Mandibular invasion of squamous cell carcinoma: factors determining surgical resection of mandible using computerized tomography and histopathologic study

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Abstract

Aim Carcinoma of the mandibular region can be considered as an important, distinct entity associated with special problems relating to diagnosis, evaluation of extension, planning of treatment, surgical techniques, treatment result and prognosis. The study was aimed to assess the accuracy of computerized tomography in demonstrating mandibular invasion, to assess the role of anatomic structures like cancellous spaces, the inferior alveolar nerve and periodontal spaces in spread of carcinomas in the mandible and to determine the spread of tumour within the mandible and the resection procedure to be carried.

Materials and methods 11 mandibular specimens which were resected for squamous cell carcinoma were examined clinically, radiographically and histopathologically. Computerized tomography 120 KV, 40 to 130ma, obtaining slices starting from the center of lesion to the clearance, of the bone involvement distally and proximal to the lesion with excellent soft tissue or cortical bone interface with bone enhancement mode was used as a principle investigating tool to assess the tumour penetration in the mandible which was confirmed by histopathologic sections.

Results A conditional probability test was conducted according to Bayes' theorem, and the results showed sensitivity 60% and specificity 77.8%, a false negative rate 40% and false positive rate 22.2%. A positive predictive value 69% and negative predictive value 70%.

Conclusion In our study the factors to be taken into consideration in deciding the type of resection are the pattern of tumour infiltration, irradiated or non irradiated mandibles, presence or absence of dentition, the inferior alveolar nerve involvement and the periodontal space involvement. The computerized tomography has a significant role in detecting the involvement of tumour in the mandible with enhanced settings.

Keywords Squamous cell carcinoma · Invasion · Mandible resection

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Introduction

Carcinoma of the mandibular region can be considered as an important, distinct entity associated with special problems relating to diagnosis, evaluation of extension, planning of treatment, surgical techniques,

treatment result and prognosis, as stated by Soderholm [5]. An accurate knowledge of the extent of invasion of a malignant lesion is of paramount importance in planning surgery. Oral squamous cell carcinoma has the ability to involve adjacent bone, necessitating excision of involved bone.

Resection of mandibular segment results in serious disabilities including impairment of chewing, swallowing, and articulation. The decision to preserve mandibular continuity requires detailed knowledge of the regional anatomy and assessment of tumour extent. Mandibular preservation was initially not recommended

because of the belief that the lingual periosteal lymphatics of the mandible were involved in drainage of tongue and floor of the mouth, based on the work of Ward and Robben [3,9,34] in 1951. Greer et al. [32] described marginal resection of mandible in 1953, but the concept was not clear until Marchetta et al. [1] at 1971 described the lymphatic drainage of oral cavity and the mechanism of bone invasion was classified by Carter et al. [32] 1981. It was due to these publications that conservative method of mandibular resection was popularized.

Mcgregor and McDonald [16,17,20,28,34] suggested that invasion of tumours was largely restricted to alveolar crest, and further studies confirmed the importance of cortical bone defects in the edentulous as a route for direct spread of tumour. Involvement of cancellous bone, make suspicious in involvement of inferior alveolar nerve and this adversely influences the possibility of limited surgical approach as reported by Southam [39].

There are several diagnostic imaging techniques available for evaluating mandibular invasion by squamous cell carcinoma. These include conventional radiography, computerized tomography, ultrasonography, isotope scanning and magnetic resonance imaging. The conventional radiograph, computerized tomography and isotope scanning are preferred techniques for detecting mandibular invasion. Computerized tomography is superior in diagnosing early lesion in cortical bone and adjacent tissues involvement when compared to magnetic resonance imaging; according to Barbara Belkin A et al. [8] and Huntley et al. [16]. Hence this imaging method was selected for this study.

The purpose of the study were,

1. To assess the accuracy of computerized tomography in demonstrating mandibular invasion
2. To assess the role of anatomic structures like cancellous spaces, the inferior alveolar nerve and periodontal spaces in spread of carcinomas in the mandible
3. To determine the spread of tumour within the mandible and the resection procedure to be carried

Material and methods

11 mandibular specimens which were resected for squamous cell carcinoma were obtained from the department of Pathology, Saveetha Dental College and Hospitals after the resection surgery.

