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Case Report

Prognostic factors of laryngeal solitary extramedullary plasmacytoma: a case report and review of literature

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Abstract: A paucity of data exists concerning the presentation, natural course and outcome of extramedullary plasmcytoma (EMP). It is difficult to determine the optimal treatment strategy and prognostic factors for EMP. We present an additional case of laryngeal EMP and systemic review relevant reports in the English and Chinese literature. We found, to our knowledge, 147 cases in larynx in the English-language literature and Chinese-literature. The most common treatment modality was radiotherapy alone. The mean survival duration was ~184 months, and the 5- and 10- year survival rates were 76.1% and 67.4%, respectively. The univariate analysis suggested that progression to multiple myeloma and amyloid deposits may be poor prognostic factors. The multivariate analysis suggested that only progression to multiple myeloma may be a poor prognostic factor. Laryngeal EMP is uncommon. Progression to multiple myeloma may be a poor prognostic factor.

Keywords: Extramedullary plasmcytoma, larynx, progression to multiple myeloma, amyloid deposits, prognosis

Introduction

Extramedullary plasmacytoma (EMP) is a rare tumour, accounting for 3% of all plasma cell neoplasms and less than 1% of all head and neck tumours [1-41]. Approximately 80-90% of EMPs occur in the head and neck, mainly in the paranasal sinuses, nasal cavity, oral cavity and pharynx [1-41]. Laryngeal EMP, which comprises ~6-18% of all EMPs, is a rare tumour but increasingly reported recently [1-41].

A paucity of data exists concerning the presentation, natural course and outcome of EMP. Therefore, it is difficult to determine the optimal treatment strategy and prognostic factors for EMP. Some studies have revealed that age, tumour size, site of origin (extramedullary versus bone), grade, M-protein and light chains, and radiotherapy dose influence the outcome in solitary plasmacytoma patients [1-41]. However, other studies have reported contrasting results. Therefore, the prognostic factors of head and neck tumours are unclear. To our knowledge, no report of the prognostic factors of a single tumour site (laryngeal solitary EMP) has been published.

In the present study, we report an additional case of solitary laryngeal EMP. We also reviewed the English- and Chinese-language literature concerning laryngeal solitary EMP and analysed the possible prognostic factors of laryngeal solitary EMP.

Case report

A 47-year-old female presented with persistent hoarseness for 3 months that progressively worsened for 2 weeks. She denied having dysphagia, pharyngalgia, dyspnea and fever, and other medical problems previously. Indirect laryngoscopy and laryngeal stroboscopy revealed a 2 × 2 cm reddish smooth mass overlying the left hemilarynx, the base from the aryepiglottic fold (**Figure 1**). Magnetic resonance imaging (MRI) of the neck revealed an irregular mass overlying the left false cord, vocal cord, and piriform sinus, and no enlarged node was present. T1-weighted imaging showed isointen-

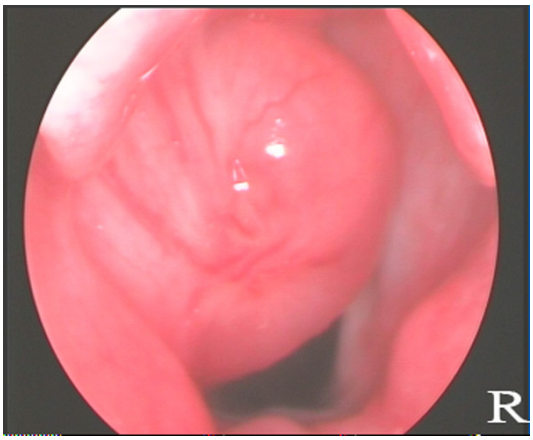

Figure 1. Laryngeal stroboscopy revealed a 2 × 2-cm reddish smooth mass overlying the left hemilarynx, the base from the aryepiglottic fold.

sity, and T2-weighted imaging showed hyperintensity. Diffusion-weighted MRI (DWI) showed that the lesion had high signal intensity, and the apparent diffusion coefficient (ADC) was 1.18 × 10^{-3} mm^2/s (**Figure 2**). These findings suggested a benign laryngeal tumour.

Prior tracheostomy with prior informed consent was necessary because of concerns regarding difficult intubation, impending respiratory crisis, and pre- and postoperative haemorrhage. Subsequently, a biopsy was performed by suspension laryngoscopy under general anaesthesia. The frozen section showed abnormal proliferation of mature-appearing plasma cells in the lesion, suggestive of a plasmacytoma. A 3.5 × 2.5 × 2 cm reddish mass in the left aryepiglottic fold, laryngeal ventricle, and false cord was completely excised via neck lateral incision (**Figure 3**). The bilateral vocal cords were normal. The postoperative histopathologic results demonstrated abnormal proliferative plasma cells arranged in a solid sheet, and these cells showed invasive growth involving the surrounding muscles and glands. Immunohistochemical staining showed that the cells were positive for CD138, CD79a, and lambda light chain (**Figure 4**), and negative for CD20, CD3 and PAX5. Ki-67 immunostaining demonstrated a low proliferation index (5%). These findings confirmed the diagnosis of plasmacytoma. A complete workup for multiple myeloma (MM) revealed normal serum electrophoresis, serum immunoglobulins, and 2-microglobulin levels. Serum calcium, uric acid, and renal function tests were normal. Bone marrow aspiration and biopsy suggested normocellular marrow with a normal architecture; all hematopoietic elements presented a normal ratio, and a whole-body skeletal emission computed tomography (ECT) survey was normal. Computed tomography of the chest, abdomen, and pelvis showed no evidence of metastatic disease. Urine examination for light chains was negative. Thus, laryngeal solitary EMP was diagnosed.

Postoperative radiotherapy was administered (50 Gy in 200-cGy fractions delivered over 30 days) to the laryngeal and corresponding neck lymph regions (**Figure 5**). Due to marked laryngeal oedema, the patient was discharged with a tracheostomy tube.

Six months after surgery, the patient developed a neck abscess, for which antibiotics were administered. The infection was subsequently controlled. One month later, the tracheostomy tube was removed successfully. Regular neck MRI, serum and urine examination, and X-ray chest films were normal. She was alive with no evidence of disease at 18 months after surgery.

Discussion

We reviewed the English-language literature using MEDLINE to conduct a PubMed/Web of Science search using the terms “plasmacytoma” or “extramedullary plasmacytoma” or “hemopoietic neoplasms” combined with “head and neck/larynx”. Articles published in Chinese journals were identified by searching the Wanfang (www.wanfangdata.com.cn), CNKI (China National Knowledge Infrastructure: http://www.cnki.net/), and Weipu (http://10.15.61.77/index.asp) databases from 1986 to 2013. We found that conclusive prognostic factors of laryngeal EMP were difficult to determine because of the small number of documented cases, alteration of biological behaviour, and insufficient data. However, useful information was obtained regarding correlated prognostic factors.

In the present review, we found 129 cases in the larynx in the English-language literature (including our case from 1968 to 2013) (**Table 1**) [1-64]. Fifty-one males and 29 females (detailed data about gender were available from 80 cases, and 43 cases were only available for the gender ratio). The male-to-female

