

CASE REPORT

# Value of imaging and aspiration cytology in the diagnosis of oncocytic carcinoma

## *Valore della radiologia e della citologia aspirativa nella diagnosi del carcinoma oncocitario*

T. PUSIOL, I. FRANCESCHETTI, I. PISCIOLI<sup>1</sup>, M.A. BELTRAME<sup>2</sup>, M. POLCE<sup>2</sup>, C. SASSI<sup>3</sup>

Institute of Anatomic Pathology, S. Maria del Carmine Hospital, Rovereto (TN); <sup>1</sup>Department of Radiology, Budrio Hospital, Budrio (BO); <sup>2</sup>Division of Otorhinolaryngology, S. Maria del Carmine Hospital, Rovereto (TN); <sup>3</sup>Clinical Department of Radiological and Histocytopathological Sciences, Imaging Diagnostic Section, Bologna University, S. Orsola Hospital, Bologna, Italy

### SUMMARY

Oncocytic carcinoma of the parotid gland is a rare neoplasm. To date 70 cases have been described in 55 reports. To the best of our knowledge the simultaneous occurrence of oncocytic carcinoma and second malignancy in another site (outside the parotid gland) has not been reported. An oncocytic carcinoma of the parotid gland is described in 56-year-old male with simultaneous breast cancer, emphasising the value of aspiration cytology and imaging procedures in the diagnosis of parotid neoplasms.

**KEY WORDS:** Parotid gland • Malignant tumours • Oncocytic carcinoma • Fine-needle aspiration cytology • Male breast cancer

### RIASSUNTO

*Il carcinoma oncocitario della parotide è raro. Sino ad oggi sono stati riportati 70 casi in 55 lavori. La contemporanea insorgenza del carcinoma oncocitario e di una seconda neoplasia maligna in altra sede non è stata mai descritta. Descriviamo il caso di un carcinoma oncocitario della parotide in un uomo di 56 anni con simultaneo sviluppo di carcinoma mammario sottolineando il valore della citologia aspirativa e delle tecniche radiologiche nella diagnosi della neoplasia parotide.*

**PAROLE CHIAVE:** Parotide • Tumori maligni • Carcinoma oncocitico • Esame citologico • Carcinoma mammella maschile

Acta Otorhinolaryngol Ital 2010;30:110-114

## Introduction

Physical examination does not always succeed in a pre-operative differential diagnosis between benign and malignant parotid tumours. Thus, diagnostic modalities, such as fine-needle aspiration cytology (FNAC) and imaging, play an important role in the work-up of patients with parotid mass lesions.

Oncocytic carcinoma (OC) of the parotid gland is a rare neoplasm. Bauer and Bauer<sup>1</sup> reported the first case in 1953 and, to date, 70 cases have been described in 55 reports. The simultaneous occurrence of OC and a second malignancy in another site has not been reported up to now. Herein, the case is described of an OC of the parotid gland, in a 56-year-old male, with simultaneous breast cancer, stressing the value of aspiration cytology and imaging procedures in the diagnosis of parotid malignancy.

