*The Journal of Laryngology & Otology (2006)*, ***120***, *885–887.*

doi:10.1017/S0022215106001642
Printed in the United Kingdom
First published online 23 May 2006

Clinical Record

# Retroperitoneal metastatic squamous cell carcinoma of the tonsil (with elevated beta human chorionic gonadotrophin): a misdiagnosis as extra-gonadal germ cell tumour

U Hofmann, MRCP, J P O'Connor, MRCS*, C S Biyani, MS, D Urol, FRCS(Urol), FEBU*, P Harnden, MD, PhD, FRCPath, MBA†, P Selby, CBE, MA, MD, FRCP, FRCR, FAMS, P M T Weston, M Ch, FRCS(Urol)*

**Abstract**

Head and neck cancers usually spread first to the regional lymph nodes but rarely may metastasize to distant sites. Metastasis to distant lymph node groups is a rare event. Furthermore, delayed multiple metastases without local recurrence is relatively uncommon. A case of retroperitoneal metastasis from a squamous cell carcinoma of the tonsil, secreting beta human chorionic gonadotrophin (β-hCG), is reported.

A 58-year-old man had undergone a tonsillectomy and chemo-radiotherapy for squamous cell carcinoma of the left tonsil and 13 months later presented with non-specific abdominal pain. The serum β-hCG levels were high and an abdominal ultrasound scan revealed hydronephrosis on the left side. A computed tomography scan demonstrated para-aortic retroperitoneal lymphadenopathy. The patient underwent an open lymph node biopsy. The initial pathological analysis was interpreted as extra-gonadal germ cell tumour and the patient received chemotherapy. A subsequent review was consistent with a metastatic squamous cell carcinoma of the tonsil, as immunohistochemical studies showed positive staining for epithelial membrane antigen and cytokeratins 5/6 but a negative reaction to placental alkaline phosphatase. Following this, the chemotherapy regimen was changed; however, a restaging scan demonstrated progression, and the patient died from aspiration pneumonia secondary to alcohol intoxication.

To our knowledge, this is the first reported case of retroperitoneal metastasis from a squamous cell carcinoma of the tonsil, secreting β-hCG and causing hydronephrosis. This case highlights the necessity of using clinical, histological, immunohistological and ultrastructural examination to establish precise diagnosis and to avoid inappropriate treatment.

**Key words: Squamous Cell Carcinoma; Tonsil; Retroperitoneal Neoplasms; HCG-Beta**

## Case report

A 58-year-old Caucasian man presented to his general practitioner with a three month history of non-specific abdominal pain. Thirteen months prior to presentation, the patient had undergone a tonsillectomy and chemo-radiotherapy for squamous cell carcinoma of the left tonsil ($T_3$ $N_0$). Regular follow up at the regional clinical oncology department had shown no sign of loco-regional recurrence. The patient smoked 70 cigarettes per day and denied any urinary symptoms. There was nothing else of note in the systemic review.

The clinical examination of the abdomen and genitalia was unremarkable. Abdominal ultrasonography demonstrated a left-sided uretero-hydronephrosis. The left kidney was reported to be small, with reduced cortical thickness, and the patient was referred to the urology department for further management.

Serum haematology and biochemistry, including prostate-specific antigen, were normal. Cystoscopy and left ureteropyelogram showed a long mid-ureteric stricture. The appearance suggested extramural compression, and insertion of a ureteric stent was attempted but failed. A computed tomography scan revealed para-aortic retroperitoneal lymphadenopathy and a 4 cm node anterior to the left common iliac vessels. An attempt to insert a percutaneous nephrostomy was complicated by a retroperitoneal haematoma, for which the patient required a blood transfusion.

To rule out an extra-gonadal germ cell tumour, serum tumour markers were requested: the serum beta human chorionic gonadotrophin (β-hCG) concentration was elevated (4405 IU/l; normal range, 0–2 IU/l), as was that of lactate dehyrogenase (1082 U/l; normal range, 313–619 U/l), while the alpha-fetoprotein level was normal. Scrotal ultrasound excluded an impalpable testicular lesion. After discussion with radiological colleagues, an open lymph node biopsy was performed under general anaesthesia. This showed fibroblastic connective and fatty tissues infiltrated by clear cells with large nuclei and prominent

From the Departments of Medical Oncology and †Pathology, St James's University Hospital, Leeds, and the *Department of Urology, Pinderfields General Hospital, Wakefield, UK.
Accepted for publication: 5 January 2006.

nucleoli. Immunohistochemistry was negative for prostate-specific antigen, carcinoembryonic antigen and Vimentin but positive for β-hCG and alpha-fetoprotein, supporting the diagnosis of a retroperitoneal germ cell tumour.

