ENIGMATIC MORPHO INSIGHT

EOSINOPHILIC NUCLEOLI

The nucleus is the largest and the most essential storage compartment of DNA in a functional living cell. This organelle contains the self-perpetuating nucleic acid (DNA) that codes for various kinds of proteins synthesized in the cytoplasm of the cell.

When observed under a microscope, the nucleus within the cells can either present as open phase nucleus or a closed phase nucleus.

Open phase nucleus is also called as vesicular nucleus. This is seen in an actively proliferating or actively synthesizing cell in which nucleus contains prominent nucleoli. It can exhibit marked variation in size and shape, occasionally with very large and bizarre forms. Usually no more than 2-3 nucleoli per cell are seen. Their number, size and shape generally are species specific and relate to the synthetic activity of the cell.[1]

In a closed phase nucleus, the nucleus is small with a defined outline and uniform nuclear chromatin that indicates that the cell is in resting phase. In such cells, the nucleolus can be seen only during interphase.

The most prominent substructure within the nucleus is the nucleolus. It is a dense non-membrane bound structure observed during interphase in a normal cell, because it dissipates during cell division.[1]

The nucleolus is the site of rRNA synthesis, transcription and processing. It is designed to fulfill the need for large-scale production of rRNA and assembly of the ribosomal subunits.[2] Ultrastructurally, it consists of components like fibrillar center, dens fibrillar component, granular component, condensed chromatin that is inactive, interstices and nucleolar vacuole.[3]

rRNAs are essential for the formation of ribosomes. This involves the assembly of the ribosomal precursor RNA with both ribosomal proteins and 5S rRNA. The genes that encode ribosomal proteins are transcribed outside of the nucleolus by RNA polymerase, yielding mRNAs that are translated on cytoplasmic ribosomes. The ribosomal proteins are then transported from the cytoplasm to the nucleolus, where they are assembled with rRNAs to form pre-ribosomal particles.[2-4]

For routine histopathological examination, tissue sections are stained with hematoxylin and eosin. Here, hematoxylin, which is a basic dye, binds to negatively charged structures like DNA, RNA and stains the nucleus hematoxyphilic in the normal interphase nuclei. Eosin, an acidic dye, which has an affinity for positively charged structures such as mitochondria, cytoplasmic proteins and ribosomal proteins, stains them eosinophilic in color.

However, in a cell that is actively synthesizing proteins and possesses increased amounts of pre-ribosomal particles (protein factories), the nucleoli are positively charged and may stain amphophilic to eosinophilic owing to their very high protein content.

The importance of ribosomal production is particularly evident in oocytes and actively growing mammalian cells in which the rRNA genes are amplified to support the synthesis of large number of ribosomes required to meet the need for protein synthesis.[2]

In cancerous cells, the cell's entry into cell cycle is always

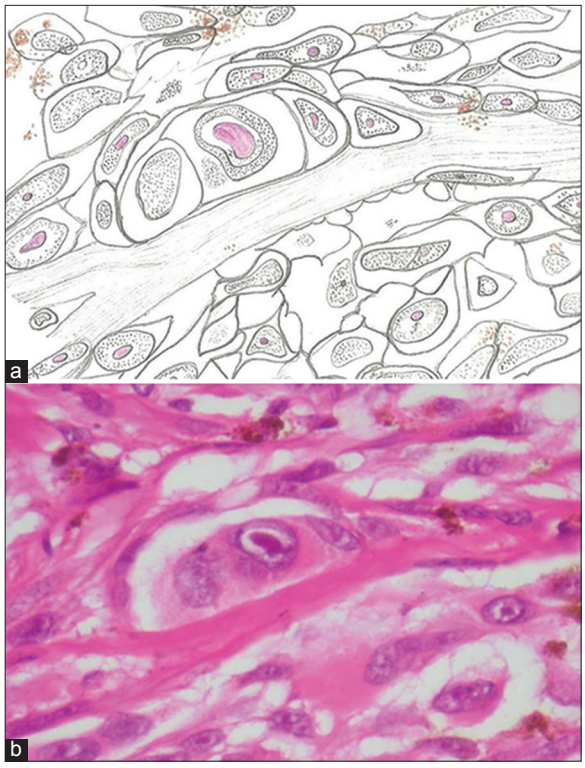

Figure 1: (a) Photomicrograph shows tumor cells with ill-defined cell borders, abundant cytoplasm and open phase nucleus with prominent eosinophilic nucleoli (H&E stain, ×400). (b) Hand-drawn illustration of the same