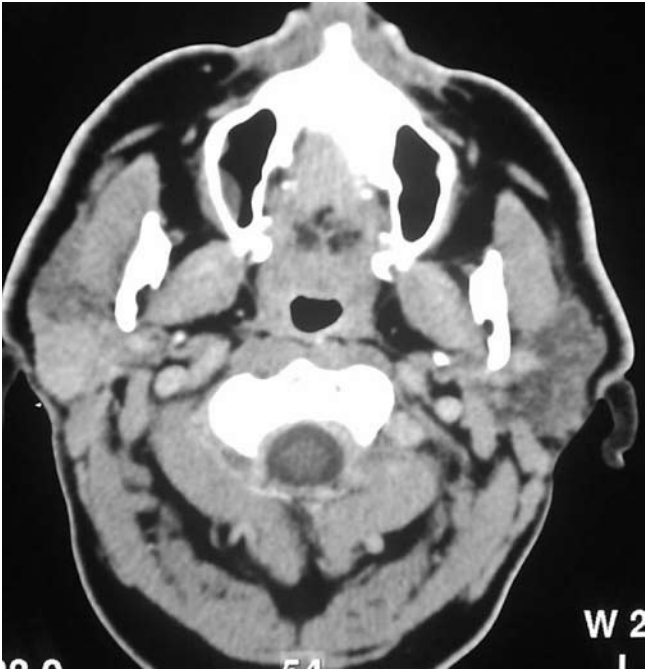
## Case presentation

In June 2006, a 56-year-old male was referred to the Otorhinolaryngology Division for a painless right preauricular mass which had been gradually increasing in size for a year. Computed tomography (CT) showed an enhanced signal of the right parotid gland with a homogeneous hyperdense mass (3.5 cm in diameter) with regular contours; on the medial site, the mass was indistinguishable from the adjacent anatomic structures (Fig. 1).

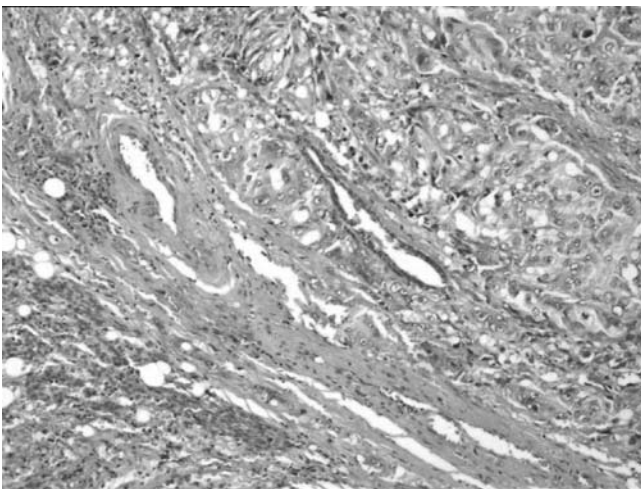
The facial nerve was functionally normal. FNAC revealed oncocytes with mild atypia. Total parotidectomy with facial nerve preservation was performed. The mass was firm, multi-nodular, unencapsulated, grey-brown and measured 3.5 x 3 cm.

The frozen section showed a malignant infiltrative growth pattern.

Histology showed the typical features of oncocytic carcinoma (Fig. 2). The tumour cells were positive for immu-



**Fig. 1.** CT shows enhanced signal of right parotid gland with homogeneous hyperdense mass (2.5 cm in diameter) with regular contours; at medial site, mass is indistinguishable from adjacent anatomic structures.



**Fig. 2.** Oncocytic carcinoma. Sheets, islands and nests of large, round to polyhedral cells, with fine, granular, eosinophilic cytoplasm and central, round, vesicular nuclei, often with prominent nucleoli (H&E 100X).

no-histochemical stain with anti-mitochondria antibody (Mitochondria antibody SPM198, Abcam).

Post-operatively, the patient received radiotherapy (6300 rad) to the surgical site. In January 2007, the patient was referred to the Surgical Division for a left mammary nodule. In the aspiration cytology, malignant cells were found. Total mastectomy with axillary lymph-adenectomy was performed. The histological examination of the surgical specimen showed invasive ductal carcinoma, grade III (Nottingham Histological Score), with metastasis in 12 axillary lymph nodes (tumour deposits > 2 mm

(pT1c pN3a M0 G3). Immuno-histochemistry analysis exhibited 90% positivity for oestrogen receptor (Estrogen Receptor  $\alpha$  clone SP1, Dako, Glostrup, Denmark), 80% for progesterone receptor (Progesteron Receptor clone SP2, Dako, Glostrup, Denmark), 40% for Ki-67 (Ki-67 clone SP6, Dako, Glostrup, Denmark). Her-2 evaluation showed a 10% of neoplastic positive cells, score 2 (HERCEP TEST, Dako, Glostrup, Denmark). FISH analysis showed Her-2 amplification. The treatment administered for breast carcinoma was Tamoxifen 20 mg/day and 17 cycles of Herceptin. For the parotid carcinoma, ultrasound follow-up was decided with no additional therapy. At present, the patient is free from disease.

