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Laryngeal carcinoma: Our experience at Obafemi Awolowo University Teaching Hospital complex, Ile-Ife, Nigeria

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Abstract

Objectives: To determine the prevalent age, frequency, pattern of presentation, investigations and outcome of management of laryngeal carcinoma in our environment.
Design: 10 year retrospective study (January 1994 to December 2003).
Setting: Teaching hospital.
Subjects: 13 patients with tissue diagnosis managed for laryngeal carcinoma.
Main Outcome Measures: The age, sex, occupation, presentation, use of cigarettes and alcohol, investigations, tissue diagnosis, outcome of management and duration of follow up were extracted from hospital records and analysed.
Results: The age of patients ranged 38 to 88 years (median 69, male: female ratio=12:1). The histopathology was squamous cell carcinoma in all. Common symptoms included hoarseness of voice and breathlessness in all the patients, cough and weight loss in seven patients and otalgia in six. Only one patient indulged in alcohol while two were regular cigarette smokers. All the patients presented in stage IV with respiratory distress necessitating emergency tracheostomy in all. Seven patients had total laryngectomy plus post-operative radiotherapy while two patients had pharyngo-laryngectomy, thyroidectomy and radical neck dissection plus post-operative radiotherapy and thyroxine supplement. Post operative complications included pharyngo-cutaneous fistula in two patients, pharyngeal stenosis, stoma stenosis, and hypocalcaemia with hypothyroidism in one patient each. The fistulae were management conservatively. Prognosis was good despite late presentation.
Conclusion: Laryngeal carcinoma occurs predominantly in males. Presentation is late with hoarseness of voice and breathlessness in our community. Soft tissue neck X-ray is a useful diagnostic tool. Scarcity of radiotherapy centres, ignorance, local taboos, poverty and poor recognition by general medical practitioners negatively affected management of the patients. Laryngeal carcinoma should be excluded when managing elderly patients for bronchial asthma.

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Introduction

Carcinoma of the larynx, like other head and neck cancers is among the most debilitating tumour in which early diagnosis remains the best predictor of survival.[1] In Spain where carcinoma of the larynx is common, it accounts for 5.6% of all malignancies.[2] During the period under review carcinoma of the larynx accounted for 3.4% of head and neck cancers confirmed in our institution. It is commoner in males and it can be glottic, supraglottic or subglottic, with the highest cure rate in glottic, followed by supraglottic tumour.[3,4]

In developing countries like ours, late presentation is a major problem in the management of most malignant diseases, often due to poverty and ignorance. At times delay in diagnosis and management may be responsible as witnessed in this review. Efforts are being made to find a useful marker to enhance early detection of this disease. Markers of alcohol abuse (Ggt, Vcm) which were thought to be useful have not shown a correlation with any feature of this disease.[5] Retinoblastoma tumour suppressor gene (Rb) may be useful in determining the presence of nodal metastasis in this disease in the near future.[6]

It is recognised that early diagnosis remains the best predictor of prognosis of this disease. Since no appropriate marker has yet been found for early detection of this tumour, and in the face of scarce facilities and personnel especially in developing nations, it becomes imperative that concerted efforts are made to increase public awareness to ensure early presentation and enhance prompt recognition by healthcare providers. This for now remains the only useful weapon to aid effective management of this disease in developing countries.

This study was carried out at Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria, which serves the needs of the rural and semi-urban population of Osun, Ondo, Ekiti, and part of Kogi, Kwara and Oyo States, all in the south west of Nigeria. It is hoped that this study will help to determine the frequency, prevalent age, pattern of presentation, and outcome of management of this disease in our environment.

Objectives: This study is aimed at determining the frequency, prevalent age, pattern of presentation, investigations and outcome of management of laryngeal carcinoma in our environment and to compare our results with studies elsewhere.

Materials and Methods

The hospital records of patients managed for carcinoma of the larynx in our institution between January 1994 and December 2003 were reviewed retrospectively. Seventeen cases were clinically diagnosed and managed as laryngeal carcinoma during the period, but only 13 cases with tissue diagnosis were included in this review. The age, sex, occupation, social habits regarding cigarette smoking and alcohol consumption, presentation, investigations, tissue diagnosis, outcome of management and duration of follow up were extracted from the records and analysed.

