

# Radiation-induced Fibrosarcoma of the Larynx: a Case Report and Review of Literature

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## Research Article

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# Radiation-induced fibrosarcoma of the larynx: a case report and review of literature

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**Abstract: Background:** Radiation-induced sarcoma(RIS) is a rare complication following radiotherapy of head and neck carcinoma. It occurs mostly within the limits of the irradiated area and always suggests a poor prognosis. **Case summary:** Herein, we reported one case of a 61-year-old male with laryngeal squamous cell carcinoma (SCC), who had a history of surgery and radiotherapy. In 2014, this patient was admitted in our hospital for increasing hoarseness five years after surgery and radiotherapy. Finally, the patient was diagnosed as fibrosarcoma and was given total laryngectomy, the patient was died in August 2019 within following up. In addition, the clinical and pathological characteristics of similar cases and their probable tumorigenesis were also reviewed. **Conclusion:** RIS is increasingly important. They usually occur mostly within the limits of the irradiated area. SCC is the most common malignant tumour in the head and neck region, and radiotherapy is a primary adjuvant therapy method. For patients receiving radiotherapy, physicians should follow up more carefully for early detection the RISs. For sarcomas occurring in head and neck region, especially RIS, complete surgical resection is the primary treatment. The choice of radiotherapy and chemotherapy should be more cautious. The prognosis of primary sarcomas or RISs is still controversial. No matter primary sarcomas or RISs, we believe that complete surgical resection should be considered as a top priority in surgery.

**Key words:** fibrosarcoma; radiation-induced sarcoma; squamous cell carcinoma; larynx; pathology

## Background

Radiotherapy can kill cancer cells regionally, but it also can be carcinogenic. Radiation-induced sarcoma

(RIS) is a rare and serious complication of radiotherapy [1]. So far, limited laryngeal RIS has been reported in the literature, and its mechanism is still unclear. Laryngeal RISs are similar to those of other common complications of radiotherapy, so it is difficult and confusing to diagnosis of RIS at early stage.

Laryngeal malignant tumour is one of the common malignant tumours in the head and neck region, and nearly 96-98% of masses were diagnosed as squamous cell carcinoma (SCC). Sarcoma is rare and accounts for less than 1% in head and neck malignant tumours, which includes fibrosarcoma, leiomyosarcoma, rhabdomyosarcoma and angiosarcoma [2]. It scarcely originates in larynx, and the report of RIS is even rarer. RIS occurs in the radiation or nearby area and it is different from original tumours by pathological diagnosis. In addition, it must exclude spontaneous sarcoma, which is induced by other incentives.

Here, we present the clinical data of a laryngeal, radiation-induced fibrosarcoma patient and review related literature to generate a preliminary investigation of RISs.

### **Case presentation**

A 61-year-old male was admitted in our hospital due to “hoarseness for 40 days” in August 2009. He had a history of smoking for more than 40 years and occasional alcoholic drinking. Physical examination showed a rough surface at the front side of the right vocal cord, and the movement of vocal cords was normal. No evidence showed regional or distant metastasis. The CO<sub>2</sub> laser cordectomy under suspension laryngoscope was implemented for the mass excision. Pathological diagnosis was a laryngeal SCC (Figure 4A,4B) and no residual tumour tissue at the resection margin. After that, the patient received radiotherapy (6MV-X-ray, 60Gy/30F) of parallel opposed fields on throat. There was no recurrence in the following 4 years.

In May 2013, a laryngoscope check showed a grey neoplasm with rough surface at anterior right vocal cords(Figure 2A). Magnetic resonance imaging (MRI) revealed changes after operation on laryngeal squamous carcinoma and radiotherapy, and the right vocal cords were thickened(Figure 3A,3B). Then the patient was admitted to another hospital and was given a neoplasm excision under suspension laryngoscope. The pathological results confirmed that the lesion was radiotherapy-related hyperplasia of fibre tissues. Six months later, this patient was admitted in our hospital for increasing hoarseness. Physical examination and laryngoscope showed hyperaemia and oedema of right vocal cords with a smooth surface and without vocal cords movement restriction(Figure 2B). The mass was cut via suspension laryngoscope and postoperative and pathological result showed larynx hyperplasia of fibrous tissues with certain atypia, impartial cells. In addition, the immunohistochemical examination was performed with markers of vimentin (+), CK (-), HHF-35 (-) and SMA (-)(Figure 4C-G). It was considered singularity fibroblast, which might appear as an advanced change after

radiotherapy.