## Discussion

The role of imaging in the assessment of a salivary gland tumour is to define the intra-glandular vs extra-glandular location, to detect malignant features, to assess local extension and invasion and to detect nodal metastases and systemic involvement.

For parotid lesions, ultrasound (US) is a sensitive and efficient procedure for relatively superficial structures accessible by high resolution US which provides excellent resolution and tissue characterization without a radiation hazard. Cervical node involvement can also be assessed. US has a limited visualization of the deep lobe of the parotid gland.

A series of reports demonstrated the superiority of magnetic resonance imaging (MRI) over CT in delineating parotid mass lesions<sup>2,3</sup>. CT evaluates the cortical involvement and the presence of calculus disease in sialoadenitis (which may mimic a tumour) in a more precise way; but MRI is superior in defining tumour characteristics and extension, particularly an eventual perineural spread.

Among MRI features, only poorly defined margin and infiltration on non-enhanced non-fatsuppressed T1-weight images yielded a significant difference between benign and malignant parotid lesions.

In the recent literature, it was reported that the sensitivity of parotid FNAC ranges from 54% to 95%, specificity from 86% to 100% and accuracy from 84% to 97%<sup>4,7</sup>.

In the study of Inohara et al., of 81 patients with a parotid mass lesion (60 benign and 21 malignant), the sensitivity/specificity/accuracy of FNAC and MRI were 90%/95%/94% and 81%/92%/89%, respectively. FNAC or MRI served equally to predict the malignant nature of parotid mass lesions<sup>8</sup>.

The role of nuclear medicine and PET scan, in the imaging of parotid masses, has not yet been established<sup>9</sup>.

In conclusion, MRI is the procedure of choice in the identification of parotid malignancy, and the combination of FNAC and MRI yielded no diagnostic advantage over either modality alone.

**Table I.** Aspiration cytology in the diagnosis of malignant oncocytoma. Review of the literature.

Authors	Findings	Diagnosis
Eneroth 1965 <sup>10</sup>	Usual oncocytes mixed with oncocytic cells with marked atypia of the nucleus as well as morphologically typical carcinoma cells	Malignant Oncocytoma
Austin 1987 <sup>11</sup>	Single cells with copious, dense, granular cytoplasm and eccentric nuclei	Not performed
Haberman 1990 <sup>*12</sup>	NOS	Consistent with oncocytoma
Abdul-Karim 1991 <sup>13</sup>	Cytologically "benign" oncocytes	Oncocytoma
Scher 1991 <sup>14</sup>	NOS	Malignancy with oncocytic features
	NOS	Malignant epithelial neoplasm with oncocytic features
	NOS	Carcinoma with oncocytic features
	NOS	
Ramakrishna 1992 <sup>15</sup>	NOS	NOS
Laforga 1994 <sup>16</sup>	Cellular polymorphism, nuclear atypia, hyperchromatism, with nuclear membrane irregularities and prominent nucleoli	Consistent with a malignant tumour, confidently of oncocytic nature
Rajan 1994 <sup>17</sup>	Cells were predominantly dissociated, showed nuclear enlargement and pleomorphism, prominent nucleoli, multinucleation and contained abundant homogeneous cytoplasm	Malignant oncocytoma
Kandiloros 1995 <sup>18</sup>	NOS	Warthin's tumour
Harrison 1995 <sup>19</sup>	Partly cohesive cluster of oncocytes showing abundant, finely granular cytoplasm, mild nuclear pleomorphism and some nuclear overlapping. Cohesive sheets of polygonal oncocytic cells with narrow intercellular spaces conferring a "squamous" appearance	Primary salivary gland neoplasm of an unusual type, with characteristics suggestive of oncocytic or possibly squamous differentiation
Ardekian 1999 <sup>20</sup>	NOS	Adenocarcinoma
Cinar 2003 <sup>21</sup>	First aspiration: NOS	Warthin's tumour
	Second aspiration: oncocytes and atypical cells	Malignant epithelial tumour
Guclu 2005 <sup>22</sup>	Oncocytes and atypical cells	Malignant epithelial tumour
Caloglu 2006 <sup>23</sup>	Atypical epithelial cells	NOS

\* Aspiration cytology was performed on metastases near left stylomastoid foramen.

