Oncologic outcomes of early glottic cancers with anterior commissure involvement treated with advanced laser cordectomies

Chirurgie endoscopique au laser des cancers glottiques précoces avec atteinte de la commissure antérieure: Résultats carcinologiques

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RÉSUMÉ

Introduction : La place de la chirurgie endoscopique au laser dans le traitement des cancers glottiques précoces est maintenant bien codifiée. La commissure antérieure (CA) est un sous-site anatomique délicat en raison de son accès difficile et du risque élevé de propagation de la tumeur de ce site au cartilage thyroïdien, à la sous glotte et à l'espace pré-épiglottique. Ces raisons rendent l'approche endoscopique controversée en cas d'atteinte commissurale antérieure.

Méthodes : Il s'agit d'une étude rétrospective monocentrique réalisée entre les années 2012 et 2015. Dix-huit patients traités avec des cordectomies au laser à un stade avancé ont été inclus.

Résultats : Toutes les tumeurs étaient classées T1 (78% étaient T1a et 12% T1b). Après chirurgie au laser, 4 patients (22,22%) avaient des marges positives. Ces patients étaient candidats à une chirurgie de second look permettant la détection et le traitement d'une maladie résiduelle. Les résultats oncologiques ont été étudiés. Deux patients ont présenté des rechutes locales dans un délai moyen de 7 mois. Le taux de contrôle local était de 88,9%, tandis que le contrôle local utilisant uniquement le laser était de 83,33%. Une patiente a subi une laryngectomie totale (TL) suivie d'une RT adjuvante après une récidive massive au niveau de la commissure antérieure avec infiltration du cartilage thyroïde. Le taux de préservation du larynx était de 94,44%. Le taux de survie globale à 3 ans a atteint 100%, tandis que la survie sans maladie à 3 ans était de 88,9%.

Conclusion : La chirurgie endoscopique au laser offre des résultats oncologiques acceptables dans le traitement du cancer T1 du larynx avec atteinte de la commissure antérieure.

Mots-clés

Cancer glottique précoce, commissure antérieure, chirurgie

SUMMARY

Introduction: The contribution of transoral laser microsurgery (TLM) in the management of early glottic cancer is now well established. The anterior commissure (AC) is a delicate anatomic subsite due to its difficult access and the high risk of tumour spread from this site to the thyroid cartilage, the subglottis and the pre epiglottic space. These reasons make the endoscopic approach controversial in case of AC involvement.

Methods: This is a single centre retrospective study performed between the years 2012 and 2015. Eighteen patients treated with advanced Va laser cordectomies were included.

Results: All tumours were staged T1 (78% were T1a and 12% T1b). After laser surgery 4 patients (22.22%) had positive margins. These patients were candidate to second look procedure allowing detection and treatment of residual disease. Oncologic outcomes were studied. Two patients experienced local relapses within a mean delay of 7 months. The local control rate was 88.9% while the local control using laser only was 83.33%. One patient underwent a total laryngectomy (TL) followed by adjuvant radiation therapy (RT) after a massive recurrence in the AC with infiltration of the thyroid cartilage. The laryngeal preservation rate was 94.44%. The 3 years overall survival rate reached 100% while the 3 years disease free survival was 88.9%.

Conclusion: the TLM offers acceptable oncologic outcomes in the treatment of T1 laryngeal cancer with AC involvement.

Key-words

Early glottic cancer- anterior commissure- laser surgery

INTRODUCTION

The contribution of transoral laser microsurgery (TLM) in the management of early glottic cancer is now well established (1). Compared to other modalities, it offers better functional results, shorter hospital stay and less morbidity rate which reduces the cost of treatment (2, 3). Another worthy advantage of the TLM consists in the easier salvage in case of relapse (4). The invasion of the AC in glottic cancers is known as a negative prognostic factor regardless the treatment modality. The pathophysiologic mechanism behind the aggressiveness of laryngeal cancer of the anterior glottis is not yet well understood. Besides this subsite is associated with an increased risk of spread to the thyroid cartilage (5). TLM is therefore controversial and even risky in case of AC involvement. In fact, Eckel proved that deep infiltration of the AC could not be well-treated by TLM (6). On the other hand the difficult access to the AC represents a real challenge for surgeons. The purpose of this single-centre study was to evaluate the oncologic outcomes of early glottic cancer with AC involvement treated with extended laser cordectomies.