The specimens were dentate, edentate or partially dentate (Fig. 1). Both segmental and hemimandibulectomy specimens were obtained. Two of the specimens were from previously irradiated patients. Preoperatively the size of the tumour, extent of the tumour was noted. The specimens were photographed and inspected for amalgam restorations, which may produce heavy metal artifact deterioration of the CT scans.

The specimens were then thoroughly fixed in 10% formalin. After formalin fixation, a consistent mark was made on each specimen to obtain the comparison of CT slice with appropriate histologic section. CT imaging was done by 120 KV, 40 to 130 ma, obtaining slices starting from the center of lesion to the clearance, of the bone involvement distally and proximal to the lesion with excellent soft tissue or cortical bone interface (Fig. 2). Bone enhancement mode was set upto give fine bone detail. The specimens were placed in plastic tray, supported in position with clinical examination gloves within the gantry, and oriented for the image slices to be taken in buccolingual direction. After scanning the soft tissue tumour adjacent to the mandible was removed. The markings were done with Indian ink correlating to CT slices by using a caliper-measuring device (Fig. 3). Specimens were decalcified in formic acid 10% and the blocks were obtained by using fine cutting blade with water coolant sprayed correlating the CT slices. The slices were processed for paraffin sectioning and subsequent staining with hematoxylin and eosin.

The CT images were reviewed with the clinical information about individual patients but without the final histopathologic report being made known to the principal investigator or the consultant radiologist.

The assessment was made on the presence or absence of bony invasion. If invasion was present, the pattern of spread was noted, giving more importance to the vulnerable areas like the periodontal ligament space in the event of a dentate or partially dentate mandible and the inferior alveolar nerve. The presence or absence of bone invasion as noted on the CT was compared with the corresponding histological sections to assess the degree of correlation.

Results

Eleven resected mandibular specimens were obtained. 8 of the specimens were

dentulous and 3 were edentate. In 8 specimens the main site of entry was the buccal mucosa, in 2, the floor of the mouth and in 1 specimen the tongue. The TNM classification was T3 (6) and T4 (5).

In all the 11 specimens the mandibular bone was involved by squamous cell carcinoma. Following Slootweg and Muller's classification the pattern of invasion was assessed as either erosive or infiltrative. The erosive pattern (N=2) was characterized by a broad pushing tumour front with a sharp tumour bone interface and evidence of active marginal bone resorption. Bone was not generally identified with in the tumour. The infiltrative pattern (N=9) showed irregular, focal infiltration by elongated strands of tumour cells into the mandibular bone (Fig. 4).

Two specimens showed an erosive pattern of spread at both the central and peripheral portions of the specimens and 9 specimens showed an infiltrative pattern of invasion at both sites. In 1 specimen the central lesion showed a well-differentiated carcinoma and the peripheral portion showed a moderately differentiated carcinoma. In another specimen the tumour periphery was limited to the soft tissues with periosteal reaction without bone involvement (Fig. 5).

In 8 dentate specimens, 7 were partially dentate and allowed assessment of the periodontal ligament space, and preferential tumour spread into the space was seen in 2 cases. Both the cases had direct extension of tumour in the space and showed an infiltrative pattern (Fig. 6) and there was no erosion of cortex.

7 of the 11 specimens which contained portions of inferior alveolar nerve did not show any evidence of tumour involvement. In 1 specimen the tumour margin surrounded the nerve bundle without infiltrating it and the pattern of invasion was 'erosive' (Figs. 7 and 8). All the specimens showed no involvement of nerve either by CT or histological findings (Fig. 9).

In 5 of the 11 specimens with bone invasion there was good correlation between CT and histological findings. In other 6 specimens, CT was not correlating to the histological findings. In 3 of the 6 specimens CT showed positive evidence of tumour and the histological findings were negative. In 1 specimen CT showed no clearance of tumour and the histological findings showed negative evidence. In 3 specimens, CT showed no evidence of tumour and histological findings showed involvement of the bone.