When malignancy is suspected on the basis of clinical or US data, MRI should be performed for all the patients candidate to surgery.

In the articles regarding FNAC and imaging of the parotid lesions, OC is not reported. Only a scrupulous review of single cases or small series of OC would permit clinical features, to be established, as well as outcome and value of FNAC and imaging in the management of this neoplasm. Regarding the 70 reported cases, age and sex were given in 61 patients. The age ranged from 30 to 93 years, with a mean and a median age of 62.7 years. Clinically, they usually presented as parotid masses. The size of the tumour ranged from 0.4 to 8 cm in maximum diameter (mean 4.01).

The function of the facial nerve was studied in 54 out of 70 patients and facial nerve paralysis was found in 16 cases.

Initial treatment was specified in 60 out of 70 patients (one patient refused the treatment) and the follow-up time was available in 44 cases, ranging from 3 to 150 months (mean 32 months).

Initial conservative surgery (tumorectomy, superficial pa-

rotidectomy) was performed in 13 cases for OC, in 3 cases for oncocytoma, in 1 case for pleomorphic adenoma, and in 1 case for undifferentiated malignant carcinoma, out of the 59 patients with clinical records of the treatment.

Radiation therapy was performed in 26 cases: in 1 case as the only treatment, in 10 cases associated with conservative surgery and in 15 cases associated with total parotidectomy.

Metastases to the cervical lymph nodes were present in 30 out of 70 patients. Other metastatic sites were lungs, liver, bone, parapharyngeal region and skin.

A total of 11 out of the 44 patients with available follow-up died of the disease and 3 from unrelated causes (pneumonia, cardio-respiratory failure and cerebro-vascular accident in the absence of local or metastatic disease).

FNAC and imaging procedures were reported in a small number of cases (Tables I-II)<sup>10-30</sup>.

In the diagnosis of OC, FNAC was first used by Eneroth<sup>10</sup>. Then, other reports described the use of this procedure in the diagnosis of this kind of neoplasm, with controversial opinions (Table I). In accordance with Harrison et al., we retain that OC aspiration cytology may

**Table II.** Radiological findings of oncocytic carcinoma: review of the literature.

Authors (first)	Procedure	Radiological findings
Whittam 1971 <sup>24</sup>	Arteriography	Left carotid arteriography. Presence of tumour vessels in the parotid swelling.
Scher 1991 <sup>14</sup>	MRI (Case 1)	2 cm mass within the deep portion of the parotid gland.
	MRI (Case 2)	Left parotid tumour with extraglandular extension.
	CT (Case 4)	Mass in the superficial portion of the parotid gland.
Negrier 1991 <sup>25</sup>	U	Neoplastic nodule with cervical lymphadenopathy.
Kondiloros 1995 <sup>18</sup>	TC	Tumour occupying superficial and deep portion of right parotid as well as a smaller tumour in upper part of left parotid.
Yoshihara 1997 <sup>26</sup>	MRI	Irregular and nonhomogeneous mass invading adjacent muscle tissue.
Mahnke 1998 <sup>27</sup>	U	Large cystic tumour.
	MRI	6.6 x 5.5 x 6 cm large tumour of left parotid gland with involvement of deep portions.
Ardekian 1999 <sup>20</sup>	CT	Nonhomogeneous mass of left parotid gland.
Kimura 2003 <sup>28</sup>	CT	4 x 4 cm isodense tumour.
Cinar 2003 <sup>21</sup>	CT	6 x 6 cm solid lesion in left superficial parotid region and several enlarged lymph nodes in parotid gland and on left side of patient's neck.
Guclu 2005 <sup>22</sup>	CT	A 3 x 3 cm solid lesion in left parotid gland.
Ozawa 2006 <sup>29</sup>	MRI	A 3.2 x 2.3 x 3.7 cm well circumscribed mass, located in superficial lobe of left parotid gland. Tumour was isointense on T1-weighted images, with no gadolinium enhancement, and of low intensity, with high-intensity area in central portion, on T2-weighted images.
Caloglu 2006 <sup>23</sup>	CT	3 x 3 x 2 cm solid lesion in left superficial parotid region.
Giordano 2006 <sup>30</sup>	CT	2 x 2.5 cm solid lesion in left parotid gland. Cervical and peri-aortic lymph nodes were not enlarged, except for one in submandibular region.