Results

The age of patients ranged from 38 to 88 (median 69.9) years with peak incidence in the seventh decade. There were 12 male patients and one female.

Presentation: All the patients presented with stage IV diseases in respiratory obstruction. They were all treated as bronchial asthma by general practitioners before referral. Hoarseness of voice and breathlessness were common symptoms in all the patients. Other symptoms were as listed in the table.

Table I: Symptoms and duration of symptoms.

Symptoms	No. of patients
Breathlessness	13
Hoarseness of voice	13
Weight loss	7
Cough	7
Oltagia	6
Dysphagia	3
Stridor	2
Odynophagia	2
Headache	1
Anterior neck swelling	1
Duration in (Months)	**No. of patients**
3-6	2
7-12	6
13-18	2
24-36	2
>60	1
Total	**13**

Social history: Two patients were regular cigarette smokers who took average of 10 sticks per day over periods ranging from six to 50years; three were casual smokers who took zero to three sticks per day while eight patients had never smoked cigarettes. Two patients took alcohol regularly, nine were occasional alcohol users and two patients have never taken alcohol. Four patients were clergymen, three were farmers, and one patient each was a teacher, soldier, trader, bricklayer, textile industry worker and civil servant.

Investigations.

- *Plain lateral neck radiograph* proved very useful in demonstrating a soft tissue mass obstructing the laryngeal lumen in all the cases.
- *Plain chest radiograph* did not show any active lung lesions in all the patients.
- The *blood chemistry* and *full blood counts* were within normal limit in all.
- *Direct laryngoscopy and biopsy* revealed transglottic tumours with areas of necrosis in all the patients. In two patients, the tumour extended to the oropharynx (base of the tongue), the anterior neck, the strap muscles and the thyroid gland.
- *Histopathology* confirmed well differentiated squamous cell carcinoma in all the patients.
- Pre-operative *pulmonary function test* confirmed adequate pulmonary reserve in all the nine patients who had definitive surgery.

Operation: All the patients had emergency tracheostomy to relief airway obstruction on presentation. This palliative measure was possible in only four patients who declined further surgical management. Seven patients had total laryngectomy plus post operative radiotherapy, while two patients had pharyngo-laryngectomy, thyroidectomy and radical neck dissection plus post operative radiotherapy and thyroxine supplement.

Surgical Complications: Included pharyngo-cutaneous fistula in two patients, pharyngeal stenosis, stoma stenosis, and hypocalcaemia with hypothyroidism in one patient each. The fistulae were managed conservatively while the pharyngeal stenosis was corrected with a two-staged delto-pectoral flap repair. Eight of the nine laryngectomees were able to achieve oesophageal speech while the remaining one could not because of pharyngeal stenosis.

Duration of Follow Up: Three patients have been followed up for 5½ years, two patients for 3½ years, one patient for two years and two patients for 1¾ years. One patient died three months after surgery from ruptured carotid artery following post operative radiotherapy while the remaining eight patients are still doing well. The four patients that declined definitive surgery and were scheduled for radiotherapy were all lost to follow up.

Discussion

Carcinoma of the larynx is one of the most debilitating human diseases. Like other head and neck tumours, the strategic location and the unique function sub-serves by the larynx accords an important clinical and social recognition to this tumour.

The age incidence of 38 to 88 (median 69.9) years observed in this series closely reflects the global age incidence of this disease.[7] Existing literature showed a male preponderance in the epidemiology of this disease, though recent publications indicate increase frequency in the number of women affected.[8,9] The 12:1 male to female ratio observed in this series is close to the 10:1 observed by Lechuga, *et al.*[8] The male preponderance led to the speculation of the different susceptibility of the tumour cells to steroid sex hormones. However, available data on the receptor status for androgens, oestrogens and progesterone in laryngeal carcinoma are controversial. A recent report by Hagedorn and Nenlich failed to demonstrate the presence of significant male and female sex hormones in laryngeal tumour specimens.[10]

Although cigarette smoking has been identified as an important aetiologic and prognostic factor of this disease,[1,3,11] only two of our patients were regular smokers, while eight never smoked cigarettes. Alcohol has also been aetiologically linked to this disease,[2,8,11] but only two patients were regular alcohol users. These findings suggest that cigarette smoking and alcohol consumption are not important aetiological factors of this disease in our community.