In all the specimens in which bone invasion was seen on CT, the tumour entered through the edentulous alveolar crest (Fig. 10) and the buccal cortical bone where erosion was evident by periosteal stripping. In 1 specimen where the main entry of tumour was lingual, the lingual cancellous bone showed involvement of cortical bone involvement (Fig. 11). In another specimen main entry of tumour was from the floor of the mouth. Cancellous bone involvement without lingual cortical bone involvement was seen (Fig. 12).

A conditional probability test was conducted according to Bayes' theorem, and the results showed sensitivity 60% and specificity 77.8%, a false negative rate 40% and false positive rate 22.2%. A positive predictive value 69% and negative predictive value 70%.

Discussion

Mandibular invasion is a determining factor for treatment planning and the prognosis of the disease. Invasion of the bone by direct extension of an adjacent carcinoma, which penetrates the thin mucosal layer of the alveolar ridge, is the most common route of mandibular infiltration [17]. Brown and Brown [9] emphasized that the attached mucosa is the main potential route of tumour entry because of the lack of periosteum in this area of the mandible. Early tumour invasion of the mandible generally occurs when the lesion is located close to the buccal sulcus or the mylohyoid crest, bringing the tumour into direct proximity to the bone.

The bone is invaded in areas of the cortical defects created by the fibrous attachment of the mucosa or by reactive inflammation associated with the tumour [9]. These findings suggest that it is justifiable to adopt a more conservative surgical approach, such as marginal resection in cases of limited superficial bone involvement. But if evidence of bone marrow invasion exists, segmental resection has to be carried out.

The frequency of bone involvement can be related to various clinical features, as the location, proximity of the mandible and the size of the tumour. Although it is reported that proximity of the tumour to the bone, not the size or stage is the determining factor in mandibular involvement, the large tumour increases the surface area and through 'fragile' osseous parts (cortical clefts and microvascular bone channels), can more easily erode the

bony surface [13,14]. Our results showed that irrespective of the primary location whether the buccal mucosa, floor of the mouth or the tongue, which were involving the mandible, invaded the cortical bone. Nomura T et al. [25] mandibular resorption was classified into three types: 1) compression type, characterized by a relatively smooth margin, surrounded by regions of osteosclerosis 2) permeated type characterized by an unclear margin and 3) moth-eaten type, characterized by a more irregular margin than that in permeated type, with extensive destruction of bone and small bone fragments scattered among the destroyed bone. In 1 specimen the tumour extended upto the periosteum without evidence of cortical bone involvement and in another specimen involvement into medullary spaces was seen without evidence of cortical bone involvement. When the tumour involves the superficial portion, this involvement can be missed in bone scans. Large tumours have a great tendency than the small ones to invade bone. In our study 10 of the 11 tumour staged T3 or T4, and showed bone infiltration.

Nomura T et al. [25] showed in his study, invasion of tumour cells into the periosteum, cortical bone, or bone marrow was histopathologically confirmed in 114 of the 176 patients (65%). The remaining 35% of our patients had no evidence of mandibular invasion and could have been treated without mandibulectomy. 65% (62 of 96) of the patients who received marginal resection had no tumour invasion to the periosteum or bone of the mandible. Although tumour cells had nearly invaded the periosteum in some patients, there was no clear evidence of tumour invasion into the periosteum or periodontal space and suggested that in dentate areas the periodontal ligament space could provide route of entry for carcinoma to bone [16]. The study could not determine the direct invasion by periodontal spaces, but once the cortical bone was involved, periodontal spaces were involved by direct contiguous extension of the tumour (Fig. 7). In our study 2 specimens showed involvement of periodontal spaces where the tumour directly infiltrated into the bone.

The grade of histologic differentiation of the tumour did not seem to correlate with presence, pattern, or extent of the bone invasion. But in our present study 10 of 11 specimens were well differentiated and showed keratinisation with extensive desmoplastic changes (Fig. 12) and 1 specimen showed moderately

differentiating type with minimal keratinisation.

