Liver Ultrasound in Oral Squamous Cell Carcinoma

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Purpose: The presence of metastases plays a fundamental role in staging of patients with head and neck cancer before treatment. The aim of this study was to determine the role of ultrasonography (US) of the liver in the evaluation of patients with oral squamous cell carcinoma (OSCC).

Materials and Methods: The records were reviewed of 131 patients with OSCC (age range 29-84 years, mean 55) who had undergone a routine plain chest X-ray, an ultrasound examination and CT scan of the head and neck and/or the thorax, an enzyme and ultrasound examination of the liver and sometimes a bone scintigraphy.

Results: US exam showed no signs of liver metastases in 126/131 patients. In the other 5 patients focal alterations of liver eco-pattern were identified, raising the possibility of liver metastases. Only one case of true positive findings of liver metastases was identified in a patient with T2, N0 OSCC of the tongue.

Conclusions: In this series we identified only one case of liver metastases from 131 patients retrospectively evaluated. Ultrasound screening in patients with OSCC seems unjustified.

Key words: squamous cell carcinomas of head and neck, ultrasonography, liver metastases

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In the evaluation of patients affected by malignant tumours in the head and neck, the identification of metastases plays a fundamental role in staging before treatment (Ferlito et al, 2001; Righini et al, 2001). The most common sites of distant metastases (DM) from squamous cell carcinomas (SCC) of head and neck are the lungs, bones and liver (Ferlito et al, 2001; Johnson, 2001; Nilssen et al, 1999).

The overall incidence of DM detected in patients with SCC in the head and neck ranges from 11% to 40% with significant differences in percentage of DM, between clinical and autopsy series (Ferlito et al, 2001; Johnson, 2001; Nilssen et al, 1999; Righini et al, 2001; Stirrett et al, 1953).

The presence of DM however, influences the management of the patient dramatically. Liver screening procedures for detection of occult metastases were introduced as a clinical tool as early as 1953 by Stirrett (Stuckensen, 2000). Recently ultrasound scanning has become the preferred method for performing this procedure. Belson et al (1980) reported the role of bone and liver scans in metastasis detection in 132 patients with head and neck cancer. Belson et al (1980) and Troell et al (1995) analysed 97 patients with SCC detecting chest, bone and hepatic metastasis.

Righini et al (2001) made a clinical retrospective study of 267 patients with cancer of the upper respiratory and digestive tract using ultrasound scanning as the screening test for the detection of liver metastasis. De Bree et al (2000) analysed screening test values in patients with head and neck cancer. A liver screening scan is routinely included in the initial pre-treatment evaluation of patients with oral squamous cell carcinoma in our institutions. Thus, the aim of this study

was to determine the role of ultrasonography (US) of the liver in the evaluation of DM in patients with SCC of the oral cavity (OSCC).

MATERIAL AND METHODS

A retrospective review of 131 patients (age range 29-84 years, mean 55) with tongue, floor of the mouth, retromolar, cheek, soft and hard palate and gingival OSCC was performed. Primary tumour stage, T and N, and tumour differentiation G were considered and related to the presence of DM. A clinical evaluation was performed on all patients, and investigations included plain chest radiography, ultrasound examination and CT scan of the head and neck and/or the thorax, ultrasound examination of the liver, and bone scintigraphy in M1 cases.

Laboratory tests for detection of liver function included assays of: gamma-glutamyl transpeptidase, aspartate aminotransferase, alanine aminotransferase, and bilirubin levels.

Liver ultrasound was performed using the Sonolayer 350 (Toshiba medical, Tokyo, Japan) fitted with a 3.75 MHz probe. Sonographic evaluation included high resolution grey scan and a colour-coded duplex sonographic scan. In all cases ultrasound scans were performed by the same experienced radiologist. Evidence of nodular areas with poor defined margin characterised by mixed pattern, with prevalence of hypoechoic pattern were considered indicative for liver metastasis.

RESULTS

Clinical T-stage assessment prior to therapy was: T1=18, T2=32, T3=22, T4=59; and N stage was: N0=62, N1=23, N2=38, N3=3, NX=3. Of the 131 patients studied, only nine (7%) had DM: in lung (5), bone (3), and liver (1).

US exam showed no signs of liver metastases in 126/131 patients. In the other 5 patients focal alterations of liver eco-pattern were identified, raising the possibility of liver metastases. Consequently these 5 patients underwent CT scan of the upper abdomen using conventional equipment in 2 cases and multislice CT in 3.