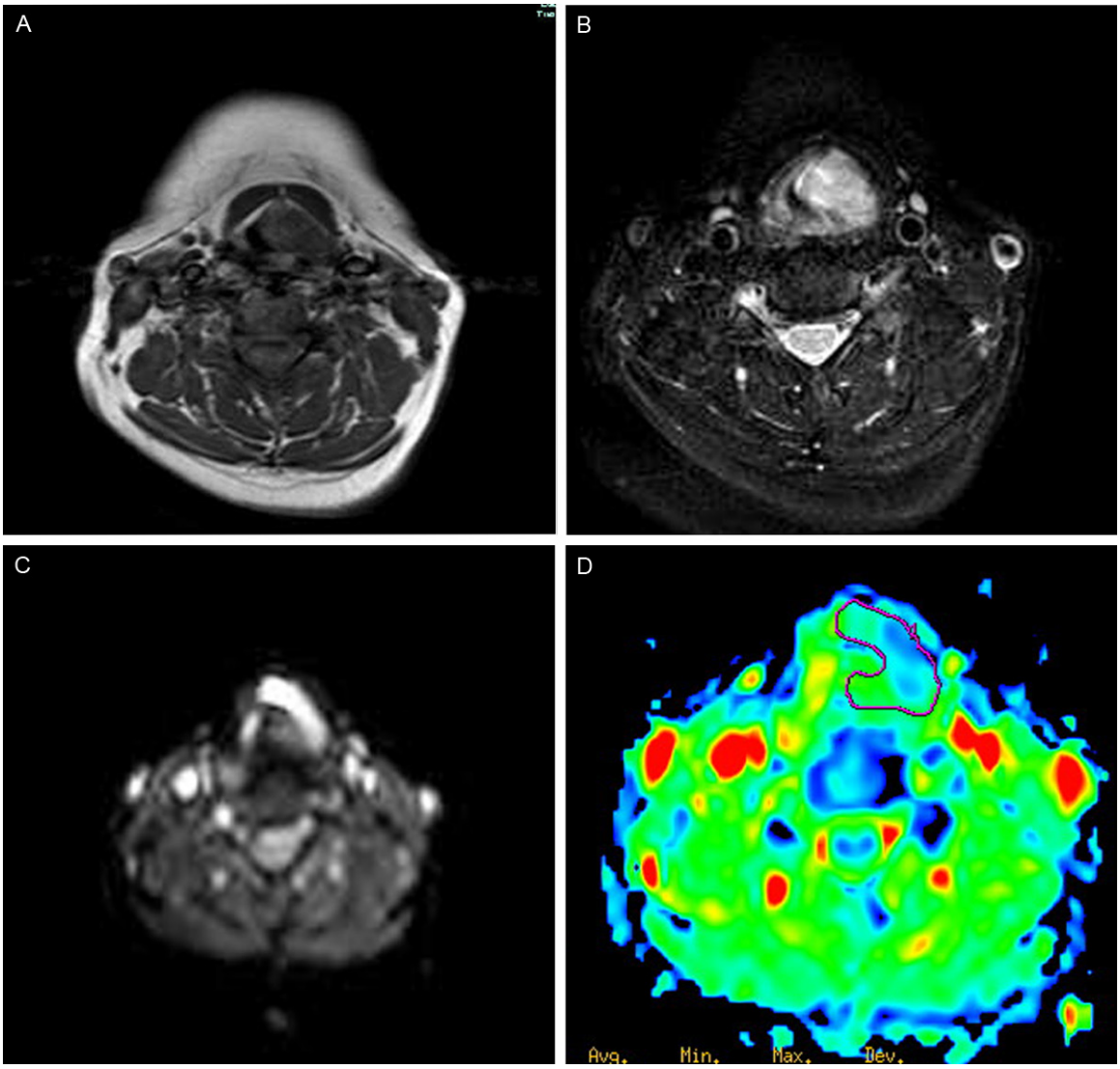

Figure 2. MRI showed an irregular mass overlying the left false cord, vocal cord, and piriform sinus, and no enlarged node was present. T1-weighted imaging showed isointensity (A), and T2-weighted imaging showed hyperintensity (B). Diffusion-weighted MRI (DWI) showed that the lesion had high signal intensity (C), and the apparent diffusion coefficient (ADC) was 1.18×10^{-3} mm^2/s (D).

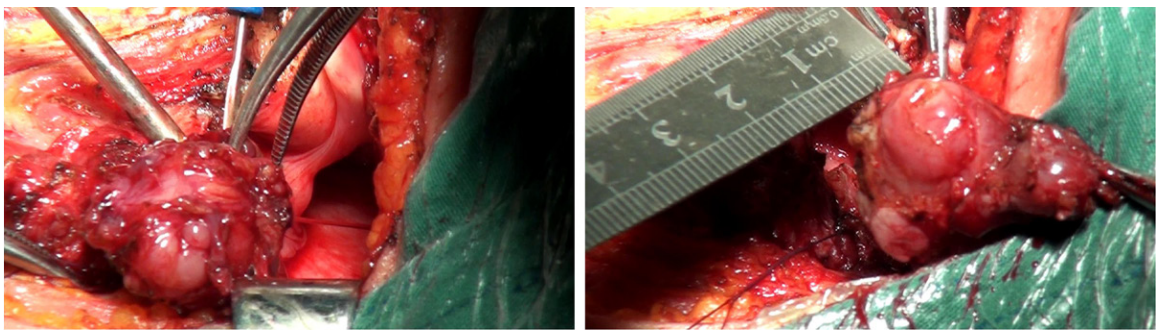

Figure 3. A 3.5 × 2.5 × 2 cm reddish mass in the left aryepiglottic fold, laryngeal ventricle, and false cord was completely excised via neck lateral incision.

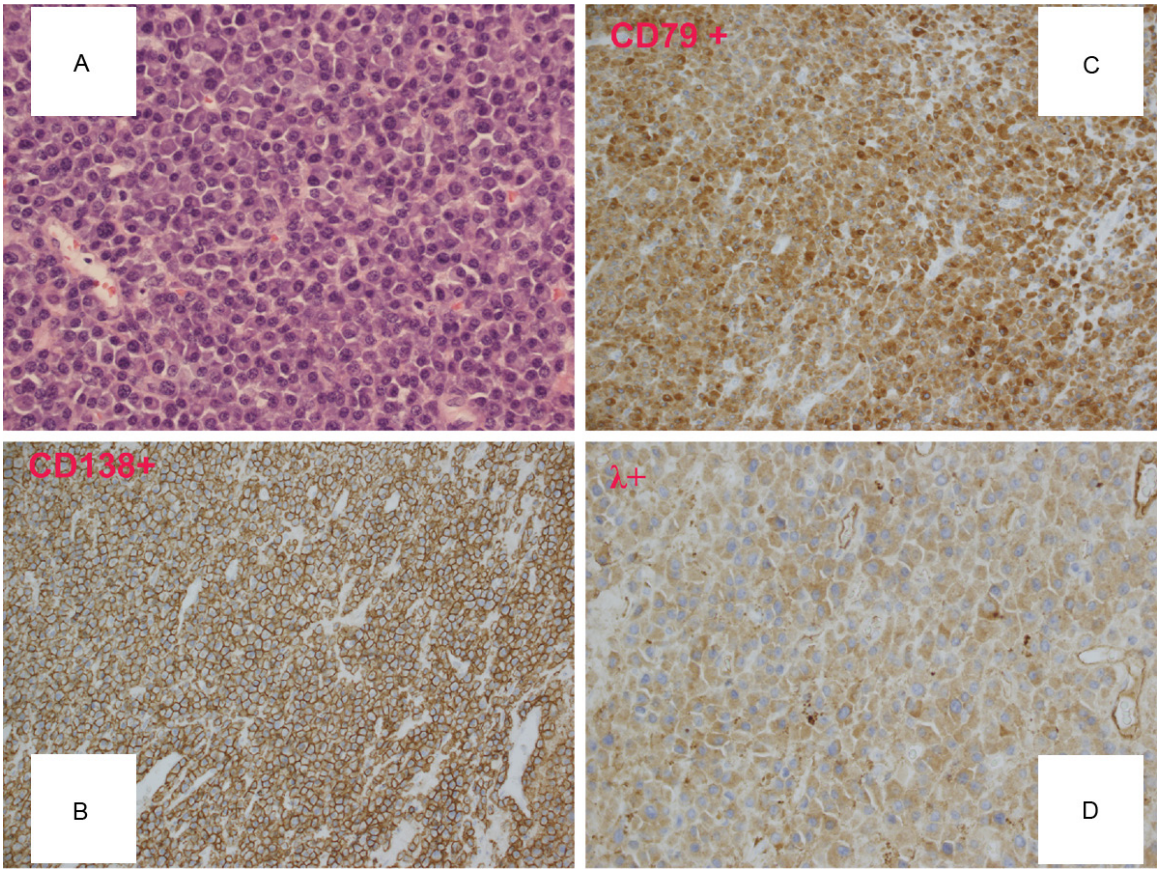

Figure 4. Pathological results demonstrated abnormal proliferative plasma cells arranged in a solid sheet, and these cells showed invasive growth involving the surrounding muscles and glands (A). Immunohistochemical staining showed that the cells were positive for CD138 (B), CD79a (C), and lambda light chain (D).