CT: Computed tomography; MRI: Magnetic resonance imaging; U: Ultrasound

display a spectrum of appearance from apparently benign to clearly malignant cells<sup>19</sup>. MRI was used in 5 cases, but the radiological reports are inadequate because the features of malignant parotid lesions (poorly defined margin and infiltration on non-enhanced non-fat suppressed T1-weight images) were not described.

In the present case, FNAC was inconclusive; CT had a limited value in determining the malignant nature of the neoplasm. We should have performed MRI but we did not manage to programme it before the surgical intervention and we based our diagnosis on the frozen section.

The simultaneous presence of two malignancies gives rise to problems in the choice of the treatment.

Consequently, the description of single cases of simulta-

neous malignant lesions could contribute to the comprehension of the biological behaviour.

Male breast cancer (MBC) is a rare tumour and accounts for less than 1% of breast cancers, but the incidence seems to be increasing<sup>31</sup>.

Some aspects of the aetiology of MBC are similar to those of the female counterpart. It has been estimated that there is a family history in about 5% of MBC patients.

In the review of the literature, OC has never been reported before in association with other primary malignancies of other sites, while MBC has only been reported in association with hepatocellular carcinoma.

MRI is the procedure of choice in the OC diagnosis when FNAC contains atypical oncocytic cells.

## References

- Bauer WA, Bauer JD. *Classification of tumors of the parotid gland. Study of one-hundred forty-three cases.* Arch Pathol 1953;55:328-46.
- Casselmann JW, Mancuso AA. *Major salivary gland masses: comparison of MR imaging and CT.* Radiology 1987;165:183-9.
- Raine C, Saliba K, Chippindale AJ, et al. *Radiological imaging in primary parotid malignancy.* Br J Plast Surg 2003;56:637-43.
- Al-Khafaji BM, Nestok BR, Katz LR. *Fine-needle aspiration of 154 parotid masses with histologic correlation.* Cancer 1998;84:153-9.
- Cohen EG, Patel SG, Lin O, et al. *Fine-needle aspiration biopsy of salivary gland lesions in a selected patient population.* Arch Otolaryngol Head Neck Surg 2004;130:773-8.
- Pitts DB, Hilsinger RL, Karandy E, et al. *Fine-needle aspiration in the diagnosis of salivary gland disorders in the community hospital setting.* Arch Otolaryngol Head Neck Surg 1992;118:479-82.