METHODS

Within our medical institute of oncology in the department of head and neck surgery, patients with early squamous cell cancer (SCC) of the Glottis are either treated by external beam radiotherapy (RT), transoral laser microsurgery (TLM) or open partial laryngectomies. Due to its lower cost and easier salvage in case of relapse, TLM should be the first choice in well selected patients. From January 2012 to January 2015, all the data of patients treated with TLM for SCC of the Glottis were retrospectively reviewed. Diagnosis was previously confirmed by histopathological evaluation.

All patients underwent suspension laryngoscopy under general anesthesia, allowing staging of the disease, evaluation of the quality of exposure and performing biopsies. Laryngeal CT scans were done in all cases. Imaging helped in staging of the disease by showing paraglottic and pre-epiglottic spaces and cartilage integrity. Tumours were then classified following the TNM UICC classification of 2009 of glottic cancers. Therapeutic decisions were made within a multidisciplinary committee taking into account the stage of the disease, the operability and the choice of the patient.

In this study, we only considered T1 patients with AC involvement. Surgical resection was done under general anaesthesia after orotracheal intubation with a carbon dioxide laser Unilas 10600, Limmer Germany used in the continuous super pulse mode with output power set to 2 to 5 Watts. An optical microscope Carl Zeiss (Carl Zeiss, Germany) connected to a camera was used during the procedure. Surgical interventions were saved in a proper data file for each patient for iconographic and legal purposes.

Exposure was either optimal in majority of cases allowing the usage of a large laryngoscope (20x18mm) or difficult requiring smaller laryngoscopes or external pushing of the cricoid cartilage. Multitudes of Optics (0, 30, 45 and 70) were used for a better vision of the AC and sub glottis. When a clear vision of the AC and the whole vocal cords (VC) structure was not possible, the intervention was cancelled and the therapeutic decision changed.

Resections were performed following the European Laryngological Society classification modified in 2007 (ELS 2007). A type Va extended cordectomy encompassing the VC, the AC and the controlateral VC when necessary was realized to all patient with AC involvement. When needed, resection of the vestibular fold was performed to improve the quality of exposure. Tumour was resected en-bloc whenever possible. Otherwise a piece-meal resection was achieved.

In no case frozen sections were performed. Specimen was fixed to a cardboard. Anterior limit was marked with ink. If margins were positive, a second look procedure (SLP) was systematically done within the two first post operative months, for the purpose to search and remove potential residual disease. SLP was also done in an interval of 6 months in cases of significant worsening of the voice.

Patients were followed every 3 months for 2 years, then every 6 months and then yearly from the 5th year. An office- based fiberoptic examination was done in every check-up. Relapses were salvaged by second TLS or by open partial or total laryngectomies.

Statistical analysis was performed with SPSS version 20 statistical software. Mean and standard deviation (SDs) were reported in descriptive statistics. Overall survival (OS) was calculated between the surgery and the date of the last consultation or the date of death of the patient. Disease free survival (DFS) was calculated between the surgery and the first relapse. The percentages of laryngeal preservation and the rate of local control using laser only were also evaluated.

RESULTS

A total of 18 patients with early glottic cancer involving the AC were treated by TLM during the period of the study. Seventeen patients were males. Mean age was 64.4±8.98, ranging between 47 and 77 years. Sixteen patients (88.9%) were cigarette smokers, 12 (66.7%) were alcohol consumers (2 daily consumers, 4 regular consumers, 6 infrequent consumers). Twelve patients (66.7%) had anterior medical history: It was hypertension and diabetes mellitus in the majority of cases.

Hoarseness was the chief complaint. Patients sought medical consultation in delays ranging between 1 to 17 months with a mean delay of 6.5 ±7.09 months. Neither dysphagia nor dyspnea was reported in any case. One incidental finding on a CT scan was recorded. It was a synchronous laryngeal tumour to a prostatic adenocarcinoma in a 75-year-old patient.

CT scan was systematic. Thirty three 33% of cases showed evident involvement of the AC. Particular attention was paid to the thyroid cartilage. Patients presenting lysis or erosion of the cartilage as well as infiltration of the paraglottic or pre-epiglottic spaces were excluded from this protocol of treatment.