In November 2014, electronic laryngoscope showed that a neoplasm occurred at the right vocal cords and sub-glottis area, and the movement of right vocal cords was limited(Figure 2C). Laryngeal magnetic resonance imaging (MRI)(Figure 3C,3D) and computed tomography (CT)(Figure 3E,3F) showed that right vocal cords and anterior commissure were thicken significantly, and the laryngeal cavity was obviously narrowed compared to the film in 2013. Pathological examination of the laryngeal biopsy specimen showed hyperplasia of spindle cells with dysplasia. Immunohistochemical studies revealed that the tumor cells was positive for Vim, and negative for CK, SMA, CD34 and Actin(Figure 4H-M). Based on the morphological finding and immunostaining, it was diagnosed as fibrosarcoma. Finally, the patient was given total laryngectomy. The patient was died in August 2019 within follow-up.

## **Discussion**

The mechanism of developing sarcoma and pathogenesis is complex, which might due to trauma, chemical tumorigenesis factors, radiation, tumourigenic factors, immune factors or genetic factors [3]. There are sporadic reported cases of RIS, such as osteosarcoma and angiosarcoma [4,5]. Nageris et al. [6] reported fibrosarcoma as a late complication of radiotherapy. In this case, the patient appeared with fibrosarcoma 5 years after laser surgery and radiotherapy of laryngeal squamous carcinoma. And radiation of radiotherapy may be one of the causes of pathogenesis. In general, the risk of RIS increased with increasing radiation dose [8], suggesting the dose of radiotherapy played a very important role in the development of RIS [7].

Diagnosis of sarcoma is clinically difficult due to the lack of specific clinical manifestations. The non-specific clinical manifestation is the persistent and progressive hoarseness. Sarcoma is easy to be omitted or misdiagnosed as it usually grows slow, and the non-ulcerated painless mass is similar to a benign tumour in appearance [9]. Currently, there is no specific diagnostic method/biomarker for sarcomas and the diagnosis is mainly based on pathological examination. The accurate of diagnosis is mainly due to the knowledge and experience of the pathologists. Usually, CK and EMA represent epithelial tumours, and vimentin is a broad immunohistochemistry marker in the diagnosis of soft tissue tumours. For soft tissue tumours, DES, HHF35 and actin represent myogenic tumours; CD31, CD34 and VEGFR represent vascular original tumours and S100 represents neurogenic tumours. In addition, there are indicators that may show proliferative activity of soft tissue tumours, such as Ki67, whose higher expression correlates with worse prognosis. With the application of electron microscopy, diagnosis has become easier [10]. In this paper, the first time, the patient was diagnosed as laryngeal SCC, with the immunohistochemical result CK(+). The second time, it was considered singularity fibroblast,

which may appear as a secondary change after radiotherapy; the immunohistochemical results were CK (-), vimentin (+), HHHF35 (-) and SMA (-). The third time, fibrosarcoma was considered, combined with immunohistochemical results of Vim (+),CK(-), SMA(-), CD34(-) and actin(-).

Surgical operation remains the preferred treatment for laryngeal sarcoma and operation methods are similar to laryngeal SCC [11], which are determined based on the scope of the tumour, the diseased lesions, tumour stage and grade level. As for RISs, a complete surgical excision becomes particularly important [12]. Due to a lack of evidence on early cervical lymph node metastases, cervical lymph node dissection is not recommended as regular treatments [13]. Thiagarajan et al. [12] reported that as with sarcomas occurring elsewhere in the body, lymph node involvement is uncommon in RISs of the head and neck, occurring in only approximately 10% of patients. Radiotherapy is mainly used as an efficient treatment for preventing local recurrence at early postoperative stage [14]. As for RISs, the choice of radiotherapy must be more cautious [12]. The therapeutic effect of chemotherapy for head sarcoma also is quite small. It is recommend that physicians should exclude metastases before any treatment for non-SCCs to avoid the wrong treatment and delay treatment [15].

