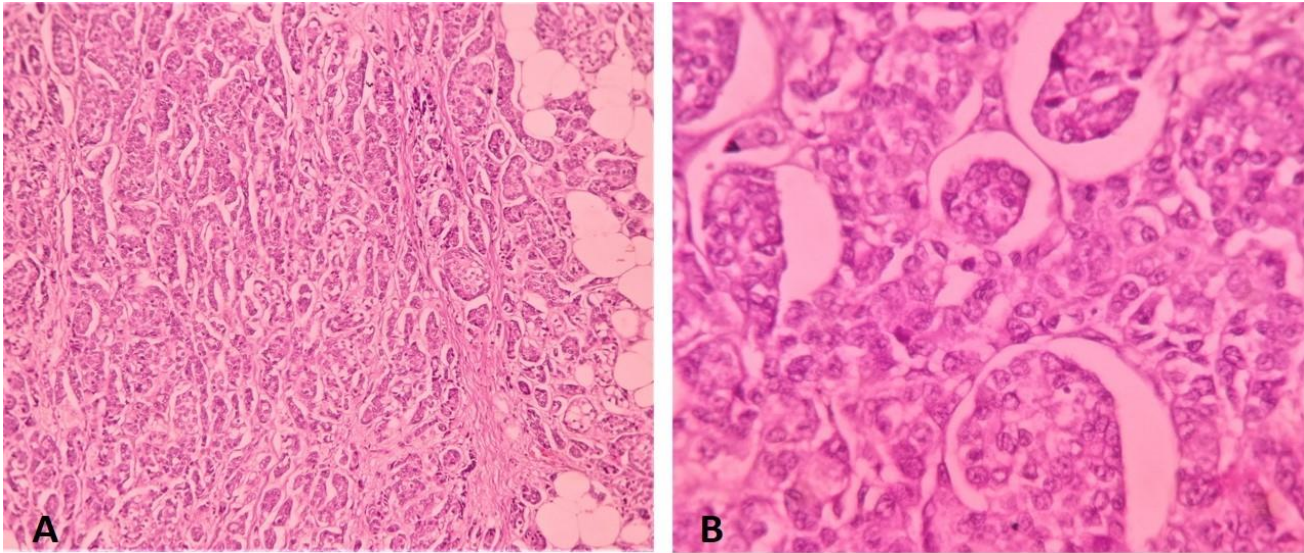


Figure 1. **A** Tumor cells arranged in sheets, cords and clusters [H&E, 100x] **B.** Tumor cells having pleomorphic vesicular nuclei and prominent nucleoli [H&E, 400x]

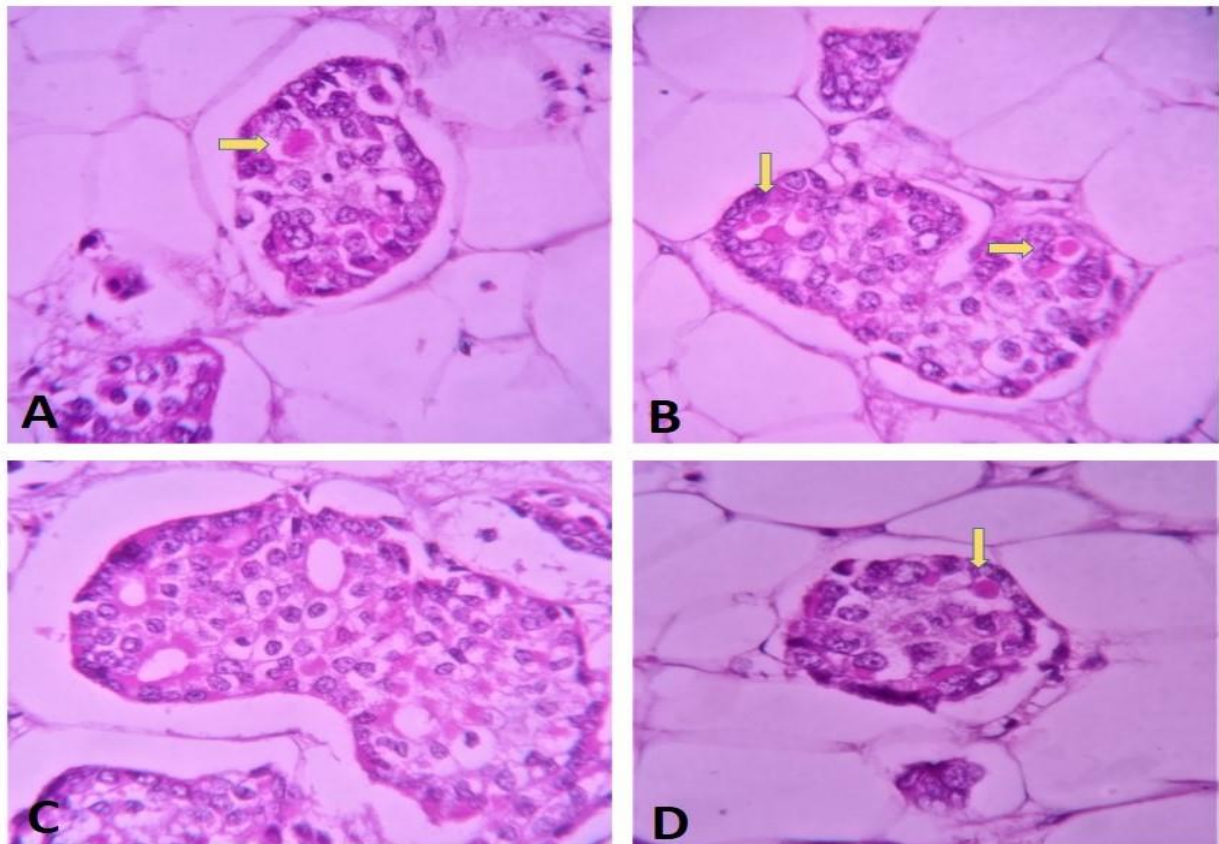


Figure 2: A-D Eosinophilic hyaline globules/ Thanatosomes (Yellow arrow) within the tumor cells and in the stroma [H&E, 400x]

Discussion

Hyaline globules have been described in literature in various non-neoplastic and neoplastic conditions. According to Papadimitriou et al. they are terminal cytoplasmic structures related to irreversible cell injury and apoptosis, resulting in cytoplasmic blebbing and condensation, with plasma protein imbibition, and formation of globoid hyaline fragments.[3] Their presence indicates high cell turnover and therefore in neoplastic conditions is usually related to high grade tumors. Thanatosomes in breast tumors were rarely reported and investigated in the literature.[1,2,11-13] Datta et. al. described Thanatosomes in invasive lobular carcinoma. D'Alfonso et al. reported two cases of malignant phyllodes tumor with numerous hyaline bodies in the stromal component of the tumors.

They also evaluated retrospectively 86 high grade breast tumors and found Thanatosomes in 16% of those high grade lesions, of which, most common was metaplastic spindle cell carcinomas (21%) followed by malignant phylloides tumor.[11] Ozerdem et. al., reported a case of conventional, spindle cell type mammary myofibroblastoma with intracytoplasmatic hyaline globules.[13] The present case showed an IDC-NST grade 2 tumor with Thanatosomes with a high Ki-67 proliferative index of 40% indicating rapid cell turnover.

Conclusion

Thanatosomes are uncommon in invasive breast carcinoma. They are related to cell injury and apoptosis. They indicate high cell turnover with high proliferation index. Pathologists should be aware of this uncommon and rarely reported histological finding.

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