Our experience in the treatment of Malignant Fibrous Histiocytoma of the larynx: clinical diagnosis, therapeutic approach and review of literature

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Abstract: Hereditary spherocytosis (HS) and Chronic myelocytic leukemia (CML) are both life threatening hematologic diseases. They are rarely seen to occur simultaneously in one individual patient. Here we demonstrate a case of HS associated with CML in this study. The patient is a young female, diagnosed with HS in 2005, and was given partial embolization of the splenic artery. She got significant remission after the procedure. In 2008, she was found abnormal in blood routine test, after bone marrow routine, chromosome and fusion gene tests, she was diagnosed with CML (chronic phase). She did not receive regular treatment until 3 months prior, and is currently being treated with Dasatimib. She achieved hematological remission, but had no significant improvement in chromosome and fusion gene figures. Due to her severe condition of hemolysis, a splenectomy or an allogeneic hematopoietic stem cell transplantation is considered.

Keywords: Malignant Fibrous Histiocytoma (MFH), CO2 Laser Cordectomy, Vocal Cord Cancer, Glottic sarcoma

1 Introduction

Malignant Fibrous Histiocytoma, MFH, is a primitive, often pleomorphic, soft tissue sarcoma characterized by fibrous tissue with fibroblasts, histiocytes and myofibroblasts [1-5]. It was first described by O’Brein and Stout in 1964, as a ‘fibrous histiocytoma or fibrous xanthoma.’ It is assumed that in fibrous histiocytoma, cells behave as phagocytes but also form connective tissue fibers; whereas in pure histiocytoma no fibers are formed [5]. In 1983, Enzinger and Weiss, described storiform-pleomorphic, myxoid, giant cells, inflammatory and angiomatoid variants [6,7].

Storiform-pleomorphic phenotype is the most frequent; few cases of low differentiation MFH can be distinguished in high-grade pleomorphic sarcoma, pleomorphic sarcoma with giant cells and inflammatory pleomorphic sarcoma [8].

MFH is the most common subtype of soft tissue sarcoma in adults, described in bone, viscera and skin [9-12], it remains a rare malignancy in the head and neck region (3-13% of all malignant lesions), and it occurs even more rarely in the larynx, 10-15% of these cases [13-15].

As all sarcomas, the development of MFH is unrelated to smoking and alcohol consumption. Some sarcomas are
related to genetic syndromes such as Li Fraumeni, neurofibromatosis, or rarely Cutis Laxa [4,16].

MFH can be correlated to hereditary mutations of oncosuppressor genes or environmental mutagens exposure as commonly reported in bowel tumors [17,18]; it is one of the most common radiation-associated sarcomas, accounting for almost 50% of all cases occurring in both bone and soft tissue [19,20].

43 cases of MFH of the larynx have been described in literature since 1972. Rolander et al. studied a review of case reports of MHF: 8 cases in supraglottic region (2 of these of epiglottis, 4 of aryepiglottic fold, 1 of Morgagni ventricle, 1 not specified); 19 glottis region (17 of vocal cords, 1 of anterior commissura, 1 not specified); 8 in subglottis region; 6 in not specified region; 1 in hemilarynx and 1 case of transglottic cancer (vocal cord and Morgagni ventricle) (Table 1).

Surgery with en-block resection of tumor is the first treatment choice: 60% of patients may survive over 5 years, and 40% over 10 years [14,15,19]. Radiotherapy is given to patients with risk of recurrence, in non-surgical patients or in cases with metastasis [20-24].

Adjuvant or neoadjuvant chemotherapy is suggested when patients have high risk of recurrence [25-27]. The prognosis is related to tumor differentiation, vascular invasion, size (over 5 cm), metastasis [25-28].

Endothelial Progenitor Cells (EPCs) a promising target of cell based therapy, just used in several benign and malignant diseases, should be a possible innovative non surgical approach [29-37].

We present one case of a cord-commissural MFH of larynx, the first treated in microlaryngoscopy with CO2 laser.

2 Case report

C.L., 84 year-old male, smoker for 50 years, was admitted to the Department of Otorhinolaryngology of the Second University of Naples in March 2009. He had had hoarseness for 8 months and there had been familial cases of tumors, such as lung adenocarcinoma. During fiberoptic laryngoscopy, we discovered a red-violaceous nodular lesion of the left vocal cord and of the anterior commissure, with hypomobility of the left vocal chord (Figure 1); there was no palpable cervical lymphadenopathy. CT-scan of the neck and thorax was performed, showing a laryngeal mass infiltrating the left vocal cord and the anterior commissural; no cervical lymph nodes and no metastases were found. Transoral endoscopic cordectomy of the left vocal cord and of anterior commissural was performed in microlaryngoscopy with CO2 (IVd) (Figure 2).

The surgical specimen was sent for histological examination.

At microscopic evaluation, a lesion, was observed, mostly formed of spindle-shaped malignant cells arranged in a fascicular/storiform pattern of growth, with several highly pleomorphic elements, in the corion. Moreover, a significant number of osteoclast-like giant-cells, with hyperchromatic and slightly atypical nuclei, were found. A focal collagen deposition, consisting of bundles of fibrillar eosinophilic material, was associated.