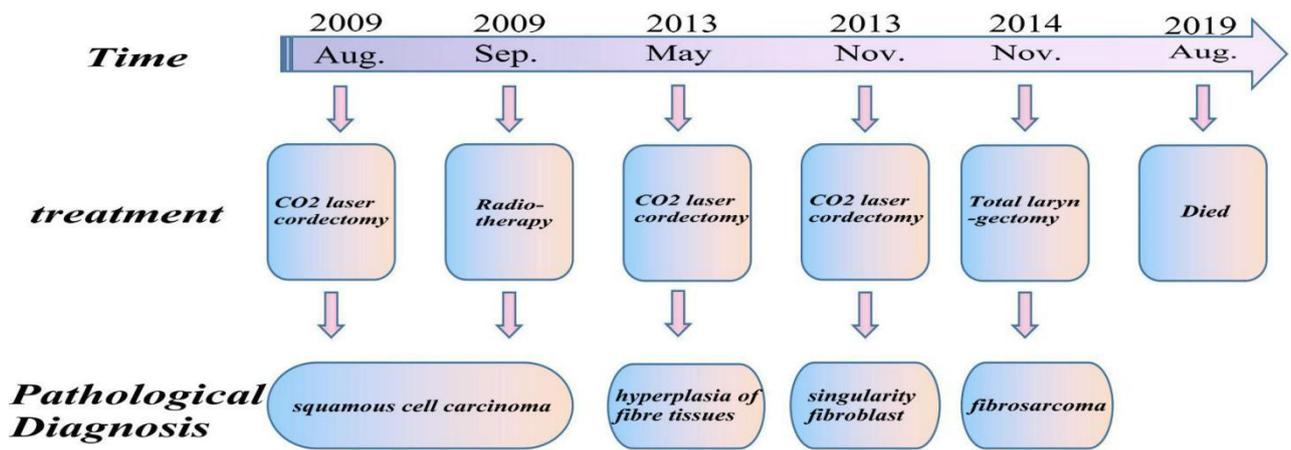
Gladdy et al. reported that RISs result in worse outcome compared with stage-matched primary soft tissue sarcomas [16]. Five-year disease-free survival rates for the former are 10–30% compared with 54% for de novo tumours, whereas Yeang et al. [17] found that patients treated with curative intent have similar outcomes regardless of whether they were radiation-induced or primary sarcomas. For the patient we reported, he was died in August 2019.

## **Conclusion**

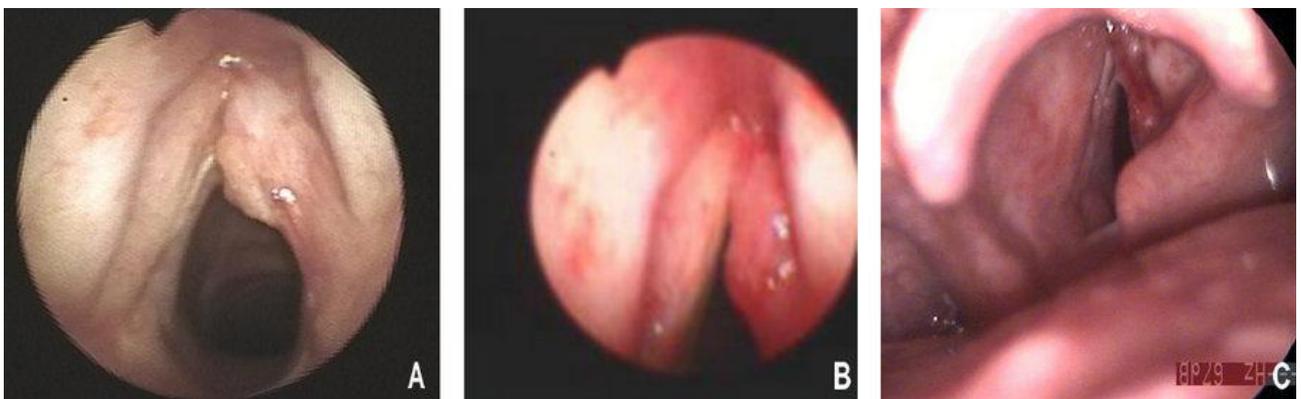
In summary, RISs usually occur within the limits of the irradiated area. SCC is the most common malignant tumour in the head and neck region; therefore, radiotherapy is a primary adjuvant therapy method. For patients receiving radiotherapy, we should follow up more carefully for early detection the RISs. For sarcomas occurring in head and neck region, especially RISs, complete surgical resection is the primary treatment. The choice of radiotherapy or chemotherapy must be more cautious. The prognosis of primary sarcomas or RISs is still controversial.