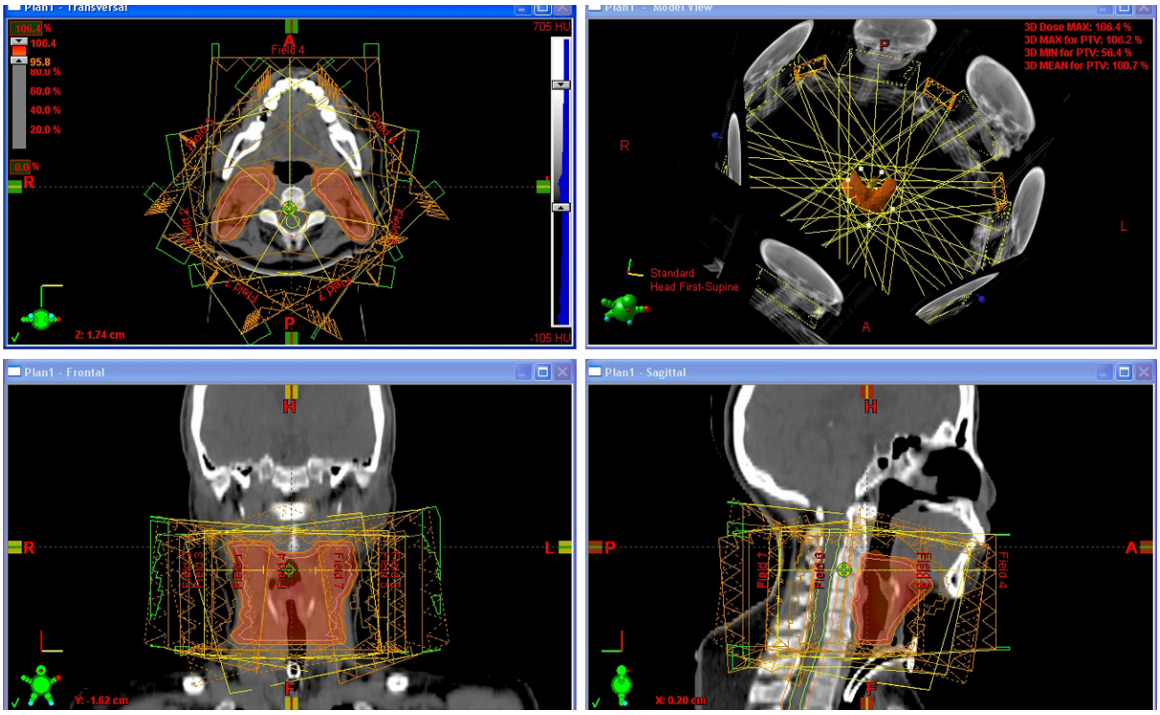

Figure 5. Postoperatively, the patient received radiotherapy (50 Gy in 200-cGy fractions delivered over 30 days) to the laryngeal andcorresponding neck lymph regions.

Table 1. 129 EMP cases in the larynx in the English-language literature

Ref	Pt	Sex/age	site	symptom	Size	Urine	Serum	ICH: Ig	ICH	Treatment	Recurrence	Metastasis	Follow-up
Present case	1	47/F	aryepiglottic fold	hoarseness	2.0 cm × 2.0 cm	NEG	NEG	IgG λ+	CD138+, CD79a+	surgery + postoperative radiotherapy (50 Gy)	No	No	7 mo ANED
Gerry 2013	2~33	median 62 yrs	larynx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ghatak 2013	34	29/Fpregnancy	vocal card	hoarseness, respiratory distress	NA	κ+	IgG κ+, β 2 -microglobulin↑	IgG κ+	NA	tracheotomy + radiotherapy (50 Gy)	No	No	16 months
Loyo 2013	35	80/F	paraglottic	hoarseness, dyspnea, stridor	NA	NEG	NEG	IgG κ+	CD38+	CO2laser hemilaryngetomy	NA	NA	NA
Baghmar 2013	36	44/M	Larynx	NA	< 5 cm	NEG	NEG	NA	NA	radiotherapy alone (45 Gy)	Yes	progression to MM	Alive/CR
Kim 2012	37	58/M	left arytenoid	No symptom	1.5 cm × 1.2 cm	NEG	NEG	IgG λ+	NA	surgical excision under direct laryngoscopy	No	No	2 yrs
De Zoysa 2012	38	62/F	left true vocal fold	hoarseness	1.1 cm × 1.0 cm	NEG	NEG	IgG κ+	CD45+, CD138+	biopsy + radiotherapy (50 Gy)	No	No	2 months
Sasaki 2012	38~41	median 64 yrs	larynx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ramírez-Anguiano, 2012	42	57/M	subglottis	dysphonia, dyspnea, stridor	NA	NEG	NEG	NA	CD138+	biopsy + radiotherapy (54 Gy)	No	No	alive 1 yr
Pichi 2011	43	73/M	cricoid	hoarseness, progressive dyspnea	2 cm	NEG	NEG	IgG κ+	CD138+	tracheotomy, biopsy, radiotherapy (40 Gy)	No	progression to MM. one yr late	died 1 yr
Zhang 2010	44	56/F	left ventricle and ventricular band	hoarseness, dysphonia	1.5 cm × 0.6 cm	κ+	NEG	IgG, IgA	synchronous squamous cell carcinoma in situ CD38+, CD138+, EMA+	vertical hemilaryngectomy + modified left neck dissection	No	No	ANED 2 yrs
Creach 2009	45	median 64 yrs	larynx	NA	NA	NA	NA	NA	NA	radiotherapy alone	No	No	NA
Creach 2009	46	NA	larynx	NA	NA	NA	NA	NA	NA	radiotherapy alone	No	No	NA
Creach 2009	47	NA	supraglottis	NA	NA	NA	NA	NA	NA	radiotherapy alone	NA	Regional lymph node	NA
Iseri 2009	48	46/F	aryepiglottic fold	laryngeal globus sensation	0.7 cm × 0.9 cm	NEG	M	IgG λ+	NA	surgery + postoperative radiotherapy (40 Gy)	No	No	ANED 2 yrs
Rutherford 2009	49	13/F	subglottic mass	hoarseness	NA	NEG	NEG	IgG λ+	CD138+, CD79a+	surgery + postoperative radiotherapy (39.6 Gy)	No	No	ANED 6 weeks
Pratibha 2009	50	49/M	both false cords ventricle and true vocal cords	hoarseness	NA	NEG	NEG	IgG λ+	NA	biopsy + radiotherapy (44 Gy)	No	No	NA
Fernández-Aceñero 2009	51	42/F	right band	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Vanan 2009	52	16/F	vocal cord.	hoarseness, sensation of foreign body	0.76 cm	NEG	NEG	IgG λ+	CD138+, CD79a+	biopsy + radiotherapy (50.4 Gy)	No	No	ANED 1 yr
Bachar 2008	53	median 64 yrs	larynx	hoarseness	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bachar 2008	54	NA	larynx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bachar 2008	55	NA	larynx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bachar 2008	56	NA	larynx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bachar 2008	57	NA	supraglottis	hoarseness	NA	NA	NA	NA	NA	NA	NA	progression to MM, average 2.8 yrs	NA
Ozbilen Acar 2008	58	43/F	vocal cord.	hoarseness, coughing	0.4 cm	NEG	NEG	IgG λ+	NA	surgery	No	No	ANED 2 yrs
Straetmans 2008	59	62/F	subglottis	stridor	1.5 cm	NEG	NEG	IgG κ+	CD138+	tracheotomy + laryngofissure + T-tube	No	No	1 yr
Straetmans 2008	60	57/M	epiglottis	haemoptoea	0.5 mm	NEG	NEG	IgG λ+	CD138+	excised by laser + radiotherapy (50 Gy)	yes 3 mo later	No	ANED 2 yrs
Kusunoki 2007	61	76/F	supraglottic	denied any laryngopharyngeal symptoms	NA	NEG	NEG	IgG κ+	CD38+	biopsy + radiotherapy	No	No	ANED 6 mos
Velez 2007	62	64/M	right hemilarynx and a small and polypoid	hoarseness	NA	NEG	NEG	IgG λ+	NA	surgery + radiotherapy	No	No	ANED 3 yrs
Lewis 2007	63	71/M	parapharyngeal space, soft palate, supraglottic region	hoarseness	NA	NEG	κ+	IgG κ+	NA	laser excision	No	No	ANED 2 yrs
Tournier-Rangeard, 2006	64	NA	larynx	NA	NA	NA	NA	NA	NA	excised biopsy + radiotherapy	NA	NA	NA
Nakashima 2006	65	39/M	left arytenoid region	without anny laryngeal symptoms	NA	NEG	NEG	IgG κ+	NA	laser excision + radiotherapy (60 Gy)	No	No	ANED 6 yrs
Nakashima 2006	66	59/M	epiglottis	stomatitis but had no other symptoms	NA	NEG	NEG	IgG κ+	NA	surgery under a direct laryngoscopy	No	No	ANED 15 yrs
Chao 2005	67	60/M	supraglottic larynx	laryngeal mass	NEG	NEG	NEG	NA	NA	excised biopsy + radiotherapy (50 Gy)	No	No	37 mo Dead
Sakiyama 2005	68	47/F	chest wall, subglottic region	a fist-sized tumor and invariable pain in the left lateral pectoral region, stenosis chest wall operation after 2 months	NA	NEG	NEG	Ig D(λ)+	NA	biopsy + radiotherapy (50 Gy)	No	No	NED 7 yrs

