

# ONCOCYTES-AN ENIGMA OR DILEMMA

Brijendra Singh\*, Meenakshi Chowdhary\*\*

\*MBBS, MS, DNB, MNAMS Additional Professor, Department of Anatomy,  
All India Institute of Medical Sciences, A.I.I.M.S-Jodhpur

\*\*BDS, PG III yr, Department of Oral & Maxillofacial Pathology & Microbiology,  
I.T.S Centre for Dental Studies & Research, Ghaziabad, Uttar Pradesh, India

## ABSTRACT

Oncocytes are epithelial cells which appear as cells with abundant, granular, eosinophilic cytoplasm, a central pyknotic nucleus, and ultrastructurally are crammed with numerous mitochondria of various sizes. Oncocytic cells are thought of as metaplastic cells formed in response to adverse changes, with the normal cells losing their original specialization. Aging is also thought to cause a functional exhaustion of mitochondrial enzymes, and a compensatory hyperplasia of mitochondria can occur, which in turn is responsible for the oncocytic change. Through this paper we had enlightened facts about oncocytes.

### Key Words:

Oncocytes, Oncocytoma, Mitochondria, Neoplasia.

## BACKGROUND:

Large cell with small irregular nuclei and dense acidophilic granules due to presence of abundant mitochondria are oncocytes.<sup>1</sup> **Synonyms:** (Oxyphil cells, hurthle cell and askenazy cell) **Oxyphil cells** are oncocytes found in oncocytoma of kidney, salivary gland and endocrine gland. In thyroid gland they are referred as **hurthle & askenazy cells**.

Neoplasm composed predominantly or exclusively of this kind of cells is called 'oncocytic'. Such tumours have been described in the overwhelming majority of organs; kidney, thyroid, lacrimal gland, pituitary gland, salivary gland, adrenal, parathyroid, preganglia, respiratory tract, paranasal sinuses, pleura, liver, pancreato-biliary system, stomach, colon, rectum, CNS, female & male genital tracts, skin and soft tissues.

### What are oncocytes?

Oncocytes are epithelial cells characterised by an abundant mitochondria, granular & eosinophilic cytoplasm, and a centrally situated nucleus. Oncocytes were first observed by Schaffer 1897 in human minor salivary glands; similar cell have been observed not only in salivary glands but also in numerous other organs.<sup>1</sup>

'**Biological significance**' of Oncocytes has not yet been revealed but they are found to occur singly or in small clusters and appear to increase in frequency

with age of individual.

Ultrastructural studies have revealed that cytoplasm of these cells is filled with numerous tightly packed mitochondria showing various pleomorphism. Pathologically a review of literature reveals that the existence of several oncocytic salivary gland lesions e.g.: nodular or diffuse hyperplastic lesion (oncoytosis, oncocytoma) benign or malignant and other tumors with less or more prominent oncocytic component. Few reports of animal study have been examined ultrastructurally.<sup>2,3</sup> During an experimental study of autoimmune sialadinitis in mice, multinodular hyperplastic foci of oncocytes were found and observed.<sup>4</sup> In light microscopy nodular hyperplastic foci measuring 1.8mm in diameter were very characteristic and rather uniform, they were often lobulated and usually circumscribed but real encapsulation was not found.<sup>4</sup> The characteristic appearance of cell displayed an oncocytic appearance i.e large cells rich in eosinophilic & fine granular cytoplasm, polyhedral or ovoid in contour with centrally situated pyknotic nuclei. Further, more varying number of basophilic fine granules scattered in cytoplasm.<sup>4,5</sup> The cells were arranged in solid masses and some were in tubular arrangement and smooth plasma membrane. In solid masses cells with lobular architecture were separated by myoepithelial cells and Oncocytes were attached to adjacent cells by junctional complexes.<sup>5</sup> Smooth plasma membrane,

### Address for Correspondence:

Dr. Brijendra Singh

Additional Professor, Department of Anatomy, All India Institute of Medical Sciences, Basni Industrial Area, Jodhpur (Rajasthan) PIN: 342005 INDIA Mobile No: 08003996900, 09811410309, drbrijendrasingh@gmail.com

large nucleus with frequent marginal indentations and indistinct nucleoli cytoplasm was highly packed with mitochondria which varied in shape and size. The mitochondrial cristae were increased in number and closely packed. No mitochondrial dense bodies or glycogen granules were seen small & dense granules were scattered in intermitochondrial areas.<sup>1,3</sup>

#### **Pathogenesis:**

Within salivary gland parenchyma adjacent to hyperplastic foci of oncocytes that occurred singly or in small groups; Intermediate type cells between oncocytes and normal salivary glands, epithelial cells have been observed which might represent the oncocytic transformation of salivary gland.<sup>5,6</sup> Epithelial cells in various stages were found in duct system. This oncocytic transformation is more frequent in granular ducts less in striated duct and still less in other regions. In early stages of oncocytic transformation non oriented mitochondria increase gradually in number and size in cytoplasm of duct cells. As oncocytic transformation progressed the cytoplasm gets filled with tightly packed randomly oriented mitochondria, the basal striations disappeared and nucleus showed pyknotic appearance. Furthermore, oncocyte transformed cells were observed to form hyperplastic foci, some of which have solid or tubular arrangement in such foci various stages of oncocytic transformation was suggestive of ability to develop hyperplastic or neoplastic lesion.<sup>4</sup>

Some authors referred oncocytes as benign epithelial cells that appear in young adult life and which may form tumour nests and cord of cells; especially in parotid gland such tumors grow slowly and are painless.