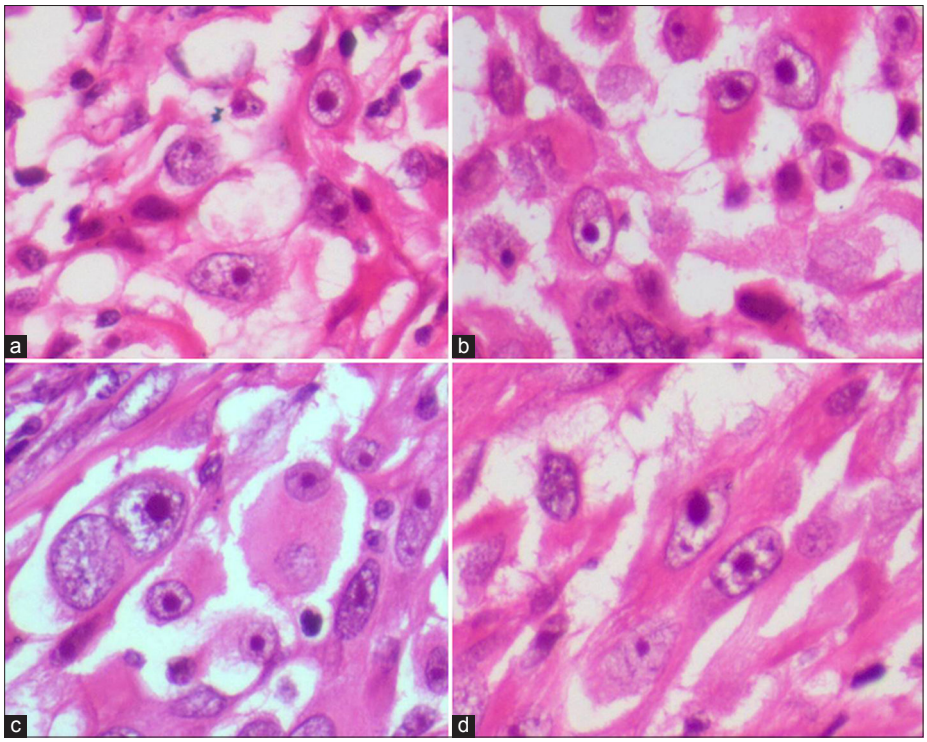

Figure 2: (a-d) Photomicrograph shows predominantly epithelioid cells with ill-defined cell borders exhibiting abundant cytoplasm and open phase nuclei with prominent inclusion-like eosinophilic nucleoli (H&E stain, ×400)

associated with up-regulation of the nucleolar function and increased nucleolar size, which is directly dependent on the rapidity of cell cycle proliferation. These changes observed are a consequence of increased metabolic requirement, including the rate of ribosome biogenesis that characterizes the proliferating cells. Hence, the nucleolus is the mirror for a series of metabolic changes that characterize cell proliferation.[3-5]

As the amount of pre-ribosomal proteins increase in these cancerous cells, they may exhibit amphophilic to eosinophilic nucleoli upon staining with hematoxylin and eosin stain.

Few lesions/pathologies where eosinophilic nuclei can be encountered include:

- Classical Reed-Sternberg cells:[6,7] The hallmark of Hodgkin's lymphoma is characterized by bilobed or multinucleated nucleus with prominent eosinophilic inclusions-like nucleoli resembling an "owl's eye"
- Malignant melanoma[8]
- Myeloid sarcoma[9]
- Carcinoid tumors[10]
- Colon carcinoma[11]
- Ewing's sarcoma[12]
- Peripheral neuroectodermal tumor[13]
- Rhabdomyosarcoma[14]
- Olfactory neuroblastoma[15]
- Nephroblastoma or Wilms' tumor[16]
- Poorly differentiated squamous cell carcinoma
- Anaplastic carcinoma.

This article illustrates this interesting feature, which was observed in a case of malignant melanoma in a 65-year-old male patient. Microscopically, the lesion presented as a highly cellular pleomorphic tumor with the tumor cells arranged in the form of fascicles, pseudo-organoid and storiform pattern. The cells were of varied morphology ranging from spindle to ovoid to epitheliod. They exhibited cellular and nuclear pleomorphism; increased mitoses and were almost completely devoid of melanin pigmentation. Most of the tumor cells showed the presence of eosinophilic nucleoli representing an actively synthesizing cell, which aided in arriving at a diagnosis of malignant melanoma. A panel of immunohistochemical markers was instituted and the diagnosis was confirmed.

A high-power view of the tumor cells along with a hand-drawn illustration of the lesion is presented in Figure 1. The H and E stained images of the tumor cells is presented in Figure 2.

ACKNOWLEDGEMENT

- Department of Oral and Maxillofacial Pathology, Krishnadevaraya College of Dental Sciences, Bangalore
- Dr. GVV Satyakiran, Postgraduate student, Department of Oral and Maxillofacial Pathology, Krishnadevaraya College of Dental Sciences.

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Access this article online

Quick Response Code:

Website: www.jomfp.in

DOI: 10.4103/0973-029X.140716

How to cite this article: Bavle RM. Eosinophilic Nucleoli. J Oral Maxillofac Pathol 2014;18:152-4.

Source of Support: Nil. **Conflict of Interest:** None declared.