Yavas 2004	69	43/F	nasopharynx, left vocal cord	nasal obstruction and hoarseness	NA	NEG	NEG	IgG κ+	NA	Biopsy + radiotherapy	NA	NA	NA
Hall 2004	70	58/M	subglottis	laryngeal obstruction	NA	NEG	NEG	IgG κ+	NA	NA	NA	NA	NA
Michalaki 2003	71	46/F	Larynx	NA	NA	NA	NA	NA	NA	radiotherapy 45 Gy	No	No	ANED 49 mo
Michalaki 2003	72	59/M	Larynx	NA	NA	NA	NA	NA	NA	radiotherapy 45 Gy	No	No	ANED 67 mo
Strojan 2002	73	65/M	False vocal cord	NA	NA	NA	NA	IgNEG κ+	NA	radiotherapy (60 Gy)	No	No	DOC at 7.8 yrs
Strojan 2002	74	72/M	true vocal cord	NA	NA	NEG	NEG	Ig NEGλ+	NA	radiotherapy (40 Gy)	No	No	DOC at 4.7 yrs
Strojan 2002	75	50/F	laryngeal ventricle right	NA	NA	Neg	NEG	IgNEG κ+	NA	radiotherapy (50 Gy)	No	No	ANED at 2.2 yrs
Soni 2002	76	65/M	subglottic region	cough, hoarseness, discrete dysphagia and shortness of breath	NA	NEG	NEG	IgG κ+	NA	Biopsy + tracheostomy + radiotherapy (60 Gy)	No	No	ANED 2 yrs
Lee 2002	77	44/F	supraglottic larynx	hoarseness	NA	NEG	NEG	negative	NA	laser excision	No	No	ANED 6 mos
Kamijo 2002	78	80/M	left false vocal fold	hoarseness	2 × 1.0 cm	NEG	NEG	negative	CD79+, Vs38C+	surgery + radiotherapy (60 Gy)	No	No	ANED 2 yrs
Uppal 2001	79	54/M	left hemilarynx	stridor	NA	NEG	NEG	NA	NA	radiotherapy alone?	No	NA	died weeks
Maheshwari 2001	80	65/M	subglottic region	dry cough, breathlessness	NA	NA	NA	NA	NA	radiotherapy alone	No	No	NED 1 yr
Saad 2001	81	79/M	glottis	no laryngeal symptom	NA	NEG	M	NA	NA	NA	NA	NA	died 6 mo
Nagasaka 2001	82	12/F	glottis	hoarseness, increasing difficulty of breathing	3 cm	NEG	NEG	IgG κ+	NA	surgery + radiotherapy (43.2 Gy)	No	No	ANED 4 yrs
Rakover 2000	83	38/M	glottis	hoarseness	NA	NEG	NEG	IgG κ+	NA	Biopsy	Yes, 3 times	No	radiotherapy (50 Gy), ANED 3 yrs
Hotz 1999	84	63/NA	multifocal sites: nasopharynx, larynx, nasalmfossa	dyspnea	NA	NA	NEG	IgG κ+	EMA	surgery + radiotherapy (45 Gy)	No	No	108 mo ANED
Hotz 1999	85	45/NA	multifocal sites: nasopharynx, larynx	dysphagia	NA	NA	NEG	IgG κ+	CD45RB, EMA	surgery + radiotherapy (55 Gy)	Yes, 47 mo, laser + chemotherapy	No	108 mo AWD
Liebross 1999	86	NA	larynx	NA	NA	NEG	NEG	NA	NA	radiotherapy alone	No	No	NA
Alexiou 1999	87	69/M	glottis	NA	NA	NEG	No	IgG κ+	NA	surgery	No	No	ANED 62 mos

Alexiou 1999	88	40/M	Aryepiglottic space and regional neck side involvement	NA	NA	NEG	elevated IgG levels	IgG κ+	elevated IgG levels	surgery + postoperative radiotherapy (40 Gy)	No	No	ANED 20 mos
Nowak-Sadzikowska 1998	89	34/M	supraglottis	hoarseness	NA	NEG	NEG	NA	NA	radiotherapy alone (54 Gy)	No	No	ANED 10 yrs
Nowak-Sadzikowska 1998	90	50/M	glottis	hoarseness	NA	NEG	NEG	NA	NA	radiotherapy alone (60 Gy)	No	No	ANED 10 yrs
Nowak-Sadzikowska 1998	91	36/M	supraglottis	asymptomatic	NA	NEG	NEG	NA	NA	radiotherapy alone (54 Gy)	No	No	ANED 10 yrs
Nowak-Sadzikowska 1998	92	68/F	supraglottis	hoarseness	NA	NEG	NEG	NA	NA	radiotherapy alone (54 Gy)	No	No	ANED 10 yrs
Nowak-Sadzikowska 1998	93	48/M	glottis	hoarseness	NA	NEG	NEG	NA	NA	radiotherapy alone (60 Gy)	No	No	ANED 10 yrs
Bhattacharya 1998	94	49/F	spiglottis, right aryeplottic fold, postcricoid space, false cords and aryteoids	dysphagia, weight loss, cachectic	NA	M-P	a high gamma globulin rate	κ+	NA	biopsy	No	No	DOD, 6 mo
Sulzner 1998	95	49/M	right aryentoid	nonproductive coughing	NA	NEG	NEG	IgG κ+	NA	radiotherapy (45 Gy)	No	No	ANED, 5 yrs
Susnerwala 1997	96	79/F	larynx	NA	NA	NEG	NEG	κ+	NA	radiotherapy (35 Gy)	No	No	ANED, 132 mo
Susnerwala 1997	97	65/M	larynx	NA	NA	NEG	NEG	κ+	NA	radiotherapy (45 Gy)	No	No	ANED, 52 mo
Rodriguez-de-Velasquez 1996	98	33/F	subglottis	hoarseness	NA	NA	NA	NA	NA	NA	NA	NA	NA
Rolins 1995	99	43/M	epiglottis	asymptomatic	2 × 2.5 cm	NEG	NEG	κ, λ+	CD14, CD15, CD5, CD19	surgery	No	No	ANED, 3 yrs
Rabinov 1993	100	48/M	subglottic region	hoarseness, stridor	NA	NA	NA	NA	NA	radiotherapy	NA	NA	NA
Mochimatsu 1993	101	54/M	laryngeal surface of the epiglottis	the sensation of a foreign body, bloody sputum, difficulty in swallowing solids	3 cm	M-P	a high gamma globulin rate of 24%, IgG, IgA, IgD, λ+	IgD+	NA	total laryngrctomy and postoperative (50 Gy) radiotherapy	No	progression to MM, 12 yrs later	died of MM, 12 yrs
Weissman1993	102	76/M	subglotic region	hoarseness, hemoptysis	3 cm × 3 cm	NEG	NEG	IgG κ+	NA	tracheotomy + surgery + radiotherapy	NA	NA	NA