#### **Location:**

Oncocytes may be found in small groups/scattered in otherwise normal organs such as thyroid gland. Though oncocytic epithelium is part of Warthin's tumor. Schaffer in 1877 observed oncocytes in salivary gland of man, but it was in 1931 Hamper did a comprehensive study and found oncocytes in serous and mixed glands of tongue, pharynx oesophagus, and trachea.<sup>5,6</sup> It was Tremblay in 1969 who reported oncocytes in thyroid, parathyroid, pituitary, adrenal, pancreas, gallbladder, fallopian tubes and lacrimal glands.<sup>6</sup> Also oncocytes were later studied in bronchial glands.<sup>7</sup>

#### **Staining of oncocytes:**

Characteristic appearance of oncocytes in H&E stain is granular appearance, eosinophilic

cytoplasm with centrally situated pyknotic nuclei.<sup>13,14</sup> Oncocytes in bronchial glands showed high enzyme activity and did not stain with periodic acid schiff stain.<sup>8</sup>

#### **Special stain:**

Mitochondria of oncocytes are strongly positive with phosphotungstic acid haematoxylin stain (PTAH stain). Immunohistochemistry showed a ductal epithelium population with ductal positivity for AE1/AE3, CK19, CK7 antibodies and basal cell positivity for P63, CK14, CK5, CK6 antibodies differentiation in oncocytic areas.<sup>9</sup> In massonfontanna staining, brownish granules in cytoplasm of oncocytic cells were positive suggestive of melanin as stained negative for berlin blue staining was indicative of melanin rather than haemosiderin in case of melaniconcocytic metaplasia of nasopharynx.<sup>10</sup>

#### **Oncocytes as an entity of age related changes:**

These cells are referred as benign epithelial cells that appear in young adult life. They are found commonly with increasing age and are supposed to be most frequent in collecting duct of bronchial glands.<sup>5,7</sup> The frequency of oncocytes as age related suggest that they are not normal but sign of degeneration. It is commonly believe that oncocytes represent a peculiar form of degeneration of epithelial cells and they have diminished secretary activity.<sup>6,11</sup>

#### **Role of oncocytes:**

Various hypothesis are laid, since oncocytes are usually found in secretory epithelial tissue and likely represent altered cells ,suggest a secretory function for ductal epithelium.<sup>12,13</sup> The term oncocyte is an unfortunate one as it may be thought to imply neoplastic change, but is a word in current usage and no other satisfactory alternative is available.

#### **Various pathological lesions involving Oncocytes:**

Oncocytic adenocarcinoma, oncocytic adenoma, metastatic oncocytic adenocarcinoma; The oncocytic metaplasia is a well established pathological entity that may occur in many organs including salivary glands, thyroid, parathyroid and kidney.<sup>10</sup> The melaniconcocytic metaplasia is usually small in size with a benign clinical course and should not be misdiagnosed with melanoma or carcinoma.<sup>11</sup> Oncocyticlipoadenoma of salivary gland is an exceptional benign tumor arising in parotid gland & submandibular gland.<sup>9</sup>

## DISCUSSION

Oncocytic lesions are characterized pathologically by an abundance of oncocytes. That is large eosinophilic and finely granular cells enriched in mitochondria; they can arise in numerous organs and tissues often in endocrine glands and have been associated with hyperplasia, autoimmunity and neoplasia.<sup>14</sup>

Neoplasm with oncocytic cells like warthin tumor, oncocytoma, oncocytic carcinoma, salivary duct carcinoma, acinic cell carcinoma, metastatic hurthle cell carcinoma from thyroid and rarely mucoepidermoid carcinoma are being pursued in study these days, trying to find out its correlation with oncocytes.<sup>15</sup>

Like, difference between clear cells and oncocytes is a question and giving it a valuable explanation of clear cell being referred as vacuolated cytoplasm that exist as aneuploidy pattern/heterogenicity while oncocytes have eosinophilic proliferation by tendency exist in diploidy pattern need experimental study follow up ; that can be an area of future prospects of interest.<sup>16</sup>

In contrast to diffuse oncocytosis remnants of original salivary tissue with acini and fatty tissue are usually present between oncocytic nodules, typical oncocytomas may possibly develop from such oncocytic proliferation by tendency to its confluent growth.<sup>17</sup>

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# Obituary



## Prof. G.L. SHAH

Date of birth	: 1.1.1955
High School	: 1971
M.B.B.S.	: 1982
M.S. Anatomy	: 1986
Lecturer	: Kasturba Medical College 1987, Karnataka
Asstt. Professor, IMS, BHU	: 1983
Professor, IMS, BHU	: 2009
One son, one daughter	: Both are married
Expired in sudden illness with cardiac arrest on 28.8.2014	