## **Figure legend**

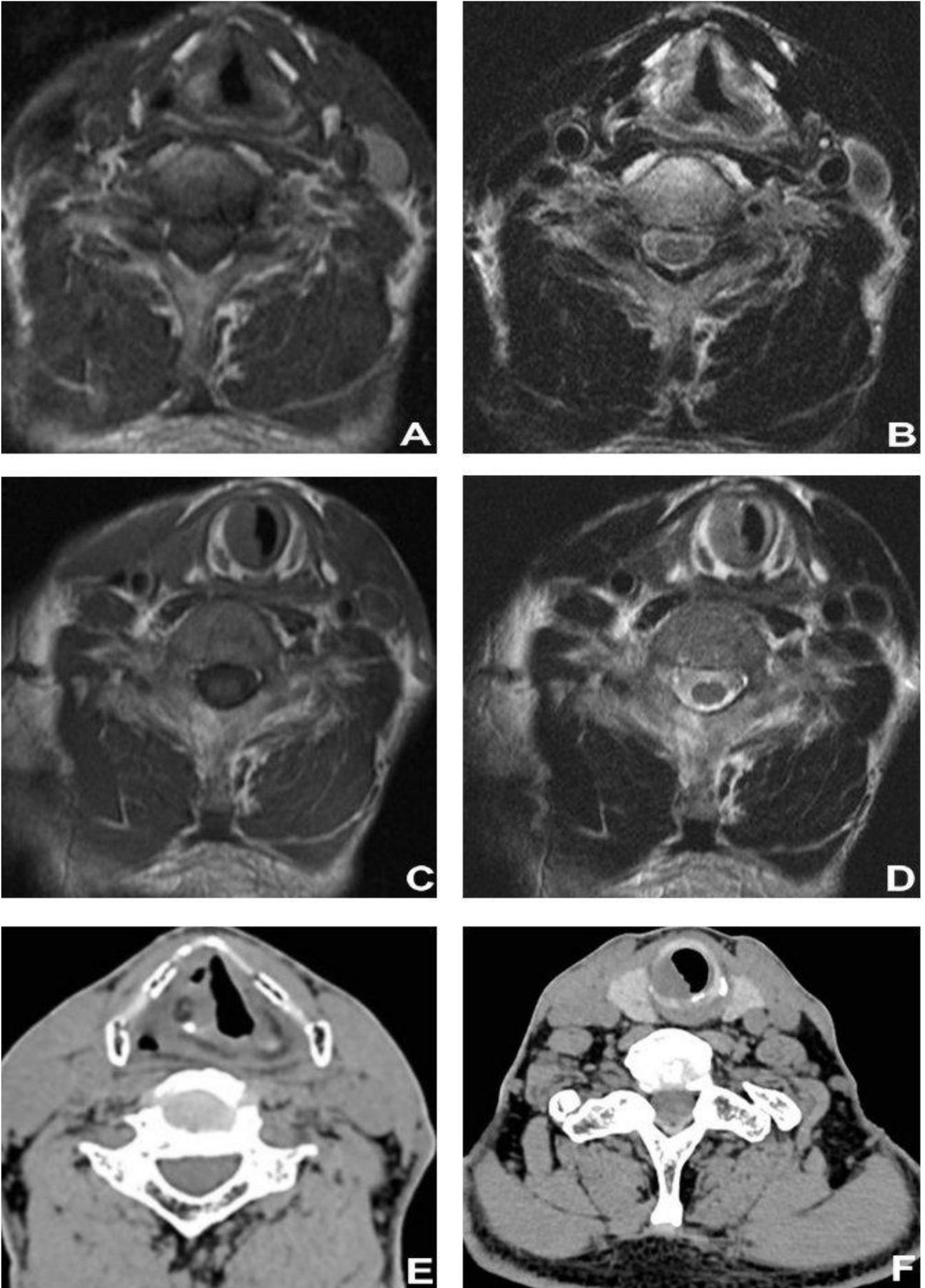
**Figure 1:** Diagnosis and treatment process of the patient