The occupations of these patients could have played a role in the genesis of this disease because exposures to conditions that induce chronic laryngeal inflammation or irritation have been associated with laryngeal carcinoma.[11,12] Voice abuse acting singly, or in combination with smoking or other irritants such as chalk, cement dust etc, can induce chronic laryngeal irritation and predispose to squamous cell metaplasia and laryngeal carcinoma. In this series, the four clergymen and the three teachers were exposed to prolonged voice usage, while the bricklayer and the textile worker were exposed to cement products and industrial wastes.

Hoarseness of voice and breathlessness presented by all our patients were the most common symptoms of laryngeal carcinoma observed by Ratiola and his co-workers.[3] Weight loss, cough and otalgia were less common while dysphagia, stridor, odinophagia, headache and neck swelling were uncommon symptoms. Referred otalgia, observed in six patients, is a useful guide in making early diagnosis in patients with family history of laryngeal carcinoma.[13]

Glottic tumours typically present earlier than supraglottic tumours.[3] Hoarseness of voice, the earliest symptom in all our patients appeared nine to10 months before the onset of respiratory obstruction and suggests early involvement of the vocal cords. It is also possible that the carcinoma could be glottic in origin that later spread and became transglottic due to neglect.

Beside direct laryngoscopy and biopsy, lateral soft tissue neck X-ray was found useful and diagnostic in all our cases. This is important because it is cheap, relatively affordable, and within reach of majority of our patients, though it may not be helpful in early diseases. Ultrasonography and computerized tomography are also valuable and effective in the diagnosis of laryngeal carcinoma.[14] Squamous cell carcinoma confirmed in all our patients reflects the common histopathology pattern of this disease.[3,15]

Beside the major task of instituting curative therapy without compromising voice and swallowing functions, poverty, ignorance and inadequate facilities

and manpower poses additional challenges in the management of this disease in our community. Some of our patients initially rejected tracheostomy because of local taboos and fear. Lack of funds was identified as a major cause of late presentation. Four patients declined surgery because of the cost and the wrong notion that the patients were old enough to die.

Treatment options in laryngeal carcinoma depend on the stage of the tumour, expected voice quality, expected quality of life, and the preference of the management team.[16] Radiotherapy is useful because squamous cell carcinoma, the main histological type, is radiosensitive, and because it preserve laryngeal functions. Early tumours (stages I & II) are preferably and effectively treated with radiotherapy. Total laryngectomy offers better results in advanced tumours, or when there is failure of irradiation therapy.[17,18] Elective neck dissection is also advocated to improve survival and because of possible occult metastasis found in close to a quarter of patients with apparently N_0 nodal status.[17,19] In this series, seven patients had total laryngectomy while two had pharyngo-laryngectomy, thyroidectomy and bilateral neck dissection and thyroxine supplement, with good results. Pharyngeal stenosis, pharyngo-cutaneous fistula, stoma stenosis and hypocalcaemia with hypothyroidism, which complicated the operations, are known complications of these procedures.[9]