The patient was transferred to the regional medical oncology centre and initially commenced on chemotherapy with cisplatin (100 mg/m$^2$, day one) and etoposide (300 mg/m$^2$, day one to three).

As a part of the central review process, the retroperitoneal tumour was re-examined and the nuclear features and pattern of infiltration were felt to be more in keeping with squamous cell carcinoma rather than germ cell tumour. Comparison with the previous tonsillar squamous cell carcinoma (Figure 1b) showed marked similarities, although the retroperitoneal tumour was more pleomorphic and cells with clear cytoplasm predominated (Figure 1a), whereas they were a smaller component of the tonsillar tumour. Further immunohistochemistry of the retroperitoneal tumour demonstrated positivity for epithelial membrane antigen (Figure 1c) and cytokeratins 5/6, whereas placental alkaline phosphatase was negative, in keeping with metastatic squamous cell carcinoma. There was a diffuse background expression of β-hCG (Figure 1d), as is usually the case in secreting tumours, and strong positivity in a portion of cells, most of which were mononuclear. No syncytiotrophoblasts were present.

The diagnosis was amended and the chemotherapy regimen changed to cisplatin (80 mg/m$^2$, day one) and 5-fluorouracil (3200 mg/m$^2$ over four days). The patient received two cycles, the second of which was reduced by 25 per cent due to grade III lethargy. His β-hCG concentration fell to 1089 IU/l, indicating a response to treatment.

The patient presented, prior to a planned third cycle of chemotherapy, with persistent, severe lethargy and worsening left lower back pain. A re-staging computed tomography scan showed a 4.3 × 4.9 cm soft tissue mass adjacent to the left common iliac artery and multiple liver metastases, confirming disease progression. The patient's β-hCG level had risen to 2987 IU/l. Chemotherapy was stopped and the patient was referred for palliative radiotherapy to the soft tissue mass causing lower backache.