Barbu 1992	103	69/M	Supraglottis	voice change and difficulty swallowing	NA	NEG	NEG	NA	NA	biopsy + radiotherapy?	No	No	ANED 3 yrs
Kost 1990	104	43/M	left vocal cord	hoarseness	NA	NA	NA	NA	NA	Radiotherapy (70 Gy)	NA	NA	NA
Gambino 1988	105	47/M	epiglottis	lump in throat, dysphagia	1.5 cm	NEG	NEG	NEG	NA	excised biopsy + radiotherapy	NA	NA	NA
Gaffney 1987	106	80/M	larynx	NA	NA	NA	NA	NA	NA	biopsy + radiotherapy (41.59 Gy)	No	No	ANED 7 mo
Gadomski 1986	107	51/F	right aryentoid fold	sore throat	NA	NA	NA	NA	NA	45 Gy radiotherapy	No	No	tumor-free at 5 yr then lost to follow-up
Gadomski 1986	108	54/F	both true cords	hoarseness	NA	NA	NA	NA	NA	total laryngrctomy and postoperative chemotherapy	No	No	died 15 yr later
Burke 1986	109	53/M	supraglottis	cough, hoarseness, hemoptysis, dyspnea	NA	NEG	IgG, M-p	NA	NA	chemotherapy	No	No	ANED 1 yr
Maniglia AJ 1983	110	61/F	subglottic region	hoarseness, hacking cough, shortness of breath	NA	gamma globulin spike	No	NA	NA	tracheostomy local resection + radiotherapy (?Gy)	Yes, 3 mo later	MM	died of MM, 41 mo
Maniglia AJ 1983	111	64/F	glottis	hoarseness, shortness of breath	NA	NEG	NEG	NA	NA	tracheostomy + arytenoidectomy + radiotherapy (50 Gy)	No	No	died 1 yr
Maniglia AJ 1983	112	73/M	subglottic region	hoarseness, shortnessof breath	NA	M-P	NEG	NA	NA	radiotherapy alone (56 Gy)	No	MM	lost f-u
Bush 1981	113	52/F	epiglottis	hoarseness	NA	NEG	NEG	NA	NA	radiotherapy (55 Gy)	No	No	Died of cancer of cervix 3 yrs later
Bush 1981	114	34/F	larynx	hoarseness	NA	NEG	NEG	NA	NA	Surgery	Yes, two times, 2.4 yrs, 1 yr after surgery	No	total 5.9 yrs, ANED 3.5 yrs after radiotherapy (55 Gy)
Bush 1981	115	52/M	vallecula	hoarseness	NA	NEG	NEG	NA	NA	radiotherapy (55 Gy)	No	No	ANED 3.5 yrs
Singh 1979	116	42/F	supraglottis	hoarseness	NA	NEG	NEG	NA	NA	tracheostomy local resection + radiotherapy (50 Gy)	No	No	ANED 29 mo
Woodruff 1979	117	34/F	larynx	NA	NA	NA	NA	NA	NA	Radiotherapy (50 Gy)	NA	NA	NA
Woodruff 1979	118	64/F	larynx	NA	NA	NA	NA	NA	NA	Radiotherapy	No	No	Died at 6.5 yrs
Gorenstein 1977	119	58/M	upper surface of right true vocal cord and ventricle	hoarseness	NA	NEG	NEG	NA	NA	excision + postoperative radiotherapy	No	No	ANED, 3 yrs
Gorenstein 1977	120	63/M	right cord and ventricle	hoarseness	NA	NEG	NEG	NA	NA	excision + postoperative radiotherapy	No	No	ANED, 25 yrs

Gorenstein 1977	121	59/M	subglottic and upper 2 tracheal rings	dyspnea, stridor	NA	NEG	NEG	NA	NA	excision through tracheotomy, electrocoagulation	No	No	ANED, 5 yrs, (Died of carcinoma of pancreas)
Gorenstein 1977	122	32/M	subglottic	hoarseness	NA	NEG	NEG	NA	NA	excision	No	No	ANED, 10 yrs
Gorenstein 1977	123	42/M	both true cords	hoarseness	NA	NEG	NEG	NA	NA	cord stripping	No	No	ANED, 5 yrs
Gorenstein 1977	124	61/M	posterior commissure and posterior vocal cords, aryepiglottic folds, arytenoids, and base of tongue	hoarseness and dysphagia	NA	NEG	NEG	NA	NA	radiotherapy alone	Yes, implantation of radon seeds	No	ANED, 6 yrs
Petrovich 1977	125	74/M	epiglottis	slowly enlarging mass on the right side of the neck	2 × 3 cm	NEG	NEG	NA	NA	radiotherapy alone	No	No	ANED 6 yrs
Muller 1976	126	44/M	supraglottic larynx	hoarseness	1 × 1 cm	NEG	NEG	NA	NA	tracheostomy	NA	NA	NA
Fishkin 1976	127	74/M	epiglottis	a slowly enlarging mass on the right side of neck, hoarseness	2 × 3 cm	κ+, λ+	M-protein, IgD, IgG λ+	IgG λ+, IgD+	NA	radiotherapy alone	Yes, 4 yrs later	No	AWD 4 yrs
Stone 1971	128	67/M	left false vocal fold	hoarseness	NA	NA	NA	NA	NA	biopsy + radiotherapy (30 Gy) + chemotherapy: cyclophosphamide, fluoxymesterone, prednisone	No	No	ANED 10 mo
Poole 1968	129	41/M	larynx, nasopharynx, multiple sites 6 at autopsy	hoarseness 8 yr, hemoptysis 4 mo	NA	NA	NA	NA	NA	excision + postoperative radiotherapy	No	No	DOD 3 yr 5 mo

Note: NA: not available; M: male; F: female; NEG: negative; MM: multiple myeloma; ANED: alive with no evidence of disease; AWD: alive with disease; DOD: die of disease.

ratio was 1.76:1. The patients ranged in age from 12 to 80 years at initial presentation, with a mean age of 57.9 years (data were not available for three patients; the mean age was available for 43 patients). Of 73 cases for which detailed symptoms were recorded, 43 (58.9%) presented with hoarseness, 7 (9.5%) presented with no symptoms, and 3 presented with a neck mass; other symptoms included dyspnoea, stridor, laryngeal globus sensation, haemoptysis, and dry cough. In 64 recorded primary sites of the larynx, 36 cases (56.2%) occurred in the supraglottic region, 16 (25.0%) in the glottis, and 12 (18.8%) in the subglottic region. Fifty-two cases involved only the larynx. Five cases occurred in the supraglottic region and glottis, while six occurred in multiple sites, including the larynx and extra-laryngeal sites. These findings differed from those of Rutherford et al., who found that the gender ratio was close to 3:1, and the distribution of the involved laryngeal sites was as follows: 25% in the supraglottic region, 21% in the glottis, and 29% in the subglottic region. The differences among the reviews may be due to improvement in diagnostic work-up, as suggested by Rutherford et al [13]. Another possible reason is that the data in the literature are incomplete.

In the Chinese-language literature, we found only 18 cases of EMP in the larynx (**Table 2**). Gender information was provided for 11 cases: 6 cases were males, and 5 females. Twelve cases occurred in the larynx, eight cases in the supraglottic region, four cases in the subglottic region, and none in the glottis [65-78].

One hundred and two cases included information regarding therapeutic modalities, and 81 of the 102 cases had complete follow-up data (**Table 3**). The most common treatment modality was radiotherapy alone, which was used in 44 cases (43.1%). Thirty patients (29.4%) received surgery and postoperative radiotherapy. Nineteen cases (18.6%) received surgery only (including three patients who received laser excision). Only two (2.0%), four (3.9%), one (1.0%) patient received chemotherapy only, a combination of radiotherapy and chemotherapy, and a combination of surgery and chemotherapy, respectively. Two patients (2.0%) received no treatment. Twenty-seven articles contained 46 cases (45 cases included information regarding treatment modalities) from 1999 and earlier and 53 articles contained 101 cases (57 cases included information regarding treatment modalities) from 1999 onward. In the cases reported before and including 1999, the most common treatment modality was radiotherapy alone (48.9%; 22/45), followed by the combination of surgery and postoperative radiotherapy in 13 cases (28.9%), surgery alone in 6 cases (13.3%), radiotherapy and chemotherapy in 1 case (2.2%), and chemotherapy in 1 case (2.2%). Two cases received no treatment. The most common treatment modality from 1999 onward was also single-modality radiotherapy (38.5%; 22/57). Seventeen patients (29.8%) were treated with the combination of surgery and postoperative radiotherapy, 13 with surgery alone (22.8%), 3 with radiotherapy and chemotherapy (5.3%), 1 with surgery and chemotherapy (1.8%), and 1 with chemotherapy (1.8%). The therapeutic methods did not change between the two periods. No major changes have occurred in the therapeutic modalities used for laryngeal EMP since the review of EMP in the head and neck by Alexiou et al. in 1999 [41]. The modality results were similar to those in a recent review of sinonasal EMP. A new development is the introduction of laser excision to the treatment of laryngeal EMP. However, only three case reports concerning this modality exist, and conclusive evidence regarding this new method requires further accumulation of data.