At the immunohistochemical exam, the lesion showed a strong and diffuse positivity to vimentin and mild reactivity for CD68, more prominently in the giant cells counterpart. Finally, a diagnosis of malignant fibrous histiocytoma (MFH) was made (Figure 3).

Figure 1: Fibrolaryngoscopy: red-violaceous nodular lesion of the left vocal cord and anterior commissure.

Figure 2: Microlaryngoscopic vision of the operative field after laser cordectomy.
Table 1: Clinical case review of MFH of the larynx.

| Author                  | Year | Ages/Sex | Location                  | Treatment/Recurrence                                           |
|-------------------------|------|----------|---------------------------|-----------------------------------------------------------------|
| Rolander et al.         | 1972 | 56/M     | Epiglottis                | Supraglottic laryngectomy, neck dissection/NER                  |
| Coyas et al.            | 1974 | 67/M     | Vocal Cord                | Tumor excision/Recurrence                                       |
| Canalis et al.          | 1975 | 53/M     | Vocal Cord                | Piecemeal excision/Recurrence                                  |
| Ribari et al.           | 1975 | 35/M     | Subglottis                | Tumor excision/Radiotherapy                                    |
| Ferlito                 | 1976 | 46/M     | Larynx                    | Total Laryngectomy + Radiotherapy/Recurrence                   |
| Johnson and Poushtes    | 1977 | 67/F     | Subglottis                | Tumor excision/Recurrence                                      |
| Ferlito                 | 1978 | 58/M     | Subglottis                | Tumor excision/Recurrence                                      |
| Ferlito                 | 1979 | 68/M     | Aryepiglottic fold        | Total Laryngectomy /NER                                         |
| Keenan et al.           | 1979 | 22/F     | Subglottis                | Tumor endoscopic excision/Recurrence                           |
| Setzen et al.           | 1979 | ND       | ND                        | ND                                                              |
| Ogura et al.            | 1980 | 22/F     | Subglottis                | Segmental cricotracheal resection/NER                          |
| Ogura et al.            | 1980 | 28/M     | Subglottis                | Partial cricotracheal resection/NER                            |
| Neblett and Coller      | 1891 | 22/F     | Morgagni Ventricle        | Partial Laryngectomy/NER                                       |
| Bremer et al.           | 1982 | 45/M     | ND                        | ND                                                              |
| Bremer et al.           | 1982 | 30/M     | ND                        | ND                                                              |
| Yokoi et al.            | 1982 | 64/F     | Vocal cord                | Tumor excision /NER                                            |
| Ferlito et al.          | 1983 | 67/M     | Vocal cord                | Total Laryngectomy + Radiotherapy/ Recurrence                  |
| Ferlito et al.          | 1983 | 51/M     | Vocal cord                | Total Laryngectomy /NER                                        |
| Ferlito et al.          | 1983 | 63/M     | Emilarynx                 | Laryngectomy and pharyngo esophagectomy /NER                   |
| Ferlito et al.          | 1983 | 8/F      | Subglottis                | ND                                                              |
| Radmass                 | 1984 | 45/M     | Vocal Cord                | Total Laryngectomy/NER                                         |
| Lobe and Katewkap       | 1984 | 67/M     | ND                        | Radiotherapy/NER                                                |
| Volmer                  | 1985 | 70/M     | Vocal Cord                | Tumor excision + Radiotherapy / NER                            |
| Godoy et al.            | 1986 | 26/F     | Subglottis                | Total Laryngectomy /NER                                         |
| Barnes e Kanbour        | 1988 | 68/M     | Vocal cord                | Total Laryngectomy /NER                                         |
| Masuda et al.           | 1989 | 80/M     | Vocal cord                | Tumor excision / NER                                           |
| Saha et al.             | 1989 | 58/M     | Epiglottide               | Tracheotomy and Radiotherapy/ Recurrence                       |
| Majumder et al.         | 1989 | 45/M     | Aryepiglottic fold        | Total Laryngectomy + Radiotherapy/NER                          |
| Jordan and Soames       | 1989 | 54/M     | Vocal cord                | Tumor excision / Recurrence                                    |
| Colev et al.            | 1989 | 57/M     | Aryepiglottic fold        | ND                                                              |
| Colev et al.            | 1989 | 64/M     | Vocal cord                | ND                                                              |
| Colev et al.            | 1989 | 75/M     | Vocal cord                | ND                                                              |
| Rosa et al.             | 1990 | 78/M     | Vocal cord                | Chordectomy/ Recurrence                                        |
| Bernaldez et al.        | 1991 | 54/M     | Vocal cord and Morgagni   | Total Laryngectomy /NER                                         |
| Weber et al.            | 1992 | ND/M     | Vocal cord                | ND                                                              |
| Weber et al.            | 1992 | ND/M     | Plica ariepiglottica      | ND                                                              |
| Harmoir et al.          | 1993 | 24/F     | ND                        | ND                                                              |
| Kuwabora et al.         | 1993 | 46/M     | Vocal cord                | CO2 laser Tumor excision /NER                                  |
| Pastore et al.          | 2001 | 32/M     | Laryngeal Vestibule       | Lateral Pharyngothyroidotomy, thyroid-hyoidpessia+radiotherapy/NER |
| Ortizbish et al.        | 2004 | 54/M     | Vocal cord                | Chordectomy with laryngofissure/ Recurrence                    |
| Ortizbish et al.        | 2004 | 67/M     | Anterior Commissura       | Tumor excision /NER                                             |
| Anghelba et al.         | 2009 | 59/M     | Vocal cord                | Tumor excision /NER                                             |
| Testa et al.            | 2015 | 84/M     | Cord-commissural          | CO2 laser Tumor excision /NER                                  |
At follow-up, laryngoscopy was performed every month for the first year after surgery and then every two months during the last three years. At the last follow-up examination, five year after surgery, the patient was asymptomatic and there was no recurrence of lesions.