On the basis of these CT findings, related with US features, a definitive diagnosis of metastasis was confirmed in only 1 case, while hepatic adenoma hypothesized in 1 case was confirmed with subsequent fine-needle aspiration biopsy (Fig. 1).

In 1 case a hepatic cavernous haemangioma was found and in the remaining 2 cases, multislice CT proved no signs of abnormal contrast enhancement of the liver and CT values of suspected areas showed reduced HU values in all phases of hepatic perfusion – indicative of multicentric steatosis. Thus only a single true case of liver metastasis was found and was histologically confirmed.

In this unique case, the patient had T2, N0 OSCC of the tongue while the grading of the cellular population was assessed as G2. The patient was further investigated for other primary tumours of the gastrointestinal tract, but no other neoplasia was found. Metastases were also found in the lung (n=5), bone (n=3), and liver (n=1) (Table 1).

DISCUSSION

Liver metastases are rare in patients with OSCC in the absence of other DM; whereas lung metastases are more frequently associated with OSCC (Belson et al, 1995; Stuckensen et al, 2000; Taylor et al, 1976). In this series of 131 patients with OSCC, we found only one case of liver metastases, accounting for less than 1%.

Crile was the first author to notice the possibility of DM associated with head and neck carcinomas (Crile, 1906; Felix et al, 1976). Belson et al (1980) reported no liver metastases in 132 patients with head and neck cancer, while Troell et al (2000) in an analysis of 97 patients reported 2 cases of hepatic metastases, stating these to be rare in the absence of other DM. Righini et al (2001) in their clinical retrospective study, found liver metastasis in 4 of 267 patients with cancer of the upper respiratory and digestive tract, with a higher incidence of liver metastases in patients with SCC of larynx. Bertrand et al (1995) analysed 200 patients with upper aero-digestive tract SCC and found an incidence of liver metastasis of 0.6%, while De Bree et al (2000) reported an incidence of 1%.

Some authors found a relation between T stage and DM, others show a clear correlation with N stage, number of lymph node metastases and involvement of lower nodes (Ferlito et al, 2001; Johnson, 2001; Papac, 1984; Taylor, 1976). Furthermore the incidence of liver metastases is significantly associated with the site of the primary tumour and with differentiation degree of tumours (Belson et al, 1995; Ferlito et al, 2001; Papac, 1984).

Belson et al (1995) outlined discrete criteria for obtaining liver scans in HN cancer patients: hepatic en-