**Figure 2:** Laryngoscope of the patient. A: May 2013; B: November 2013; C: November 2014

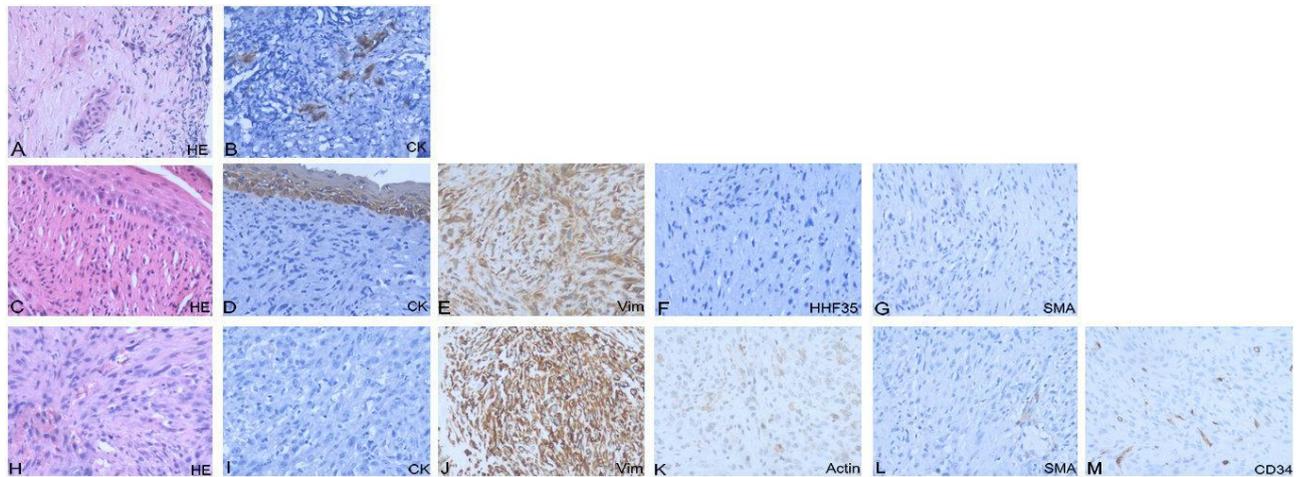


**Figure 3:** magnetic resonance imaging (MRI) and computed tomography (CT) data of the patient. A&B: magnetic resonance imaging (MRI), May 2013. C&D: magnetic resonance imaging (MRI), November 2014. E&F: computed tomography (CT), November 2014



**Figure 4:** pathological examination data of the patient (magnification power: 200X).A-B:Diagnosed as

laryngeal squamous cell carcinoma in August 2009. C-G:Diagnosed as singularity fibroblast in November 2013 .H-M:Diagnosed as fibrosarcoma in November 2014.



### Abbreviations

RIS:Radiation-induced sarcoma;SCC:squamous cell carcinoma;MRI:Magnetic resonance imaging;CT:computed tomography

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### Authors' contributions

Gong Wei – wrote the manuscript and contributed to the collected of the clinical date;Huang Donghai – is the corresponding author, has overseen all aspect of the manuscript.

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Not applicable

### Availability of data and materials

All data generated during this study are included in this manuscript.

### Declarations

### Ethics approval and consent to participate

The Ethics approval of this study was approved by the Ethic Committee of the Xiangya Hospital of Central South University.

### Consent for publication

Written informed consent was obtained from the patient for the publication of any potentially identifiable images included in this manuscript.

## Competing interests

The authors declare that they have no competing interests.