Although total laryngectomy has been proven to be of value in the management of advanced laryngeal carcinoma, the needs to preserve laryngeal function has led to increasing preference for other conservative forms of management. Recent reports showed that partial laryngectomy is a good alternative to total laryngectomy. Beside preservation of laryngeal function, it prevents emotional distress associated with permanent tracheostomy without compromising survival.[1,20-22] Sequential chemo-radiation also allows laryngeal preservation in over 65% of patients without compromising survival.[23] In combination therapy, radical laryngectomy plus radiotherapy has been shown to be more effective in loco-regional control compared to radiotherapy plus chemotherapy.[24,25] Unfortunately many of our patients could not undergo post operative radiotherapy because of the high cost, scarcity and a long waiting period. The prognosis is good despite late presentation. Eight of the nine laryngectomies were able to achieve oesophageal speech. Only one patient with pharyngeal stenosis and pharyngo-cutaneous fistula could not. One patient died from a ruptured carotid following radiotherapy three months after surgery, while the remaining eight are still doing well with an average duration of follow up of 46.5 months. Although the duration of follow up is short, it is reasonably long enough for local recurrence to manifest. Tryka *et al*, showed that most local or nodal recurrence and distance metastases were evidenced within 11 to 22months after surgery.[26] Four patients that declined definitive surgery were lost to follow up.

In view of the local problems associated with radiotherapy, surgery may remain the sole treatment of this disease in our environment. With the good results now reported with partial laryngectomy,[1,20,21] our emphasis for early tumours is towards partial resection. Less than 2% of American otolaryngologists still believe that total laryngectomy should be done for operable tumours.[16] Apart from determining the prevalent age, pattern of presentation and challenges of managing laryngeal carcinoma in our developing society, it is hoped this article will raise awareness and assist in early recognition and management of laryngeal carcinoma.

Conclusion

In our community laryngeal carcinoma occurs predominantly in male, and presentation is late with hoarseness of voice and breathlessness. In developing nations where sophisticated facilities are lacking, soft-tissue neck X-ray is a useful diagnostic tool. Scarcity of radiotherapy centres, ignorance, local taboos, poverty, and poor recognition by general medical practitioners negatively affected management of these patients. Laryngeal carcinoma should be excluded when managing middle aged and elderly patients for bronchial asthma.

References

1. Gan X, Zhou Y, Cai L. Prognosis of laryngeal carcinoma in youth. *Zhonghua Er Bi Yan Hou Ke Za Zhi* 1996;31(4):201-2
2. Zapater E, Campos A, Fortea M, Armengot M, Basterra J. Prognostic factors in supraglottic laryngeal cancer: a review of 74 cases. *Acta Otorrinolaringol Esp* 2000 Mar; 51(2):120-8.
3. Raitiola H, Pukander J, Laippala P. Glottic and supraglottic laryngeal carcinoma: differences in epidemiology, clinical characteristics and prognosis. *Acta Otolaryngol* 1999;119(7):847-51.
4. Grau JJ, Cuchi A, Traserra J, Firvida JL, Arias C, Blanch JL, *et al.* Follow-up study in head and neck cancer: cure rate according to tumor location and stage. *Oncology* 1997 Jan-Feb;54(1):38-42.
5. Avalos E, Martin A, Porras E, Martinez E, Araujo J, Cordoba J, *et al.* Biological markers of alcohol abuse in patients with carcinoma of the larynx. *Acta Otorrinolaringol Esp* 1998 Aug-Sep;49(6):465-6.
6. Takes RP, Baatenburg de Jong RJ, Schuuring E, Hermans J, Vis AA, Litvinov SV,*et al.* Markers for assessment of nodal metastasis in laryngeal carcinoma. *Arch Otolaryngol Head Neck Surg* 1997 Apr;123(4):412-9.
7. Singh B, Alfonso A, Sabin S, Poluri A, Shaha