Table 1 Metastases

Name	Age	Sex	Primary site	Histology	Grading	TNM	Stage	Liver enzyme elevation
AB	56	F	Cheek	Squamous	G1	T1 N0 M0	I	
CE	67	F	Cheek	Squamous	G2	T4 N2 M0	IV	
CO	60	M	Cheek	Squamous	G2	T2 N0 M0	II	GGT,BIL >
DB	74	F	Cheek	Squamous	G1	T1 N2 M0	IV	
DI B	51	M	Cheek	Squamous	G2	T2 N0 M0	II	
FE	77	M	Cheek	Squamous	G1	T1 N0 M0	I	
FE	76	M	Cheek	Squamous	G1	T1 N0 M0	I	
GA	69	F	Cheek	Squamous	G3	T3 N2 M0	IV	
IO	68	M	Cheek	Squamous	G1	T2 N0 M0	II	
LO	72	M	Cheek	Squamous	G2	T4 N0 M0	IV	
MA	74	M	Cheek	Squamous	G2	T2 N0 M0	II	
MA	23	M	Cheek	Squamous	G1	T2 NO MO	II	
NA	55	M	Cheek	Squamous	G2	T1 N1 M0	III	AP >
NI	64	M	Cheek	Squamous	G1	T2 N0 M0	II	
PA	83	F	Cheek	Squamous	G2	T3 N0 M0	III	
PE	78	F	Cheek	Squamous	G2	T2 N0 M0	II	
RA	61	M	Cheek	Squamous	G1	T1 N0 M0	I	
SA	55	M	Cheek	Squamous	G1	T2 N1 M0	III	
SA	64	F	Cheek	Squamous	G1	T1 N0 M0	I	GOT;GPT;GGT >
SI	66	F	Cheek	Squamous	G1	T4 N1 M0	IV	
SO	46	F	Cheek	Squamous	G1	T1 N0 M0	I	GPT >
TA	57	F	Cheek	Squamous	G1	T1 N1 M0	III	
VO	70	M	Cheek	Squamous	G1	T2 N0 M0	II	BIL >
ZI	50	M	Cheek	Squamous	G1	T1 N0 M0	I	
AB	70	M	Cheek	Squamous	G1	T4 N1 M0	IV	
AB	67	M	Cheek	Squamous	G1	T2 N1 M1	III	
BI	73	M	Cheek	Squamous	G1	T3 NX M0	III	
BR	69	F	Cheek	Squamous	G1	T2 N0 M0	II	
MO	66	M	Cheek	Squamous	G1	T4 N0 M0	IV	GOT;GPT;GGT;AP >
AE	62	M	Floor of the mouth	Squamous	G2	T1 N1 M0	III	GGT >
BO	73	M	Floor of the mouth	Squamous	G1	T2 N0 M0	II	
CI	68	M	Floor of the mouth	Squamous	G1	T1 N2 M1	IV	GGT;GOT;GPT;BIL >
CO	70	M	Floor of the mouth	Squamous	G1	T4 N2 M0	IV	GGT,GOT,AP >
CR	51	M	Floor of the mouth	Squamous	G1	T2 N2 M0	IV	GGT,GOT,GPT,AP,BIL>
D'AN	73	F	Floor of the mouth	Squamous	G1	T1 N0 M0	I	
DE M	52	M	Floor of the mouth	Squamous	G1	T4 N2 M0	IV	GGT,BIL>
DI D	60	F	Floor of the mouth	Squamous	G1	T4 N2 M0	IV	GOTe GPT>
FO	71	F	Floor of the mouth	Squamous	G2	T4 N2 M0	IV	
GA	59	M	Floor of the mouth	Squamous	G1	T4 N1 M0	IV	GGT >
GU	76	M	Floor of the mouth	Squamous	G1	T2N0M0	II	
IU	60	M	Floor of the mouth	Squamous	G1	T4 N3 M0	IV	
LA	65	M	Floor of the mouth	Squamous	G2	T2 NX M0	II	GGT >
LA	55	M	Floor of the mouth	Squamous	G1	T4 N2 M0	IV	GPT >
LO	72	M	Floor of the mouth	Squamous	G2	T2 N0 M0	II	GGT,BIL >
MA	65	M	Floor of the mouth	Squamous	G1	T4 N2 M0	IV	
MA	40	M	Floor of the mouth	Squamous	G1	T2 N0 M0	II	GGT >
MA	70	M	Floor of the mouth	Squamous	G1	T2 N1 M0	III	
OR	82	M	Floor of the mouth	Squamous	G3	T4 N2 M1	IV	
PA	69	M	Floor of the mouth	Squamous	G1	T2 N2 M0	IV	
RU	82	M	Floor of the mouth	Squamous	G2	T3 N1 M1	III	
SA	81	M	Floor of the mouth	Squamous	G2	T2 N2 M0	IV	
SI	71	M	Floor of the mouth	Squamous	G2	T4 N0 M0	IV	
SI	72	M	Floor of the mouth	Squamous	G1	T2 N0 M0	II	