Once the tumour penetrates the cortical rim, it invades the mandible diffusely along a broad front, quickly invading the inferior alveolar canal and further migrating in a horizontal fashion along the canal [39] (Fig. 6). Panday M et al. [21] showed 20% of the cases in his study had spread through the canal of inferior alveolar nerve with or without invasion of inferior alveolar nerve. In our study there was no involvement of the inferior alveolar nerve except in 1 specimen where the tumour surrounded the nerve without infiltrating it.

Brown and Brown [9] proposed the attached mucosa as the major portal of entry of the tumour in to the mandible in the edentulous and dentate mandible, in which the mandible is not protected by the periosteum. Sharpey's fibres bind the oral mucosa in to the occlusal surface of the edentulous ridge and in a wide attachment around the alveolar bone supporting the teeth. It is the attachment of these fibres in to the bone that results in the cortical defects seen on the edentulous ridge. As in our study, 5 of 8 dentate specimens showed extensive involvement of tumour in the cancellous marrow and presented with micro deposits.

In 11 specimens, the CT showed good correlation in assessing the positive margins in 9/13(69%) sections and negative margins in 14/20(70%) sections. In 6 sections CT did not reveal bony erosion and they were histologically proven to be positive. The positive predictive value in our study was 69% with negative predictive value 70% comparing to 89% and 63% studies carried out by ND Kalavrezos et al. [18] the sensitivity was 60% and specificity was 77.7% comparing to 78% and 80% [18] in the studies conducted earlier assess the predictability and reliability of the CT scans in mandibular bone involvement showed a false positive rate of 4.7% [33], 22% [18] and 28% [10]. In our study, the false positive rate was 22.2%, 4 of the 11 specimens showed no involvement of nerve either by CT or histological findings. There was a standard protocol in assessing the specimens as the specimens were examined the soft tissue attached to it and they were coronal scanned. The result of the present study does not forward the use of CT alone as a modality to assess the involvement of the bone. Andreia Perrella et al. [1] showed 1mm slice thickness, 1mm of interval of reconstruction for second time, 80 kVp, 512 x 512 matrix, and a bone tissue filter

Fig. 1 Resected segmental specimen

Fig. 2 CT sliced segmental resected specimen

Fig. 3 CT slice transformed to resected specimen

Fig. 4 Histopathological picture showing infiltrative margin of squamous cell carcinoma (25x)

Fig. 5 Picture shows arrosive pattern of tumour tissue along spicule of osteoid (25x)

Fig. 6 CT picture shows no involvement of bone

Fig. 7 Picture shows erosion of alveolar crest without involvement of neurovascular canal

Fig. 8 Picture shows transverse section of nerve bundle surrounded by tumour tissue (25x)

Fig. 9 Picture showing transverse section of nerve bundle without involvement (10x)

Fig. 10 CT Picture showing erosion of bone in alveolar crest of edentulous ridge

Fig. 11 Picture showing erosion of lingual cortical bone

Fig. 12 Picture shows micro deposits of squamous cell carcinoma (25x)

settings showed specificity of 100% and sensitivity of 75% in detecting the loci number of multilocular lesion, and detecting medullary involvement 97% and 72% respectively. Ogura I et al. [27] showed the dental CT images is a useful as prognostic indicator of mandibular bone invasion and cervical metastasis with gingival carcinoma. They provide the

accurate extent of bone resorption which is useful tool in planning resection. Mukherji SK et al. [40] showed sensitivity of 96% and specificity of 87%, positive predictive value of 89% and negative predictive value of 95% in axial contrast enhanced CT (3-mm thick contiguous sections) in which the bone algorithm settings were a width of 3500 H and level

of 700H. In evaluating the mandible involvement the uses of other scans such as MRI, bone scans [9] and Positron Emission Tomography (PET) scan [24] in which previous studies have shown better predictability and reliability.