AR, Sundaram K, *et al.* Outcome differences in younger and older patients with laryngeal cancer: a retrospective case-control study. *Am J Otolaryngol* 2000 Mar-Apr;21(2):92-7.
8. Lechuga R, Martin C, Minguez I, Cajade J, Velez M, Labella T. Study and incidence of carcinoma of the larynx in women. *Acta Otorrinolaringol Esp.* 2000 Mar; 51(2):129-32.
9. Greisen O, Carl J, Pedersen M. A consecutive series of patients with laryngeal carcinoma treated by primary irradiation. *Acta Oncol* 1997;36(3):279-82.
10. Hagedorn HG, Nerlich AG. Analysis of sex hormone receptor expression in laryngeal carcinoma. *Eur Arch Otorhinolaryngol* 2002 Apr;259(4):205-10.
11. Koufman JA, Burke AJ. The etiology and pathogenesis of laryngeal carcinoma. *Otolaryngol Clin North Am* 1997 Feb;30(1):1-19.
12. Doskov D. A system for the objective screening of dysphonia and the possibilities for its application in exposed workers. *Int Arch Occup Environ Health* 1998 Sep;71 Suppl: S79-80.
13. de Bondt RB, Balm AJ, Hilgers FJ, Tan IB. Referred earache; an important symptom of head-and-neck cancers. *Ned Tijdschr Geneeskd* 1998 Aug 1;142(31):1753-6 Comment in: *Ned Tijdschr Geneeskd.* 1998 Nov 21;142(47):2594.
14. Kabacinska A. Evaluation of the usefulness of ultrasonic examination of the pre-epiglottic space in patients with laryngeal carcinoma. *Ann Acad Med Stetin* 1998;44:197-207.
15. Kowalska B, Stankiewicz C, Mikaszewski B, Zaorski P, Polawska K, Kozlowski *et al.* Long term result of treatment of laryngeal carcinoma (1981-1990). *Otolaryngol Pol* 2000;54 Suppl 31:240-1.
16. DiNardo LJ, Kaylie DM, Isaacson J. Current treatment practices for early laryngeal carcinoma. *Otolaryngol Head Neck Surg* 1999 Jan;120(1):30-7.
17. Stankiewicz C, Kowalska B, Mikaszewski B, Brzoznowski W. Bilateral neck dissections. *Otolaryngol Pol* 2000;54 Suppl 31:142-4.
18. Levine PA, Brasnu DF, Ruparelia A, Laccourreye O. Management of advancedd stage laryngeal cancer. *Otolaryngol Clin North Am* 1997 Feb;30(1):101-12.
19. Mikaszewski B, Stankiewicz C, Kowalska B, Brzoznowski W. Effectiveness of elective neck dissection in patients with laryngeal carcinoma. *Otolaryngol Pol* 2000;54 Suppl 31:145-7.
20. Zhang L, Luan X, Pan X, Xie G, Xu F, Liu D, *et al.* Surgical management of supraglottic laryngeal carcinoma in 182 patients with special emphasis on functional preservation. *Zhonghua Zhong Liu Za Zhi* 2002 Jan;24(1):59-61.
21. Zacharek MA, Pasha R, Meleca RJ, Dworkin JP, Stachler RJ, Jacobs JR, *et al.* Functional outcomes after supracricoid laryngectomy. *Laryngoscope* 2001 Sep; 111(9):1558-64.
22. Klatka J, Kupisz K. A case of laryngeal carcinoma recurrence in the neck lymphatic system after total laryngectomy and combined method treatment. *Otolaryngol Pol* 1998; 52(5):597-9.
23. Rosenblatt E, Siegelmann-Danieli N, Zidan J, Haim N, Kuten A. Preservation of the larynx in advanced cancer experiences at the Oncology Department, Rambam Medical Center, Haifa. *Harefuah* 2000 Oct;139(7-8):271-4,326.
24. Nguyen TD, Malissard L, Theobald S, Eschwege F, Panis X, Bachaud JM, *et al.* Advanced carcinoma of the larynx: results of surgery and radiotherapy without induction chemotherapy (1980-1985): a multivariate analysis. *Int J Radiat Oncol Biol Phys* 1996 Dec1;36(5):1013-8.
25. Finizia C, Geterud A, Holmberg E, Lindstrom J, Lundgren J, Kuylenstierna R, *et al* Advancedd laryngeal cancer T3-T4 in Sweden: a retrospective study 1986-1990. Survival and locoregional control related to treatment. *Acta Otolaryngol* 1996 Nov; 116(6):906-12.
26. Tryka E, Semczuk B, Katedry I, Kliniki Otolaryngologii AM, Lublinie. Failure of surgical treatment in patients with laryngeal neoplasm treated at the Department of Otolaryngology Medical Academy in Lublin. *Otolaryngol Pol* 1995; 49 Suppl 20:349-53.