REVIEW ARTICLE

Oncocytic mania: A review of oncocytic lesions throughout the body

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ABSTRACT. Oncocytic lesions are characterized pathologically by an abundance of oncocytes, that is by enlarged, 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. The causes and mechanisms that transform a normal cell into an oncocyte remain to be elucidated. Aim of this article is to review the most common oncocytic lesions, highlighting their key pathological features and clinical significance. (J. Endocrinol. Invest. 34: 383-394, 2011) ©2011, Editrice Kurtis

INTRODUCTION AND COMMON FEATURES OF ONCOCYTIC LESIONS

Oncocytic lesions comprise a heterogeneous group of conditions characterized pathologically by the presence of oncocytes. Oncocytes (swollen cells) are enlarged, bold cells with a characteristic cytoplasm that appears deeply eosinophilic (oxyphilic) and finely granular due to the abundance of mitochondria. Oncocytes were first described in the early 1890s by Schaffer in a histological review of numerous human organs (1), and then confirmed in 1898 by Askanazy in the thyroid (2) and by Welsh in the parathyroid glands, where he named them “oxyphilic cells” (3). These early descriptions went unrecognized for about three decades until 1931 when Hamperl confirmed their presence in the salivary glands and coined the term “oncocytic” (4), later expanded to “oncocytoma” (5).

We have queried PubMed database using “oncocyt*” and “oxyphil*” keywords, and reviewed the 10 volumes on the classification of human tumors published by the World Health Organization: central nervous system (volume 1), hematopoietic and lymphoid tissues (volume 2), digestive system (volume 3), breast and female genital organs (volume 4), soft tissue and bone (volume 5), skin (volume 6), urinary system and female genital organs (volume 7), endocrine organs (volume 8), head and neck (volume 9), and lung, pleura, thymus, and heart (volume 10). We organized this review in 3 sections. First, we will summarize the common features of oncocytic lesions. Next, we will review the major oncocytic lesions throughout the body, summarized in Table 1, following an anatomical layout and underlying the more notable clinical entities. Finally, we will present current views on the pathogenesis of oncocytic lesions.

Oncocytic lesions originate mainly from epithelial cells and occur in 2 main types of settings: during inflammation and autoimmunity, where they are considered a form of metaplasia (a reversible change of the epithelial cell into a different epithelial cell, oncocytic metaplasia); and during a neoplastic process of benign (oncocytoma) or malignant nature (oncocytic carcinoma). There is not universal agreement on the extent of oncocytic transformation needed to classify a lesion: in general, in metaplasia there is only partial substitution of the epithelium by oncocytes (6). Oncocytic lesions are typical of adults, between the 5th and 7th decade of life (7, 8), but have also been described in children (9, 10). They are often asymptomatic and discovered serendipitously during diagnostic procedures performed for unrelated reasons. More rarely, they present with signs and symptoms of mass effect, due to compression of the nearby structures. Therefore, pain (11-13), weight loss (14, 15), obstruction, bleeding (16, 17), and organ-specific symptoms (like decreased visual acuity, and hearing impairment) are described.

Oncocytic lesions lack distinctive radiological features. Their diagnosis is based on microscopic examination of the resected specimen. Using the routine hematoxylin and eosin stain, oncocytes appear as enlarged (10-15 μm) cells arranged in a solid trabecular or organoid pattern. Their cytoplasm is finely granular and deeply eosinophilic (acidophilic) (Fig. 1). This characteristic cytoplasmic appearance is due to an increased number and size of mitochondria, as first suggested in 1936 by Eisen in a patient with Riedel thyroiditis (18). The nucleus is enlarged and often shows a prominent nucleolus (Fig. 1). Special stains can enhance oncocytic features: phosphotungstic acid hematoxylin emphasizes mitochondrial clumps, resulting in a dense blue cytoplasmic granularity; Luxol fast blue reacts with lipoproteins; dyes like cresyl violet and thionin stain oncocytes with more than one color (metachromasia); and periodic acid-Schiff is positive due to the high glycogen and mucin content (19, 20). Electron microscopy clearly reveals the increased number of mitochondria and their often swollen and bizarre form. It also
highlights the paucity of other subcellular organelles, the desmosomal attachment between oncocytes, and the increased content of β-type glycogen in the cytosol (8), a finding consistent with the high uptake of oncotic lesions display on positron emission tomography using fluorodeoxyglucose (11, 21). Detection of increased mitochondrial DNA (22) and mitochondrial antibodies (19, 20) supports the diagnosis of oncocytes.

Surgery is the treatment of choice for oncotic lesions and is curative for the benign forms (23). Even for malignant lesions the prognosis is usually good since recurrences and nodal metastases are rare (24, 25). Due to the low radiosensitivity of oncotypic tumors, post-operative radiotherapy is usually not indicated unless extensive local involvement and/or positive margins are present. The role of chemotherapy remains controversial (24, 25).

ONCOYTIC LESIONS OF THE HEAD AND NECK

Brain
Oncotic changes can be seen in meninges (26, 27), choroid plexus (10), or cerebellar vermis (28), although they are extremely rare. Meningiomas exhibit a wide range of morphologic ap-