The optimal surgery for squamous cell carcinoma of the oral cavity should fulfill 3 basic requirements; (1) it must

remove the primary tumour as well as those tissues that are at risk, (2) it should be technically simple, biomechanically sound and have low complication rate, (3) it should preserve or permit reconstruction of the mandible arch, particularly in anterior lesions, to restore normal mandibular function and facial appearance. In our study, 8 hemimandibulectomy specimens, 2 segmental and 1 marginal mandibulectomy specimens were studied, and the need of hemimandibulectomy could be justified only in 1 case where the tumour extended upto the angle of the mandible inferiorly and to the coronoid and condyle superiorly. One must be aware that the tumour may be entering the bone at the junction of the attached and reflected mucosa, which can be 10mm below the crest of the ridge. If a rim resection is planned, the margin of safety should be estimated from the junction of the attached and reflected mucosa rather than the crest of the ridge.

Marginal resection can be carried out safely if the tumour is not involving the bone, and to create adequate safe margin of resection. Patients with 'early' invasion of the bone, especially of the arrosive pattern are good candidates for conservative surgery. If doubt arises about the extent of bone involvement, segmental resection remains as a good alternative. In symphyseal lesions a segmental resection leaves a deformity, which is difficult to reconstruct, and the advantage of resecting 10 mm below the crest of the ridge can be taken. The height of anterior mandible is more in the dentate cases and a safe margin of 1 cm can be maintained for the continuity of the mandible and this procedure cannot be carried out in the edentulous atrophic mandibles.

When the tumour invades through the occlusal surface of the mandible [17], the dentoalveolar portions should be removed. A horizontal dentoalveolar osteotomy combined with an oblique lingual sloping cut should be performed as the lingual cortical bone is also involved in designing segmental resection to the posterior mandible, a vertical cut upto the level of the mental foramen and a posterior sub-sigmoid osteotomy are most suitable. A hemimandibulectomy can be performed when it is suspected that the tumour involves the entire mandible as they extend into the angle and the condyle and the coronoid region including the inferior alveolar nerve.

Conclusion

Our limited data suggest that the main tumour entry may be through the alveolar crest with the buccal or lingual cortical surfaces, in which the cortical clefts or the microvascular blood vessels tend to be more suspicious. The periodontal space plays a very little role in direct spread of tumour but when direct extension involves them, tumour infiltrates deep into the bone. The sensitivity of CT 60% was low compared to other studies. The accuracy of the results may be altered by the standards used in obtaining the images. The specificity 77.8%, negative predictive value 70%, positive predictive value 69% suggest the need of MRI and bone scans in assessing the tumour spread within the mandible. CT appears to be useful in detecting the early involvement but the extent of the tumour cannot detect the tumour spread into the medullary cavity. 1mm slice thickness, 1mm of interval of reconstruction for second time, 80 kVp, 512 x 512 matrix, and a bone tissue filter settings showed good specificity and sensitivity in detecting the loci number of multilocular lesion, and detecting medullary involvement. In our study there was no involvement of inferior alveolar nerve, the concept of encroachment of tumour on to the nerve rather than by perineural spread is accepted.

The factors to be taken into consideration in deciding the type of resection are the pattern of tumour infiltration, irradiated or non irradiated mandibles, presence or absence of dentition, the inferior alveolar nerve involvement and the periodontal space involvement.

The resection of mandible can be done by the following guidelines:

1. When the tumour margin is on the mucosa and does not show involvement of bone a marginal resection of mandible with adequate margin on both direction preserving the mandible lower border can be done.
2. When there is involvement of buccal and lingual mucosa, the mandible can be resected giving 1cm margin below the involvement, if 1 cm margin cannot be achieved a segmental resection can be carried out.
3. If the tumour is involving mandible and showing only involvement of cortical surface 1 cm margin clearance can be given and marginal resection can be carried.
4. When the tumour shows erosive pattern of involvement in mandible a segmental

resection with adequate clearance can be given.

5. When tumour involvement is near to the inferior alveolar nerve canal a rim resection involving the mandibular canal including the tumour with adequate margin can be carried.
6. When the tumour is involving the body of mandible, ramus and angle of mandible a hemimandibulectomy can be carried.

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