Table 1 Continued

Name	Age	Sex	Primary site	Histology	Grading	TNM	Stage	Liver enzyme elevation
SO	44	M	Floor of the mouth	Squamous	G3	T4 N2 M1	IV	
TO	61	M	Floor of the mouth	Squamous	G1	T4 N1 M0	IV	BIL >
VF	61	M	Floor of the mouth	Squamous	G2	T2 N0 M0	II	
BE	77	F	Gingival mucosa	Squamous	G1	T1 N0 M0	I	
CA	61	F	Gingival mucosa	Squamous	G1	T1 N2 M0	IV	
CM	53	F	Gingival mucosa	Squamous	G1	T2 NO Mo	II	
DM	54	M	Gingival mucosa	Squamous	G2	T4 N2 M0	IV	GOT;GPT;GGT >
LA	66	F	Gingival mucosa	Squamous	G1	T3 N1 M0	III	GOT;GPT;GGT >
NA	52	M	Gingival mucosa	Squamous	G1	T4 N2 M0	IV	
NA	60	F	Gingival mucosa	Squamous	G1	T2 N0 M0	II	
SI	25	F	Gingival mucosa	Squamous	G1	T4 N1 M0	IV	
CA	45	M	Hard palate	Squamous	G1	T4 N0 M0	IV	GGT >
CE	74	M	Hard palate	Squamous	G2	T4 N2 M0	IV	
CS	73	F	Hard palate	Squamous	G1	T3 N0 M0	III	
DI T	77	F	Hard palate	Squamous	G2	T2 N0 M0	II	
GU	80	F	Hard palate	Squamous	G1	T4 N2 M0	IV	BIL >
GE	55	M	Retro-molar trig	Squamous	G3	T4 N2 M0	IV	AP >
TA	40	M	Retro-molar trig	Squamous	G1	T2 N0 M0	II	
AA	60	M	Retro-molar trig.	Squamous	G1	T4 N0 M0	IV	
FE	76	F	Retro-molar trig.	Squamous	G2	T4 N0 M0	IV	
FO	66	M	Retro-molar trig.	Squamous	G2	T1 N0 M0	I	
FR	48	M	Retro-molar trig.	Squamous	G1	T4 N2 M0	IV	
IA	69	M	Retro-molar trig.	Squamous	G1	T4 N2 M0	IV	
JA	70	M	Retro-molar trig.	Squamous	G2	T1 N0 M0	I	
RA	45	F	Retro-molar trig.	Squamous	G1	T4 N2 M0	IV	
SA	60	F	Retro-molar trig.	Squamous	G2	T2 NO MO	II	
SO	43	M	Retro-molar trig.	Squamous	G1	T4 N1 M0	IV	GGT,GOT,GPT,BIL >
CI	72	M	Soft palate	Squamous	G1	T4 N0 M0	IV	
LU	46	M	Soft palate	Squamous	G2	T3 N0 M0	III	
AM	38	M	Tongue	Squamous	G2	T1 N3 M0	IV	
BA	61	M	Tongue	Squamous	G2	T1 N1 M0	III	
BE	68	M	Tongue	Squamous	G1	T4 N2 M0	IV	GOT >
BS	44	F	Tongue	Squamous	G3	T3 N1 M0	III	
CA	83	F	Tongue	Squamous	G2	T2 N0 M0	II	
CE	53	M	Tongue	Squamous	G2	T4 N2 M0	IV	
CM	68	M	Tongue	Squamous	G1	T1 N2 M0	IV	
CO	71	M	Tongue	Squamous	G2	T2 N0 MO	II	
DA	45	F	Tongue	Squamous	G2	T4 N3 M0	IV	AP >
D'A	69	M	Tongue	Squamous	G1	T4 N0 M0	IV	
D'AN	42	M	Tongue	Squamous	G2	T2 N0 M0	II	
DE	68	F	Tongue	Squamous	G1	T2 N0 M0	II	
DE R	68	M	Tongue	Squamous	G2	T2 N0 M1	IV	GGT;GPT >
DE S	62	F	Tongue	Squamous	G1	T3 N0 M0	III	
DO	83	M	Tongue	Squamous	G2	T2 N2 M0	IV	
ES	23	M	Tongue	Squamous	G2	T4 N1 M1	IV	
ES	69	F	Tongue	Squamous	G1	T1 N1 M0	III	
ES	75	F	Tongue	Squamous	G2	T2 N0 M0	II	
FA	66	F	Tongue	Squamous	G1	T4 N2 M0	IV	GGT,GOT,AP >
FE	77	F	Tongue	Squamous	G2	T2 N0 M0	II	
FR	58	M	Tongue	Squamous	G2	T1 N0 M0	I	
GE	78	M	Tongue	Squamous	G2	T3 N1 M0	III	
LE	44	F	Tongue	Squamous	G2	T2 N0 M0	II	
LU	64	M	Tongue	Squamous	G1	T2 N2 M0	IV	

Table 1 Continued

Name	Age	Sex	Primary site	Histology	Grading	TNM	Stage	Liver enzyme elevation
MA	29	F	Tongue	Squamous	G1	T3 N0 M0	III	
MA	80	F	Tongue	Squamous	G1	T2 N0 M0	II	
MA	65	F	Tongue	Squamous	G1	T1 N0 M0	I	
MA	61	F	Tongue	Squamous	G1	T1 N1 M0	III	
MA	73	M	Tongue	Squamous	G2	T4 N2 M1	IV	
MA	65	M	Tongue	Squamous	G1	T2 N0 M0	II	
ME	74	F	Tongue	Squamous	G1	T4 N2 M0	IV	AP >
OR	48	F	Tongue	Squamous	G1	T3 N0 M0	III	
PA	59	M	Tongue	Squamous	G1	T4 N2 M0	IV	
PA	52	M	Tongue	Squamous	G1	T2 N1 M0	III	
PI	55	M	Tongue	Squamous	G1	T1 N0 M0	I	BIL >
PO	73	F	Tongue	Squamous	G2	T1 N0 M0	I	
RU	73	F	Tongue	Squamous	G2	T1 N0 M0	I	
SA	57	F	Tongue	Squamous	G2	T1 N1 M0	III	GOT;GPT;AP;BBIL >
SA	61	M	Tongue	Squamous	G1	T4 NX M0	IV	
SA	40	M	Tongue	Squamous	G1	T1 N0 M0	I	AP >
SI	69	M	Tongue	Squamous	G1	T4 N1 M0	IV	
SO	73	M	Tongue	Squamous	G2	T4 N1 M0	IV	
TA	68	M	Tongue	Squamous	G3	T4 N2 M0	IV	
TE	66	M	Tongue	Squamous	G1	T3 N2 M0	IV	
ZI	74	M	Tongue	Squamous	G1	T1 N0 M0	I	
AA	56	M	Tongue	Squamous	G1	T4 N2 M1	IV	
CV	68	M	Tongue	Squamous	G1	T1 N2 M0	IV	GGT >
DI M	53	M	Tongue	Squamous	G2	T2 N0 M0	II	GOT,GPT,BIL>
MO	62	M	Tongue	Squamous	G1	T2 N0 M0	II	BIL >