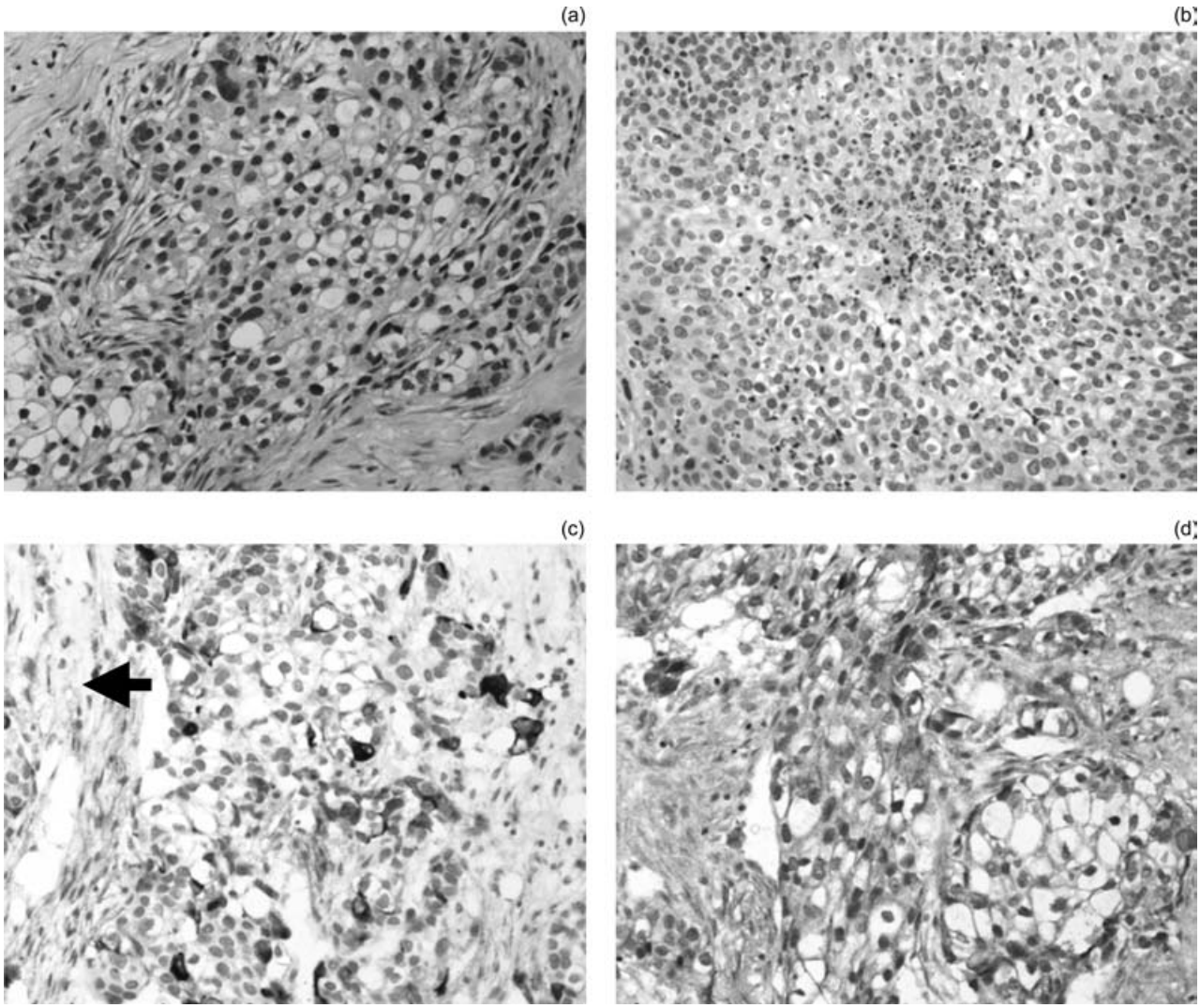


FIG. 1

(a) Primary squamous cell carcinoma of the tonsil, showing cells with clear cytoplasm admixed with cells with eosinophilic cytoplasm. (b) Retroperitoneal metastasis showing a predominance of clear cells and more pleomorphism than in the primary tumour. (c) Retroperitoneal metastasis showing diffuse background positivity for beta human chorionic gonadotrophin (due to secretion by malignant cells) and a small number of strongly positive cells (arrow). (d) Retroperitoneal metastasis showing positivity for epithelial membrane antigen in a high proportion of cells (H&E; ×200).

https://doi.org/10.1017/S0022215106001642 Published online by Cambridge University Press

Unfortunately, the patient was readmitted seven days later with aspiration pneumonia secondary to alcohol intoxication and died rapidly.

A postmortem examination reported a retroperitoneal tumour encasing the lower left ureter and para-aortic lymphadenopathy, together with multiple liver metastases. Lung sections showed focal evidence of bronchopneumonia and small islands of metastatic squamous cell carcinoma. No testicular abnormality was demonstrated. There was no evidence of a nasopharyngeal tumour. Comparisons were made with the original tonsillar pathology. The concluding diagnosis was metastatic disease secondary to the previous tonsillar squamous cell carcinoma.

## Discussion

Retroperitoneal tumours are either primary or secondary in origin. Primary lesions include sarcomas and lymphoma, whereas secondary tumours most commonly arise from the cervix, prostate or bladder and, rarely, from extra-gonadal germ cell tumours. However, lymphatic-borne metastases can arise from most solid organs. Such metastases encase the lower ureter and cause obstruction in over 60 per cent of cases by two years. Following diagnosis, the obstruction should be relieved by urinary diversion and the primary tumour managed appropriately. Prognosis depends on the primary lesion but is usually poor.[1]

Human chorionic gonadotrophin is a glycoprotein hormone with two dissimilar subunits (α and β), which is normally synthesized by trophoblastic tissue. Elevated serum levels are most common in pregnancy but are also seen in the presence of trophoblastic tumours. Levels of β-hCG may also be raised in the presence of malignancies of the liver, gastro-intestinal tract, kidney and adrenal cortex and also due to seminomatous testicular tumours.