- <sup>7</sup> Zbaren P, Schar C, Hotz AM, et al. *Value of fine-needle aspiration cytology of parotid gland masses*. Laryngoscope 2001;111:1989-92.
- <sup>8</sup> Inohara H, Akahani S, Yamamoto Y, et al. *The role of fine-needle aspiration cytology and magnetic resonance imaging in the management of parotid mass lesions*. Acta Otolaryngol 2008;128:1152-8.
- <sup>9</sup> Alvi A, Myers EN, Carrau RL. *Malignant tumors of the salivary glands*. In: Myers EN, Suen JY, editors. *Cancer of the head and neck*. WB Saunders Co., Philadelphia. PA. 1996. p. 525-61.
- <sup>10</sup> Eneroth CM. *Oncocytoma of major salivary glands*. J Laryngol Otol 1965;79:1064-72.
- <sup>11</sup> Austin MB, Frierson HF, Feldman PS. *Oncocytoid adenocarcinoma of the parotid gland. Cytologic, histologic and ultrastructural findings*. Acta Cytol 1987;31:352-6.
- <sup>12</sup> Haberman RS, Rogers WA, Haberman PH. *Malignant oncocytic adenocarcinoma of the parotid gland with metastasis to bone*. Surg Pathol 1990;3:221-6.
- <sup>13</sup> Abdul-Karim FW, Weaver MG. *Needle aspiration cytology of an oncocytic carcinoma of the parotid gland*. Diagn Cytopathol 1991;7:420-2.
- <sup>14</sup> Scher RL, Feldman PS, Lambert PR. *Oncocytic malignancy of the parotid gland*. Otolaryngol Head Neck Surg 1991;105:868-76.
- <sup>15</sup> Ramakrishna B, Perakath B, Chandi SM. *Malignant multinodular oncocytoma of the parotid gland*. Indian J Cancer 1992;29:230-3.
- <sup>16</sup> Laforga JB, Aranda FI. *Oncocytic carcinoma of parotid gland: fine-needle aspiration and histologic findings*. Diagn Cytopathol 1994;11:376-9.
- <sup>17</sup> Rajan PB, Wadehra V, Hemming JD, et al. *Fine needle aspiration cytology of malignant oncocytoma of the parotid gland: a case report*. Cytopathology 1994;5:110-3.
- <sup>18</sup> Kandiloros D, Segas J, Papadimitriou K, et al. *Malignant oncocytoma of the parotid with oncocytic change of the contralateral gland*. Am J Otolaryngol 1995;16:200-4.
- <sup>19</sup> Harrison RF, Smallman LA, Young JA, et al. *Oncocytic carcinoma of the parotid gland: a problem in fine needle aspiration diagnosis*. Cytopathology 1995;6:54-8.
- <sup>20</sup> Ardekian L, Manor R, Peled M, et al. *Malignant oncocytoma of the parotid gland: case report and analysis of the literature*. J Oral Maxillofac Surg 1999;57:325-8.
- <sup>21</sup> Cinar U, Vural C, Basak T, et al. *Oncocytic carcinoma of the parotid gland: report of a new case*. Ear Nose Throat J 2003;82:699-701.
- <sup>22</sup> Guclu E, Oghan F, Ozturk O, et al. *A rare malignancy of the parotid gland: oncocytic carcinoma*. Eur Arch Otorhinolaryngol 2005;262:567-9.
- <sup>23</sup> Caloglu M, Yurut-Caloglu V, Altaner S, et al. *Oncocytic carcinoma of the parotid gland*. Onkologie 2006;29:388-90.
- <sup>24</sup> Whittam DE. *Malignant oncocytoma of the parotid gland*. Brit J Surg 1971;58:851-3.
- <sup>25</sup> Negrier MLM, Rivel J, Pinsolle J. *Carcinome oncocytaire de la glande parotide*. Ann Pathol 1991;11:359-69.
- <sup>26</sup> Yoshihara T, Satoh M, Yamamura Y, et al. *Ultrastructural study of oncocytoma and oncocytic carcinoma of the parotid gland*. J Clin Electron Microsc 1997;30:31-6.
- <sup>27</sup> Mahnke C. *Malignant oncocytoma of the parotid gland: Case report and review of the literature*. Australian J Oto-Laryngol 1998;7:1-5.
- <sup>28</sup> Kimura M, Furuta T, Hashimoto S, et al. *Oncocytic carcinoma of the parotid gland. A case report*. Acta Cytol 2003;47:1099-102.
- <sup>29</sup> Ozawa H, Fujii M, Matsunaga T, et al. *Oncocytic carcinoma of the parotid gland*. J Otolaryngol 2006;35:189-92.
- <sup>30</sup> Giordano G, Gabrielli M, Gnetti L, et al. *Oncocytic carcinoma of parotid gland: a case report with clinical, immunohistochemical and ultrastructural features*. World J Surg Oncol 2006;21:54-9.
- <sup>31</sup> Weiss JR, Moysich KB, Swede H. *Epidemiology of male breast cancer*. Cancer Epidemiol Biomarkers Prev 2005;14:20-6.

Received: January 25, 2009 - Accepted: June 8, 2009

Address for correspondence: Dott.ssa I. Franceschetti, Istituto di Anatomia Patologica, Ospedale di S. Maria del Carmine, Piazzale S. Maria 6, 38068 Rovereto (TN), Italy, Fax: +39 0464 403029. E-mail: ilaria.franceschetti@apss.tn.it