largement or nodularity with abnormal liver function. They concluded that routine scanning is a non-worthwhile procedure.

Ferlito et al (2001) showed how extensive screening for DM detection is rarely justified in patients with SCC of the upper digestive tract, and we agree with the opinion that only some histological types of primary tumours and higher stages of SCC and tumour location could justify screening, such as liver ultrasound.

Adenoid cystic carcinoma, basalyoid squamous cell carcinoma, and neurcendocrine carcinomas have a greater propensity to DM as do primary tumours of the oropharynx and hypopharynx, particularly in advanced T stage (Ferlito et al, 2001). Considering OSCC, only advanced stage (III or IV) or poorly differentiated histological types are associated with a relatively high frequency of DM, and the lung is the preferential site, while liver metastases are quite rare (Ferlito et al, 2001).

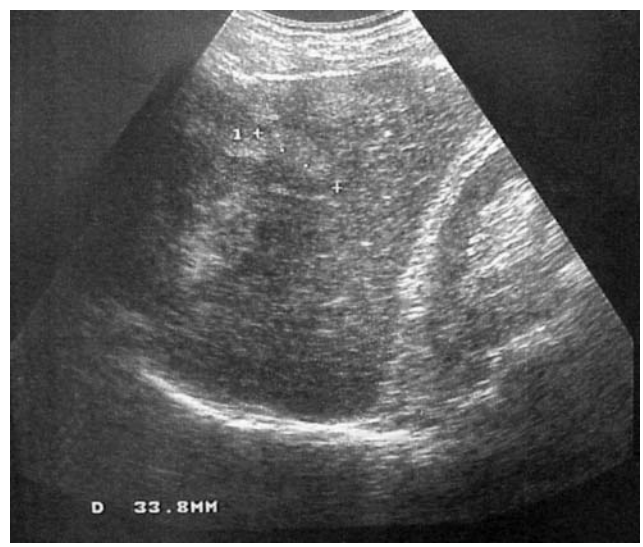

Fig. 1 Liver ultrasound (Sonolayer 350, Toshiba Medical, Tokyo, Japan) evidences a nodular area with poorly defined margin with prevalence of hypoechoic pattern suggestive for liver metastasis.

Clinically, liver metastases are asymptomatic in early stage. Laboratory tests have been used as a screening method for liver metastases but are neither specific nor sensitive, while radio-immunochemical sampling of tumours antigens, such as carcinoembryonic antigen and alpha-fetoprotein, show high sensitivity but very low specificity; and consequently imaging techniques such as US and CT, represent an important potential screening tool for detecting liver metastases (Johnson, 1996; Stuckensen, 2000).

US is relatively inexpensive and easy to perform, and its accuracy is higher than 90% (Felix et al, 1976).

On the other hand, US is extremely operator-dependent. In cases of detected US alterations with unequivocal characteristics, more specific examinations such as abdominal CT scan or an MRI were indicated (Arunachalam et al, 2002; Nilssen et al, 1999; Stirrett et al, 1953; Stuckensen et al, 2000; Tan et al, 1999). In the present series, 4 cases of suspected metastases when studied with CT scans demonstrated non-metastatic lesions.

CONCLUSIONS

Liver metastases rarely occur in SCC of the oral cavity. Ultrasound scanning is a relatively inexpensive and accurate technique for the detection of liver metastases, and the procedure is not associated with any radiation exposure (De Bree, 2000; Tan et al, 1999; Troell, 1995). It serves as a sufficient confirmatory test in patients with elevated liver enzyme and positive tumour markers (Johnson, 2001).

However, our data confirm that because of the low frequency of liver metastases found by ultrasound scanning, this screening does not appear to be justified.

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