Eighty-seven cases included recurrence data: nine patients (10.3%) experienced local recurrence. Five recurrent cases (62.5%) received radiotherapy alone, two cases (25.0%) received surgery alone, and one case (12.5%) received a combination of surgery and radiotherapy. The recurrence time was 3 months to 4 years after treatment. Rakover et al. reported that a 38-year-old male case experienced three episodes of recurrence [38]. Eighty-eight cases included data concerning metastasis: nine patients (10.2%) progressed to MM. The recurrence rate and progression to MM in the present review were lower than those of EMP in the head and neck review by Alexiou et al. (22.0% and 16%, respectively) [41].

In all 147 patients (in the English- and Chinese-language literature), 82 cases included follow-up data Sixty-six patients (80.5%) were alive, including 61 patients (74.4%) who were alive with no evidence of disease (ANED) and 5

Table 2. 18 EMP cases in the larynx in the Chinese-language literature

Ref	Pt	Sex/age	site	symptom	Size	Serum	ICH: Ig	ICH	Treatment	Recurrence	Metastasis	Follow-up
Zang 2011	130	79/F	right arytenoid and aryepiglottic fold	difficulty breathing, foreign body feeling, dyphagia	3.5 cm × 3.0 cm	No	κ+	Vimentin+, CD20 focal+, CD68 focal +, CD138+, Ki_{67} 70%	sugery	No	No	2 yr ANED
Jiang 2010	131	42/F	epiglottis	dysphagia, difficulty breathing	NA	NA	NA	NA	biopsy + postoperative chemotherapy	NA	NA	NA
Tan 2009	132	mean age: 56 years	larynx	hoarseness	NA	NEG	NA	NA	surgery	NA	NA	NA
Zhong 2008	133	67/M	subglottic region	stridor 5 mo, dyspnea 3 days	1.5 cm	NA	NA	NA	biopsy + postoperative radiotherapy, chemotherapy	No	No	3 mo ANED
Zheng 2007	134	NA	laryngeal ventricle	hoarseness	NA	NEG	IgG λ+	NA	biopsy + postoperative radiotherapy, chemotherapy	No	No	15 yr ANED
Yu 2007	135	NA	laryngeal ventricle		NA	NA	NA	NA	surgery + posteroperative radiotherapy	No	No	4 yr ANED
	136	NA	laynx	NA	NA	NA	NA	NA	radiotherapy + chemotherapy	No	No	6 mo ANED
Lu 2006	137	34/F	Epiglottis	discomfort in throat	NA	NA	NA	NA	surgery + chemotherapy	No	No	1 yr ANED
Zhu 2005	138	44/M	left laryngeal ventricle	hoarseness	2 cm	NA	κ+	LCA+, CK-, PCNA+	surgery	No	No	2 yr ANED
Wang 2004	139	mean age: 55 years	larynx	NA	NA	NEG	NA	NA	NA	NA	NA	NA
Ao 2003	140	67/F	subglottic region	difficulty breathing, cough	NA	NEG	NA	NA	surgery	No	No	5 yr ANED
	141	64/F	subglottic region	hoarseness	NA	NEG	NA	NA	Surgery + postoperative radiotherapy	No	No	NA
Wang 2002	142	43/M	epiglottis, aryepiglottic fold, false vocal cord		NA	NEG	NA	NA	biopsy + radiotherapy	yes	two years later, progression to MM	chemotherapy, 16 mo, AWD
Han 2001	143	56/M	left laryngeal ventricle	hoarseness	1.2 cm × 2 cm × 1 cm	No	NA	NA	Surgery + postoperative radiotherapy	No	No	12 yr ANED
Zhou 2000	144~146	NA	larynx	hoarseness	NA	NA	NA	NA	surgery + posteroperative radiotherapy (45 Gy)	NA	NA	NA
Pan 2000	147	48/M	subglottic region	cough, difficulty breathing	1.5 cm	NA	NA	NA	surgery	No	No	4 yr NED

Note: NA: not available; M: male; F: female; NEG: negative; MM: multiple myeloma; ANED: alive with no evidence of disease; AWD: alive with disease.

Table 3. 81 cases of laryngeal EMP had complete follow-up data

Pt	Sex/age	site	Urine	Serum	other	cervical lymph node	Size	ICH: Ig	ICH	Treatment	Recurrence	Metastasis	Follow-up
1	47/F	aryepiglottic fold	NEG	NEG	No	No	2.0 cm × 2.0 cm	IgG λ+	CD138+, CD79a+	surgery + postoperative radiotherapy (50 Gy)	No	No	7 mo ANED
34	29/Fpregnancy	vocal card	κ+	IgG κ+, β 2 -microglobulin↑	No	No	NA	IgG κ+	NA	tracheotomy + radiotherapy (50 Gy)	No	No	ANED 16 months
37	58/M	left arytenoid	NEG	NEG	No	No	1.5 cm × 1.2 cm	IgG λ+	NA	surgical excision under direct laryngoscopy	No	No	ANED 2 yrs
38	62/F	left true vocal fold	NEG	NEG	No	No	1.1 cm × 1.0 cm	IgG κ+	CD45+, CD138+	biopsy + radiotherapy (50 Gy)	No	No	ANED 2 months
42	57/M	subglottis	NEG	NEG	NO	NO	NA	NA	CD138+	biopsy + radiotherapy (54 Gy)	No	No	ANED 1 yr
43	73/M	cricoid	NEG	NEG	No	No	2 cm	IgG κ+	CD138+	tracheotomy, biopsy, radiotherapy (40 Gy)	No	progression to MM. one yr late	died 1 yr
44	56/F	left ventricle and ventricular band	κ+	NEG	coexistence of SCC	No	1.5 cm × 0.6 cm	IgG, IgA	synchronous squamous cell carcinoma in situ CD38+, CD138+, EMA+	vertical hemilaryngectomy + modified left neck dissection	No	No	ANED 2 yrs
48	46/F	aryepiglottic fold	NEG	M	No	No	0.7 cm × 0.9 cm	IgG λ+	NA	surgery + postoperative radiotherapy (40 Gy)	No	No	ANED 2 yrs
49	13/F	subglottic mass	NEG	NEG	amyloid deposition	No	NA	IgG λ+	CD138+, CD79a+	surgery + postoperative radiotherapy (39.6 Gy)	No	No	ANED 6 weeks
52	16/F	vocal cord.	NEG	NEG	No	No	0.76 cm	IgG λ+	CD138+, CD79a+	biopsy + radiotherapy (50.4 Gy)	No	No	ANED 1 yr
58	43/F	vocal cord.	NEG	NEG	No	No	0.4 cm	IgG λ+	NA	surgery	No	No	ANED 2 yrs
59	62/F	subglottis	NEG	NEG	No	No	1.5 cm	IgG κ+	CD138+	tracheotomy + laryngofissure + T-tube	No	No	1 yr AWD
60	57/M	epiglottis	NEG	NEG	No	No	0.5 mm	IgG λ+	CD138+	excised by laser + radiotherapy (50 Gy)	yes 3 mo later	No	ANED 2 yrs
61	76/F	supraglottic	NEG	NEG	No	No	NA	IgG κ+	CD38+	biopsy + radiotherapy	No	No	ANED 6 mos
62	64/M	right hemilarynx and a small and polypoid	NEG	NEG	Amyloid deposits	No	NA	IgG λ+	NA	surgery + radiotherapy	No	No	ANED 3 yrs
63	71/M	parapharyngeal space, soft palate, supraglottic region	NEG	κ+	No	No	NA	IgG κ+	NA	laser excision	No	No	ANED 2 yrs
65	39/M	left arytenoid region	NEG	NEG	No	No	NA	IgG κ+	NA	laser excision + radiotherapy (60 Gy)	No	No	ANED 6 yrs
66	59/M	epiglottis	NEG	NEG	No	No	NA	IgG κ+	NA	surgery under a direct laryngoscopy	No	No	ANED 15 yrs
67	60/M	supraglottic larynx	NEG	NEG	No	No	NEG	NA	NA	excised biopsy + radiotherapy (50 Gy)	No	No	37 mo Dead (NED)
68	47/F	chest wall, subglottic region	NEG	NEG	No	No	NA	Ig D(λ)+	NA	biopsy + radiotherapy (50 Gy)	No	No	ANED 7 yrs