The tumour was localised in the right VC in 6 cases (33.3%), in the left VC in 8 cases (44.4%) and bilateral in 4 cases (22.2%). No supra or sub glottic extension were identified. Mobility was preserved in all cases. Exposure quality was optimal in sixteen patients and difficult in two patients. Histopathological examination showed a squamous cell carcinoma (SCC) in all cases. It was well differentiated in 14 patients (77.8%) and moderately differentiated in 4 patients (22.2%). The epidemiological and clinical findings are summarized in table 1.

Among the 18 patients, 14 (77.8%) were classified T1a and 4 (22.2%) were classified T1b (tumour infiltrating the 2 VCs). No regional or distant metastasis was identified.

All patients underwent a type Va cordectomy. Resection of the ventricular fold was required in 3 cases (16.7%) to improve the exposure. one case of Intraoperative bleeding happened, it was jugulated by local dabbing and administration of haemostatic IV agents. Antibiotics and corticoids were administrated to all patients during the post-operative time. This therapy was extended 5 to 6 days after discharge.

Table1: Epidemiological and clinical findings

Epidemiological and clinical findings	
Parameters	**Results**
Patients	18
Men: woman	17:1
Mean age	64.4 ± 9
Cigarette smokers	16 (88.9%)
Alcohol consumers	12 (66.7%)
Mean consultation delay	6.5 ±7.09 months
Side (Right: left: bilateral)	6: 8: 4
Tumour T stage (T1a: T1b)	14 : 4
Tumour differentiation (well differentiated: moderately differentiated)	14: 4
Exposure quality (optimal: difficult)	16:2

Mean hospital stay was 3.6 days ±1.1, ranging between 3 and 7 days. No tracheotomies were needed in any case. Two post-operative complications were noted. The first was an inhalation pneumonia treated by antibiotherapy and a naso-gastric tube during the hospitalisation period. The evolution was favorable and the patient was discharged after 6 days. The second complication was anterior emphysema following the resection of a T1a tumour in a 76-year old woman. It was treated conservatively by antibiotic, proton pomp inhibitors and vocal resting. She was discharged after 7 days and kept a severe hoarseness.

Margins were positive in 4 cases (22.2%). A SLP was systematically performed for these patients within an interval of 2 months. Two of them underwent a second CO2 laser resection. The other 2 underwent Tucker partial laryngectomy. Two other patients required a SLP for severe voice impairment. No evidence of residual disease was found in both cases. However, an anterior synechiae was identified and resected. We waited 6 months at least before SLP when margins were free. Post-operative findings are summarized in table 2.

Another case of anterior synechiae was recorded. It was during follow up one year after TLM. Lesion was resected. Histopathological examination showed no signs of malignancy.

The 3 years OS was 100%. One patient presented a local recurrence in the ipsilateral VC 6 months after surgery. He was salvaged by a second TLM. Another patient presented a massive relapse in the AC in an interval of 8 months. CT showed an invasion of the thyroid cartilage

and the subcutaneous tissue. The patient underwent a total laryngectomy with bilateral modified radical neck dissection followed by an adjuvant radiotherapy. The three years DFS was 88.88%. The ultimate local control using laser only was 83.33%. The laryngeal preservation rate was 94.44%.

Table2: Post operative findings

Post operative findings	
Parameters	**Results**
Mean hospital stay	3.6 days ±1.1
Postoperative complication (early: late)	(2: 2)
-inhalation pneumonia	1
-cervical emphysema	1
-Glottic web	2
Positive margins	4 (22.2%)
Second look procedure	4
Number of recurrences	2
Mean delay to recurrence	7 months

DISCUSSION

Management of early laryngeal cancer with AC involvement is still controversial. In absence of a clear consensus, many surgical and none surgical therapeutic approaches have been proposed. In fact the contribution of this sub site and its related structure in the tumour infiltration is not well understood. The chief anatomic concern was to define the role of the AC ligament otherwise known as ''Broyles ligament'' in the spread of laryngeal glottic cancer. It's now more likely that this anatomic structure forms a barrier to tumour spread (7). However, it cannot prevent from subglottic and supraglottic extension or invasion of the thyroid cartilage(7). Anterior spread through the thyro-cricoid membrane represents another additional risk. From another side, as reported by Peretti et al (8), adequate target exposure remains one of the limits of TLM. Therefore, according to the same authors, AC involvement is a debated TLM indication. Complete or partial vestibulectomy was proposed as a solution to improve the vision as false vocal folds could hinder exposure of AC, especially when dealing with bulky tumours (8, 9).

