Salivary gland tumors are rare, comprising less than 3% of all neoplasms of the head and neck region. The majority of salivary tumors are located in the parotid gland (70%), followed by the minor salivary glands (22%) and the submandibular glands (8%) [1]. Oncocytic tumors comprise only 1% of all salivary gland tumors [2]. Oncocytic carcinomas are even more uncommon, representing 11% of all oncocytic salivary gland neoplasms, 0.5% of all epithelial salivary gland malignancies and 0.18% of all epithelial salivary gland tumors [3]. Oncocytic carcinoma arising in the salivary glands, first described by Bauer and Bauer in 1953, is a rare, predominantly oncocytic neoplasm [3,4]. Moreover, oncocytic carcinoma arising in the submandibular gland is an extremely rare tumor and only 11 cases have been reported to date [5]. We report a 51-year-old man with a previously benign oncocytoma in his submandibular gland that transformed from a benign morphology to malignant cellular atypia and mitosis. To our knowledge, the current report is the first published case of a malignant transformation from benign oncocytoma to oncocytic carcinoma of the submandibular gland. The proliferative activity of the tumor cells was evaluated immunohistochemically using antibodies against Ki-67.

Key Words: benign oncocytoma, Ki-67 immunohistochemical stain, malignant transformation, oncocytic carcinoma, submandibular gland


CASE PRESENTATION

A 51-year-old man presented with a recurrent mass in his left submandibular gland in August, 2008, and a prior diagnosis of benign oncocytoma in the same location. In February, 2005, he underwent total tumor ablation for the benign oncocytoma in his left submandibular gland. Pathological examination of the resected tissue of the earlier specimen revealed an encapsulated tumor (Figure 1A) composed of uniform oncocyes with fine chromatin and indistinct nucleoli (Figure 1B). Mitotic figures were rarely found.
At the current presentation, he had a painless swollen mass in the previously resected area. This lesion had been slowly growing for 4 months. On clinical examination, the mass was about 3.0 × 2.5 cm in size, hard, rubbery and fixed. A palpable cervical lymphadenopathy was also found. The facial nerve and other cranial nerves functioned normally. Neck sonography revealed one well defined heterogeneous mass lesion in the left submandibular space, measuring 3.3 × 2.8 cm in size. Several lymph nodes surrounding the tumor were swollen, with the largest one measuring about 1.2 × 0.9 cm in size. Computed tomography of the neck demonstrated one enlarged mass lesion about 3.0 cm in diameter in the left submandibular region (Figure 2A) and an enlarged lymph node, of about 1.4 cm in diameter, anterior to the submandibular mass (Figure 2B). Because recurrence of the oncocyteoma was suspected, radical tumor resection with unilateral, modified neck dissection (levels I–III) was performed in September 2008.

Microscopically, the resected tumor revealed infiltrating growth and was composed of atypical oncocytes arranged in solid sheets. Marked nuclear atypia, cellular polymorphism and mitoses were observed (Figure 3A). Focal areas of necrosis were also found. The tumor had invaded the surrounding tissue, including the muscular tissue, perineural spaces and lymphatic vessels (Figure 3B). Three of the four lymph nodes were enlarged, with the largest one measuring about 1.2 × 0.9 cm in size. The tumor was well encapsulated, with uniform oncocytes with abundant eosinophilic granular cytoplasm, fine chromatin, indistinct nucleoli and rare mitoses (hematoxylin and eosin; original magnification, 400×).

Figure 1. (A) The tumor was well encapsulated (hematoxylin and eosin; original magnification, 100×). (B) Uniform oncocytes with abundant eosinophilic granular cytoplasm, fine chromatin, indistinct nucleoli and rare mitoses (hematoxylin and eosin; original magnification, 400×).

Figure 2. (A) Axial computed tomography revealed a mass with central necrosis in the left submandibular region (arrows). (B) One enlarged lymph node was found anterior to the mass (arrow).
nodes contained tumor metastases. Therefore, the diagnosis of oncocytic carcinoma was established.

We performed immunohistochemical stains with antibodies against Ki-67 (MIB-1, DAKO) to evaluate the proliferative activity of the earlier and current tumors. The frequency of Ki-67-positive cells was lower (<1%) in the patient’s previous oncocytoma (Figure 4A) than in the current oncocytic carcinoma (15–30%) (Figure 4B). We assumed from these clinical and immunohistochemical findings that this malignant tumor had transformed from the previously benign oncocytoma. The patient received postoperative adjuvant radiotherapy in the left submandibular tumor bed (total 66 Gy), left submental space and ipsilateral neck (total 59.4 Gy). He had no evidence of recurrence after 6 months of follow-up.

**DISCUSSION**

The German pathologist Hürthle was the first researcher to describe oncocyes as components of normal canine thyroid glands in 1894 [6]. The term oncocye was only coined in 1931 by Hamperl to describe cells within Warthin’s tumor with abundant granular eosinophilic cytoplasm [7]. The predominant ultrastructural feature of oncocyes is marked mitochondrial hyperplasia [8]. Oncocytes have since been described in many human tissues, including the salivary gland, lacrimal gland, ocular caruncle, parathyroid, thyroid, pituitary, esophagus, liver, pancreas, kidneys, adrenals, testicles and ovaries [2–4,9,10]. The diagnostic criteria of oncocytic carcinoma are as follows: (1) no encapsulation; (2) local invasion;
Available chemotherapeutic agents do not provide sustained remission [19–21]. In addition, patients who underwent aggressive initial surgical intervention had significantly better prognoses than those treated conservatively [11]. Meanwhile, Nakada et al concluded that distant metastasis appeared to be the most important prognostic feature of oncocytic carcinoma [23].

To our knowledge, immunohistochemical transformation from benign oncocytoma to oncocytic carcinoma of the submandibular gland has never been reported. Further investigation of the prognosis of patients with oncocytic carcinoma of the submandibular gland is warranted as more cases are reported.

**REFERENCES**


下顎腺良性嗜酸細胞瘤轉變為惡性嗜酸細胞瘤：
病例報告

李宗勳¹ 林永松¹ 李文瑛² 吳泰清³ 張世倫⁴
財團法人奇美醫學中心 ¹耳鼻喉部 ²病理部 ³放射部

下顎腺惡性嗜酸細胞瘤是一種極罕見的腫瘤，根據我們所能查到的文獻資料顯示，
截至目前為止只有十一例病例報告被文獻記載，而由下顎腺良性嗜酸細胞瘤轉變為惡性
嗜酸細胞瘤的病例，在世界上是從來沒有被發表過的。由於下顎腺惡性嗜酸細胞瘤
如此罕見，本報告提出一 51 歲男性，於 2005 年曾接受左側下顎腺良性嗜酸細胞瘤手
術切除，於 2008 年於左側下顎腺的相同位置發現另一個腫瘤，經手術切除後，透過
臨床及免疫組織化學染色技術 Ki-67 表現數目多寡，我們合理的認定此復發的腫瘤已
經由過去的良性嗜酸細胞瘤轉變為惡性，藉提出此一罕見病例以供討論，並於本報告
中將惡性嗜酸細胞瘤流行病學、診斷、治療與預後做一簡短的文獻回顧。

關鍵詞：良性嗜酸細胞瘤，Ki-67 免疫組織化學染色法，惡性轉變，惡性嗜酸細胞瘤，下顎腺
（高雄醫誌 2010;26:327–32）

收文日期：98 年 9 月 7 日
接受刊載：98 年 10 月 13 日
通訊作者：張世倫醫師
財團法人奇美醫學中心耳鼻喉部
710 台南縣永康市中華路 901 號