71	46/F	Larynx	NA	NA	NA	NA	NA	NA	NA	radiotherapy 45 Gy	No	No	ANED 49 mo
72	59/M	Larynx	NA	NA	NA	NA	NA	NA	NA	radiotherapy 45 Gy	No	No	ANED 67 mo
73	65/M	False vocal cord	NA	NA	No	No	NA	IgNEG κ+	NA	radiotherapy (60 Gy)	No	No	DOC at 7.8 yrs
74	72/M	true vocal cord	NEG	NEG	No	No	NA	Ig NEGλ+	NA	radiotherapy (40 Gy)	No	No	DOC at 4.7 yrs
75	50/F	laryngeal ventricle right	Neg	NEG	No	No	NA	IgNEG κ+	NA	radiotherapy (50 Gy)	No	No	ANED at 2.2 yrs
76	65/M	subglottic region	NEG	NEG	No	No	NA	IgG κ+	NA	Biopsy + tracheostomy + radiotherapy (60 Gy)	No	No	ANED 2 yrs
77	44/F	supraglottic larynx	NEG	NEG	No	No	NA	nega-tive	NA	laser excision	No	No	ANED 6 mos
78	80/M	left false vocal fold	NEG	NEG	No	No	2 × 1.0 cm	nega-tive	CD79+, Vs38C+	surgery + radiotherapy (60 Gy)	No	No	ANED 2 yrs
79	54/M	left hemilarynx	NEG	NEG	No	Yes	NA	NA	NA	radiotherapy alone?	No	MM	died weeks
80	65/M	subglottic region	NA	NA	NA	NA	NA	NA	NA	radiotherapy alone	No	No	ANED 1 yr
82	12/F	glottis	NEG	NEG	Amyloid deposits	No	3 cm	IgG κ+	NA	surgery + radiotherapy (43.2 Gy)	No	No	ANED 4 yrs
83	38/M	glottis	NEG	NEG	No	No	NA	IgG κ+	NA	Biopsy	Yes, 3 times	No	radiotherapy (50 Gy), ANED 3 yrs
84	63/NA	multifocal sites: nasopharynx, larynx, nasalmfossa	NA	NEG	No	No	NA	IgG κ+	EMA	surgery + radiotherapy (45 Gy)	No	No	108 mo ANED
85	45/NA	multifocal sites: na-sopharynx, larynx	NA	NEG	No	No	NA	IgG κ+	CD45RB, EMA	surgery + radiotherapy (55 Gy)	Yes, 47 mo, laser + chemo-therapy	No	108 mo AWD
87	69/M	glottis	NEG	No	No	No	NA	IgG κ+	NA	surgery	No	No	ANED 62 mos
88	40/M	NEG	elevat-ed IgG levels	No	No	NA	NA	elevat-ed IgG levels	surgery + postop-erative radiotherapy (40 Gy)	No	No		ANED 20 mos
89	34/M	supraglottis	NEG	NEG	No	No	NA	NA	NA	radiotherapy alone (54 Gy)	No	No	ANED 10 yrs
90	50/M	glottis	NEG	NEG	No	No	NA	NA	NA	radiotherapy alone (60 Gy)	No	No	ANED 10 yrs
91	36/M	supraglottis	NEG	NEG	No	No	NA	NA	NA	radiotherapy alone (54 Gy)	No	No	ANED 10 yrs
92	68/F	supraglottis	NEG	NEG	No	No	NA	NA	NA	radiotherapy alone (54 Gy)	No	No	ANED 10 yrs
93	48/M	glottis	NEG	NEG	No	No	NA	NA	NA	radiotherapy alone (60 Gy)	No	No	ANED 10 yrs
94	49/F	spiglottis, right aryeplottic fold, post-cricoid space, false cords and aryteoids	M-P	a high gamma globulin rate	HIV	No	NA	κ+	NA	biopsy	No	No	DOD, 6 mo
95	49/M	right aryentoid	NEG	NEG	No	No	NA	IgG κ+	NA	radiotherapy (45 Gy)	No	No	ANED, 5yrs
96	79/F	larynx	NEG	NEG	No	yes	NA	κ+	NA	radiotherapy (35 Gy)	No	No	ANED, 132 mo
97	65/M	larynx	NEG	NEG	No	yes	NA	κ+	NA	radiotherapy (45 Gy)	No	No	ANED, 52 mo

99	43/M	epiglottis	NEG	NEG	No	No	2 × 2.5 cm	κ, λ+	CD14, CD15, CD5, CD19	surgery	No	No	ANED, 3 yrs
101	54/M	laryngeal surface of the epiglottis	M-P	a high gamma globulin rate of 24%, IgG, IgA, IgD, λ+	No	No	3 cm	IgD+	NA	total laryngrctomy and postoperative (50 Gy) radiotherapy	No	progression to MM, 12 yrs later	died of MM, 12 yrs
103	69/M	Supraglottis	NEG	NEG	No	No	NA	NA	NA	biopsy + radiotherapy?	No	No	ANED 3 yrs
106	80/M	larynx	NA	NA	No	No	NA	NA	NA	biopsy + radiotherapy (41.59 Gy)	No	No	ANED 7 mo
107	51/F	right aryentoid fold	NA	NA	No	No	NA	NA	NA	45 Gy radiotherapy	No	No	tumor-free at 5 yr then lost to follow-up
108	54/F	both true cords	NA	NA	No	No	NA	NA	NA	total laryngrctomy and postoperative chemotherapy	No	No	died 15 yr later
109	53/M	supraglottis	NEG	IgG, M-p	amyloid deposition	No	NA	NA	NA	chemotherapy	No	No	ANED 1 yr
110	61/F	subglottic region	gamma globulin spike	No	amyloid deposition	No	NA	NA	NA	tracheostomy local resection + radiotherapy (?Gy)	Yes, 3 mo later	MM	died of MM, 41 mo
111	64/F	glottis	NEG	NEG	amyloid deposition	No	NA	NA	NA	tracheostomy + arytenoidectomy + radiotherapy (50 Gy)	No	No	died 1 yr
112	73/M	subglottic region	M-P	NEG	amyloid deposition	No	NA	NA	NA	radiotherapy alone (56 Gy)	No	MM	lost f-u
113	52/F	epiglottis	NEG	NEG	cervix carcinoma	No	NA	NA	NA	radiotherapy (55 Gy)	No	No	Died of cancer of cervix 3 yrs later
114	34/F	larynx	NEG	NEG	No	No	NA	NA	NA	Surgery	Yes, two times, 2.4 yrs, 1 yr after surgery	No	total 5.9 yrs, ANED 3.5 yrs after radiotherapy (55 Gy)
115	52/M	vallecula	NEG	NEG	reticulum-cell sarcoma of the left inguinalnodes	No	NA	NA	NA	radiotherapy (55 Gy)	No	No	ANED 3.5 yrs
116	42/F	supraglottis	NEG	NEG	No	No	NA	NA	NA	tracheostomy local resection + radiotherapy (50 Gy)	No	No	ANED 29 mo
118	64/F	larynx	NA	NA	NA	NA	NA	NA	NA	Radiotherapy	No	No	Died at 6.5 yrs
119	58/M	upper surface of right true vocal cord and ventricle	NEG	NEG	No	yes	NA	NA	NA	excision + postoperative radiotherapy	No	No	ANED, 3 yrs
120	63/M	right cord and ventricle	NEG	NEG	No	No	NA	NA	NA	excision + postoperative radiotherapy	No	No	ANED, 25 yrs