Beta human chorionic gonadotrophin immunoreactivity has been described in oral squamous cell carcinoma, in particular in poorly differentiated tumours.[2] Serum levels of β-hCG may correlate with outcome in patients with squamous cell carcinoma of the oral cavity and oropharynx. A shorter recurrence-free survival time has been demonstrated in patients with pre-operatively elevated serum β-hCG when compared with patients with normal levels.[3]

The incidence of distant metastasis in head and neck squamous cell carcinoma is relatively small in comparison with that of other malignancies; this is influenced by the location of the primary tumour, the initial T and N stage, and the presence or absence of loco-regional control above the clavicle. The most frequent site of distant metastasis from squamous cell carcinoma is pulmonary (66 per cent of distant metastases); other sites include bone (22 per cent), liver (10 per cent), skin, mediastinum and bone marrow.[4]

- **This paper describes a case of retroperitoneal metastasis from squamous cell carcinoma of the tonsil, secreting beta human chorionic gonadotrophin (β-hCG)**
- **This is the first reported case of retroperitoneal metastasis from a squamous cell carcinoma of the tonsil, secreting β-hCG and causing hydronephrosis**
- **This case highlights the necessity of using the clinical, histological, immunohistological and ultrastructural examination to establish the precise diagnosis and avoid inappropriate treatment**

In a retrospective study of 1244 patients, approximately 5 per cent of the patients who achieved loco-regional control of their head and neck carcinoma developed distant metastases (of which 52 per cent were lung metastases (including mediastinal metastases), 12 per cent bone metastases and 5 per cent liver metastases), whereas 18 per cent of the patients with a loco-regional relapse of the tumour had distant metastases. Factors that significantly increased the risk of distant metastasis in this group of patients were advanced local and regional (metastatic neck nodes) extension of the primary tumour and location of the tumour at the hypopharynx or epiglottis.[5] Metastasis to other lymph node groups is a rare event. Alavi *et al*. reported five patients with metastases to the axillary, inguinal or anterior intercostal lymph nodes; all patients received combined surgery and radiotherapy to the primary site and lymph nodes and all developed a local recurrence.[6]

Metastatic tonsillar carcinoma very rarely presents as a cause of malignant retroperitoneal urinary obstruction. In our case, the diagnosis was initially reported as an extragonadal germ cell tumour due to histological appearance and raised tumour marker levels, assuming that the likelihood of this being metastatic disease secondary to the previous squamous cell carcinoma would be small. Extragonadal germ cell tumours are treatable; however, occasionally these tumours can be aggressive in nature and require prompt management. Because of these features, our patient was started on chemotherapy before the final comparison of lymph node biopsy and previous tonsillar carcinoma was made. Diagnostic difficulties may be encountered in the histological interpretation; this case highlights the necessity of using clinical, histological and immunohistochemical examination to establish the precise diagnosis in order to avoid misdiagnosis.

## References

1 Richie JP. Neoplasms of the testis. In: Walsh PC, Retik AB, Vaughan ED, Wein AJ, eds. *Campbell's Urology*, 7th edn. Philadelphia: W B Saunders, 1998;2411–52
2 Bhalang K, Kafrawy AH, Miles DA. Immunohistochemical study of the expression of human chorionic gonadotropin-beta in oral squamous cell carcinoma. *Cancer* 1999;**85**: 757–62
3 Hedstrom J, Grenman R, Ramsay H, Finne P, Lundin J, Haglund C *et al*. Concentration of free hCGbeta subunit in serum as a prognostic marker for squamous-cell carcinoma of the oral cavity and oropharynx. *Int J Cancer* 1999;**84**: 525–8
4 Ferlito A, Shaha AR, Silver CE, Rinaldo A, Mondin V. Incidence and sites of distant metastases from head and neck cancer. *ORL J Otorhinolaryngol Relat Spec* 2001;**63**:202–7
5 Leon X, Quer M, Orus C, del Prado Venegas M, Lopez M. Distant metastases in head and neck cancer patients who achieved loco-regional control. *Head Neck* 2000;**22**:680–6
6 Alavi S, Namazie A, Sercarz JA, Wang MB, Blackwell KE. Distant lymphatic metastasis from head neck cancer. *Ann Otol Rhinol Laryngol* 1999;**108**:860–3

Address for correspondence:
Mr Chandra Shekhar Biyani,
Consultant Urologist,
Pinderfields General Hospital,
Aberford Road,
Wakefield WF1 4DG, UK.

Fax: +44 (0) 1924 212921
E-mail: shekharbiyani@hotmail.com

Mr C S B Biyani takes responsibility for the integrity of the content of the paper.
Competing interests: None declared