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# Figures

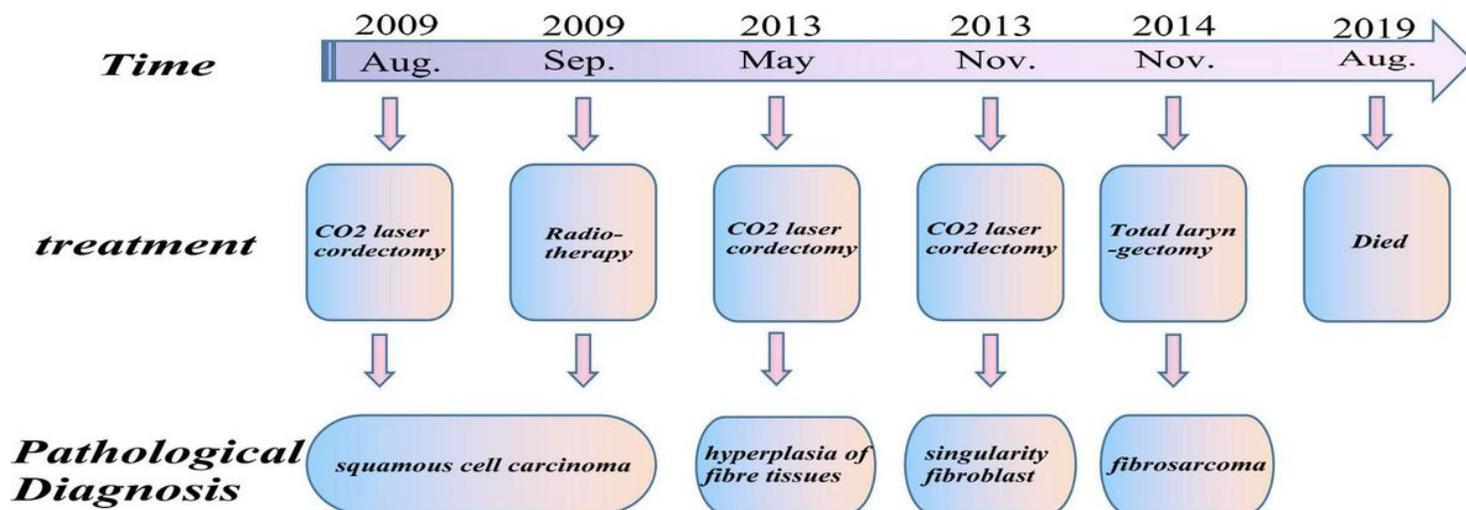


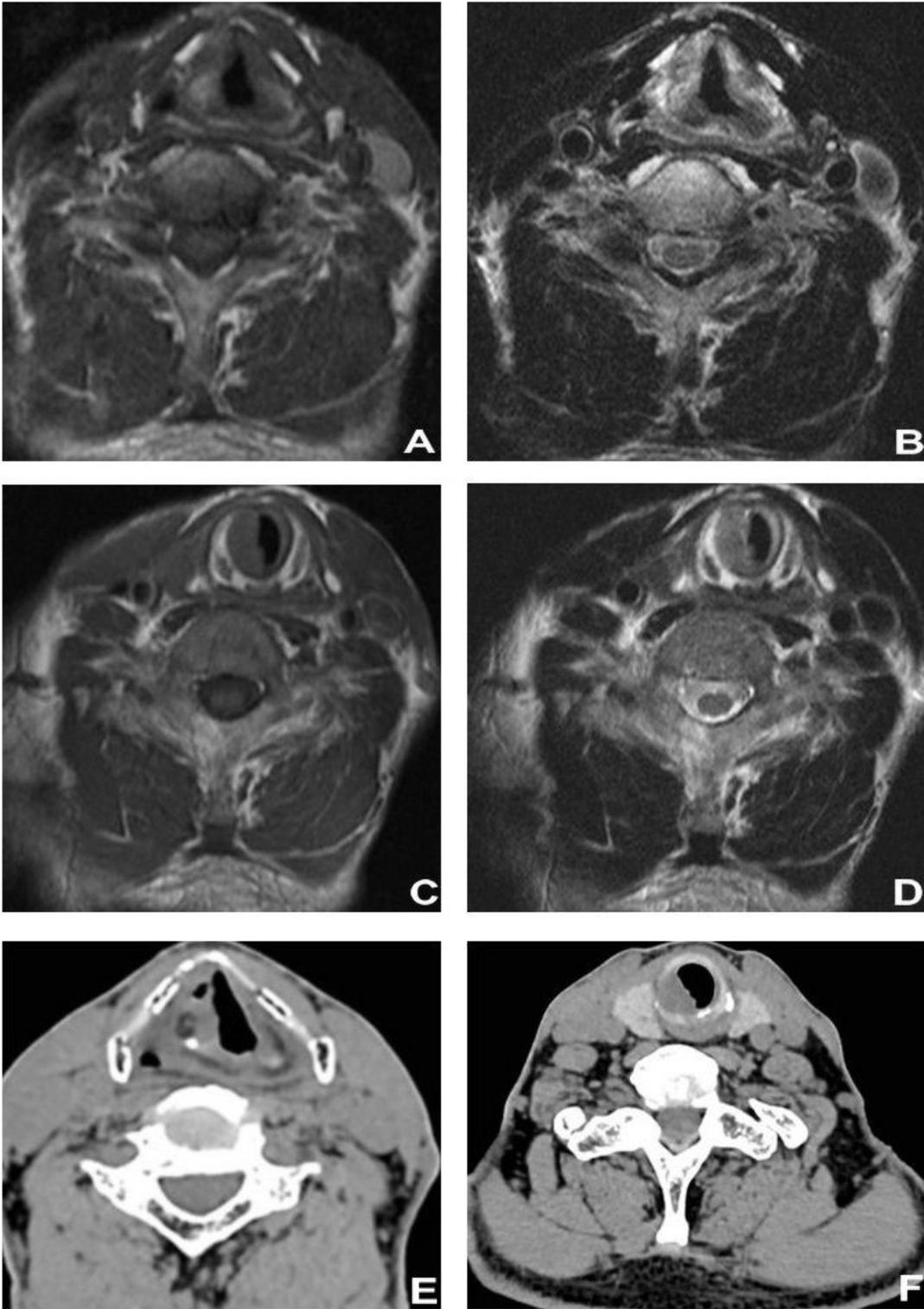
Figure 1

Diagnosis and treatment process of the patient



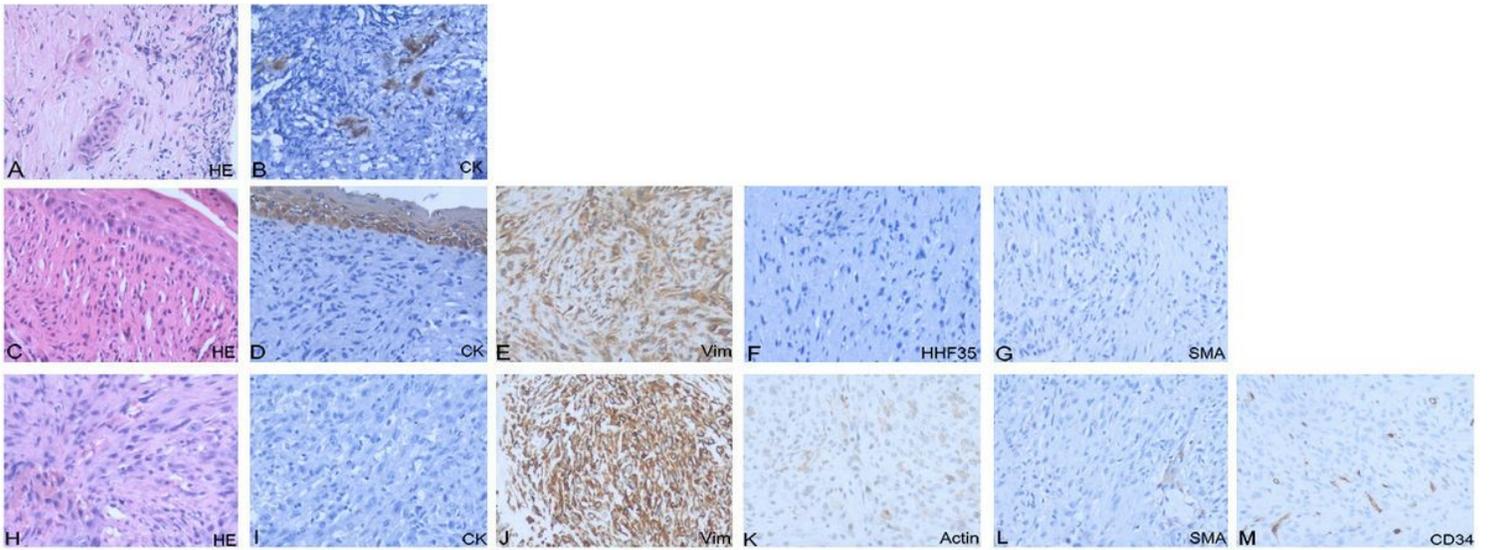
Figure 2

Laryngoscope of the patient. A: May 2013; B: November 2013; C: November 2014



**Figure 3**

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**Figure 4**

pathological examination data of the patient (magnification power: 200X). A-B: Diagnosed as laryngeal squamous cell carcinoma in August 2009. C-G: Diagnosed as singularity fibroblast in November 2013. H-M: Diagnosed as fibrosarcoma in November 2014.