121	59/M	subglottic and upper 2 tracheal rings	NEG	NEG	No	No	NA	NA	NA	excision through tracheotomy, electrocoagulation	No	No	ANED, 5 yrs, (Died of carcinoma of pancreas)
122	32/M	subglottic	NEG	NEG	No	No	NA	NA	NA	excision	No	No	ANED, 10 yrs
123	42/M	both true cords	NEG	NEG	No	No	NA	NA	NA	cord stripping	No	No	ANED, 5 yrs
124	61/M	posterior commissure and posterior vocal cords, aryepiglottic folds, arytenoids, and base of tongue	NEG	NEG	No	No		NA	NA	radiotherapy alone	Yes, implantation of radon seeds	No	ANED, 6 yrs
125	74/M	epiglottis	NEG	NEG	No	yes	2 × 3 cm	NA	NA	radiotherapy alone	No	No	ANED 6 yrs
127	74/M	epiglottis	κ+, λ+	M-protein, IgD, IgG λ+	No	enlarging mass on the right side of neck	2 × 3 cm	IgG λ+, IgD+	NA	radiotherapy alone	Yes, 4 yrs later	No	AWD 4 yrs
128	67/M	left false vocal fold	NA	NA	NA	NA	NA	NA	NA	biopsy + radiotherapy (30 Gy) + chemotherapy: cyclophosphamide, fluoxymesterone, prednisone	No	No	ANED 10 mo
129	41/M	larynx, nasopharynx, multiple sites 6 at autopsy	NA	NA	NA	NA	NA	NA	NA	excision + postoperative radiotherapy	No	No	Died of disease 3 yr 5 mo
130	79/F	right arytenoid and aryepiglottic fold	NEG	NEG	No	No	3.5 cm × 3.0 cm	κ+	Vimentin+, CD20 focal+, CD68 focal+, CD138+, Ki_{67} 70%	sugery	No	No	2 yr ANED
133	67/M	subglottic region	NA	NA	NA	NA	1.5 cm	NA	NA	biopsy + postoperative radiotherapy, chemotherapy	No	No	3 mo ANED
134	57/M	laryngeal ventricle	NEG	NEG	No	No	0.3 cm × 0.3 cm	IgG λ+	NA	biopsy + postoperative radiotherapy, chemotherapy	No	No	15 yr ANED
135	NA	NEG	NEG	No	No	NA	NA	NA	surgery + postoperative radiotherapy	No	No	No	4 yr ANED
136	NA	laynx	NEG	NEG	No	No	NA	NA	NA	radiotherapy + chemotherapy	No	No	6 mo ANED
137	34/F	Epiglottis	NEG	NEG	No	No	NA	NA	NA	surgery + chemotherapy	No	No	1 yr ANED
138	44/M	left laryngeal ventricle	NEG	NEG	No	No	2 cm	κ+	LCA+, CK-, PCNA+	surgery	No	No	2 yr ANED
140	67/F	subglottic region	NEG	NEG	No	No	NA	NA	NA	surgery	No	No	5 yr ANED
142	43/M	NEG	NEG	No	No	NA	NEG	NA	biopsy + radiotherapy	yes	two years later, progression to MM	NA	chemotherapy, 16 mo, AWD
143	56/M	left laryngeal ventricle	NEG	NEG	No	No	1.2 cm × 2 cm × 1 cm	NA	NA	Surgery + postoperative radiotherapy	No	No	12 yr ANED
147	48/M	subglottic region	NEG	NEG	No	No	1.5 cm	NA	NA	surgery	No	No	4 yr ANED

Note: NA: not available; M: male; F: female; NEG: negative; MM: multiple myeloma; ANED: alive with no evidence of disease; AWD: alive with disease; DOD: die of disease.

(6.1%) who were alive with disease (AWD). Twelve patients (14.7%) died of disease, and two patients (2.4%) died of other conditions (one died of cancer of the cervix, and the other of carcinoma of the pancreas). Two patients (2.4%) were lost to follow-up. The mean survival duration was ~184 months, and the 5- and 10-year survival rates were 76.1% and 67.4%, respectively. The overall 5-year survival rates for the two periods (from 1999 and earlier and from 1999 onward) were 73.5% and 79.7%, respectively (χ^2 = 0.733; *P* = 0.392). Patients receiving a combination of radiotherapy and chemotherapy had the most favourable outcome, with 100.0% (5/5 patients) being classified as ANED or AWD. The latter finding was similar to that of sinonasal EMP reported by D'Aguillo et al [79]. However, the number of patients undergoing this therapeutic method in the two reviews was limited, and so no conclusions could be drawn. Regarding the patients who underwent a combination of surgery and postoperative radiotherapy, radiotherapy alone, and surgery alone, 80.0% (16/20), 74.3% (26/35), and 94.7% (18/19) were classified as ANED or AWD, respectively. On univariate analysis, the overall 5-year survival rates according to the treatment modality (combination surgery and postoperative radiotherapy, radiotherapy alone, and surgery) were 84.0%, 73.2%, and 85.7%, respectively (χ^2 = 4.733; *P* = 0.192; incomplete data were excluded).

In addition to the therapeutic modalities, some reports revealed that age, tumour size, site of origin (extramedullary versus bone), grade, M-protein and light chains, and radiotherapy dose influenced the outcome in solitary plasmacytoma patients. However, other studies reported contrasting results. Nevertheless, these prognostic factors indicated overall EMP in the head and neck region, not a single primary site in the head and neck. In the present review, we collected 147 laryngeal EMPs, although some data were insufficient. On univariate analysis, progression to MM was found to be a poor prognostic factor. The 5-year overall survival rates of patients with laryngeal EMP without progression to MM and patients with laryngeal EMP with progression to MM were 83.7% and 30.0%, respectively (χ^2 = 19.642; *P* < 0.001). We found that recurrence, gender, age, and primary site in the larynx did not influence the survival rate. The overall 5-year survival rate of patients with laryngeal EMP without recurrence *vs.* that of those with recurrence was 80.2% *vs.* 71.1%, respectively (χ^2 = 0.256; *P* = 0.613). The overall 5-year survival rates in females and males were 69.3% and 77.8%, respectively (χ^2 = 2.346; *P* = 0.309). The overall 5-year survival rates of patients with laryngeal EMP younger than 60 years and those older than 60 years were 79.2% and 70.1%, respectively (χ^2 = 1.986; *P* = 0.371). The overall 5-year survival rates in patients with EMP at primary sites in the supraglottic region, glottis, subglottic region, and multiple sites were 81.6%, 76.4%, 77.1%, 65.5%, respectively (χ^2 = 0.009; *P* = 0.909).

Some studies have found that light chain restriction is a prognostic factor [45, 80]. In our review, the type of light chain was recorded for 35 cases by means of immunohistochemistry of tissue sections. Twelve cases (34.3%) were positive for lambda (λ), and 23 cases (65.7%) were positive for kappa (κ). Favourable outcomes in patients who were λ positive and κ positive occurred in 91.7% (11/12) and 87.0% (20/23), respectively (χ^2 = 0.542, *P* = 0.924).

In our review, we found only nine cases (10.8%; 83 of 147 patients with laryngeal EMP had data concerning amyloid deposits, and 74 cases had complete follow-up data) with coexistent amyloid deposits. The overall 3-year survival rates in patients with laryngeal EMP coexistent with and without amyloid deposits were 92.9% and 68.6%, respectively (χ^2 = 10.152; *P* = 0.001). The latter finding differed from previous reports [53]. Previously, the presence of amyloid deposits was suggested to raise the suspicion of plasmacytoma if found in a laryngeal biopsy specimen, and appears to have no adverse effect on the prognosis of EMP of the head and neck [53]. The univariate analysis suggested that amyloid deposits may be a poor prognostic factor.

Adenopathy may be the first indication of disease in some cases, and may not influence the prognosis. Ten to twenty percent of patients with EMP may develop cervical lymph node metastasis. In our review, only seven cases of metastasis to the lymph nodes (8.4%; 83 cases were mentioned regardless of metastasis to the lymph nodes) were reported in laryngeal EMP. The overall 5-year survival rates in laryngeal EMP patients with or without cervical lymph node metastasis were 78.9% and 83.0%, respectively (χ^2 = 1.179; *P* = 0.555).

In our review, only two cases were found to express urinary Bence-Jones protein, and three cases were found to express serum myeloma protein. These data did not undergo a rigorous statistical analysis.

On multivariate analysis (Cox proportional hazards model), only progression to MM was a poor prognostic factor ($P = 0.002$). Gender, age, recurrence, primary site, coexistence of amyloid deposits, and cervical lymph node involvement were not significantly associated with the prognosis.

The present systematic review possessed several limitations. First, the review included several case reports and had some bias. Second, no uniformity was found regarding the stage, grade, treatment modality, and outcomes. Thus, the present review lacked the strength of a randomized controlled trial of laryngeal EMP and so no conclusions could be drawn.

In conclusion, we reported here a case of laryngeal EMP and reviewed the English- and Chinese-language literature concerning laryngeal solitary EMP; 147 cases of laryngeal EMP were identified. We suggest that the progression of laryngeal EMP to MM might only occur through prognostic factors.

Disclosure of conflict of interest

None.

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