All tumours in our series were classified T1. T1b tumours were approached during a single laser session. Approaching these tumours during 2 laser sessions beginning with the most affected side is recommended as it may reduce the formation of anterior glottic web(10).T2 and even T3 tumours were included in other studies (11-13). The Intraoperative detection of inner cortex infiltration of the thyroid cartilage (T3) should be considered as an absolute contraindication of curative resection by TLM (8, 14).

Four patients (22.2%) had positive margins. Stephenson and al (13), reported a significantly higher rate of involved margins with the AC-involved group. In the study of Hakeem and al (11), the percentages of negative margins in the AC-involved group was 77.05%. However, it reached 94.47% in the AC-free group. This difference was statistically significant (p= <0.0001).

In our series, patients with positive margins required a second look procedure. Other authors recommend a SLP systematically in case of AC involvement (15). We treated Residual disease either by relaser or partial open laryngectomies. External beam radiotherapy (RT) was also proposed as an adjuvant treatment (13). As reported by Stephenson and al (13), patients with AC involvement needed more adjuvant RT in comparison with AC-free group (statistically significant p= 0.0005).

Two patients (11.1%) relapsed after treatment. The mean delay to relapse was 7months. For Chone this delay approaches 15 months ranging between 5 and 39 months (16). In the series of Hakeem and al patients with T1a tumours had a local recurrence rate equals to 16.67% in the AC-involved group and 18.5% in the AC-free group while these rates in patients having T1b tumours were respectively 42.85% and 30.43% (11). These differences were not statistically significant contrarily to T2 lesions for the same authors (11). Rödel and al (17), reported the same local control rate in the T2 lesions reaching 76% whether the AC were involved or not. Pearson and al (18), reported no local recurrences occurring in early tumours (pT1 and pT2) group. These divergences could be explained by the technical limitations, the quality of exposure, the tumour bulk and the resourcefulness of the surgeon.

Recurrences where salvaged in our series either by TL followed by adjuvant RT in one patient after a massive relapse in the AC. The other patient was treated during a second TLM. Open partial laryngectomies were used as salvage modality by some surgeons (1, 16, 19). However, this approach remains not well established. Marioni and al recommend TL even for small tumours as this modality is more predictable and technically easier (20). Few

studies discussed the role of open partial laryngectomies after failure of TLM. Lucioni and al (21), treated 17 patients by salvage horizontal partial laryngectomies after failure of laser. Forty seven (47%) among these patients presented a second relapse, 62% were treated by total laryngectomies. These authors recommend a TL for T2 patients with bilateral lesions. To our knowledge, no studies discussing the salvage modalities after failure of TLM in treating tumour with AC involvement were reported. Only one patient underwent a TL in our series. The laryngeal preservation rate was 94.44%. In the literature, AC-free groups had slightly better laryngeal preservation rates compared to the AC-involved groups rates (11, 13, 22, 23). These differences were statistically significant in the study of Hoffmann et al (24).

The 3 years overall survival rate was 100%. Disease free survival rate was 88.9%. These rates were respectively 96.7% and 83.3% for Mendelsohn and al (12). Hakeem and al (11), achieved a 5 years overall survival rate of 90.16% in the AC-free group and 86.38% in the AC-involved group (p= 0.642). Oncologic outcomes are summarized in table 3.

Table3: Oncologic outcomes

	Oncologic outcomes		
	Overall survival	**Local control**	**Laryngeal preservation**
Our series	100% (3 years)	88.9%	94.4%
Hakeem et al[11]	90.16% (5 years)	(T1a: 83.33%, T1b: 57.14%, T2: 65.21%)	95.8%
Stephenson et al[13]	95.2	96.7%	96.7%
Mendelsohn et al[12]	96.7% (5 years)	83.3%	93.3%
Chone et al[16]	-	79%	96%

CONCLUSION

According to this study, TLM is a reliable treatment alternative in the management of early glottic cancer with AC involvement. Despite the limited small number of patients and the retrospective aspect, this report remains in agreement with most of the previous studies (11-13, 16, 18). The reduced rate of local control and laryngeal preservation was not significant for many authors (11, 13, 16, 25). However, it has been reported an increased significant risk of positive margins associated with patients treated by TLM for early glottic cancer with AC involvement (11, 13). Besides these patients required more adjuvant RT (13). Therefore, optimal exposure, proper instrumentation and advanced surgical skills are needed in the management of these tumours.

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