**Ethical approval:** The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors’ institutional review board or equivalent committee.

**Informed consent:** Informed consent has been obtained from all individuals included in this study.

### 3 Discussion

In 1964, O’Brein and Stout first defined MHF, in order to describe a histiocytic-like tumor with predominant fibroblasts [5]. MFH of the larynx is a rare disease, comprising approximately less than 2% of all head and neck tumors [19]. It is divided histologically into five variants: stori- pleomorphic, myxoid, giant cells, inflammatory and angiomatous. Immunohistochemistry is needed to differentiate MFH from other malignant tumors such as sarcomatoid carcinoma (AE1/AE3-negativity), malignant schwannoma and melanoma (S100-negativity), angiosarcoma (CD3- negativity), rhabdomyosarcoma (myoglobin-negativity) [7].

The neoplastic cells of MFH are positive to vimentin and CD68 (histiocytic marker) and focally positive to S100 (neuroectodermic marker) and smooth muscle actin (SMA) [7]. Age related incidence ranges from 4 to 84 (our patient) years; only one case occurring in a child (8 year-old female, 2.3% of all cases) [9], 8 cases (4 female and 4 male, 18.2% of all cases) [9] all between 20-30 years old. MFH is more common in male patients than in female (M:F, 4:1) [20]. Radiotherapy is given when patients have high risk of recurrence, in non-operated patients or in cases with metastasis; adjuvant or neoadjuvant chemotherapy is suggested when patients have high risk of recurrence [20-24]. The prognosis is related to tumor differentiation, vascular invasion, size (over 5 cm), resection margins, metastasis: 60% of the patients may survive over 5 years, and 40% of the patients may survive over 10 years [25-27].

Of the 43 cases of MFH of the larynx described since 1972 (Rolander et al.: 8 cases occurred in the supraglottic region (2 of these of epiglottis, 4 of aryepiglottic fold, 1 of Morgagni ventricle, 1 not specified); 19 in glottis region (17 of vocal cords, 1 of anterior commissura, 1 not specified); 8 in the subglottis region; 6 in unspecified regions; 6 in unspecified regions; 1 in hemilarynx and 1 case of transglottic cancer (vocal cord and Morgagni ventricle) (Table 1). We have indicated treatments, recurrences and follow-ups in tab.1 [20]. Surgical intervention is the first choice of treatment and the majority of authors used demolitive surgical techniques: total, partial or supraglottic laryngectomy; traditional cordectomy, tumor excision, partial cricotracheal resection; in 1994 Kuwabara et al., described a glottic MFH (vocal cord) treated with CO\textsubscript{2} laser [22]. In our case CO\textsubscript{2} laser treatment wasn’t associated to vocal cord lesion or paralysis [38].

In literature 8 Italian cases of MFH occurring in Italy were described from 1976 (Ferlito et al.) [23] to 2001 (Pastore et al.) [24], 7 male and 1 female, mean age 49.7 ± 2 glottic cases, 2 supraglottic, 2 ipoglottic, 1 transglottic and 1 undetermined (Table 2) [20-22].

### 4 Conclusions

Our case represents the second case in literature of commissural MFH. Ortiz Bish et al. in 2004 described the first in 2004 [39], a 64 year old male who underwent traditional tumor excision and 6 months after surgery he did
not present any recurrences [25-27]. We performed CO\textsuperscript{2} laser tumor excision, the first time used in Italy for MFH of larynx.

Five years after surgery, without any adjuvant treatment, did not present any recurrence.

Malignant fibrous histiocytomas are a very rare mesenchymal neoplasm of the larynx. At present, no guidelines for laryngeal MFH exist because of lack of evidence-based data, the treatment of choice is surgical, in some cases associated with radiotherapy and chemotherapy. An innovative approach should be considered a cell-based therapy using Endothelial Progenitor Cells (EPCs) [29-37]. EPCs pathogenic mechanisms involving in vascular and non-vascular diseases includes several biomarkers and Ca\textsuperscript{2+} toolkit. [40-49].

We found 43 cases of MFH of the larynx, in literature the presented case is the second cord-commissural case described and the only commissural one treated with CO\textsuperscript{2} laser surgery.

Conflict of interest statement: Authors state no conflict of interest.

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