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Main Article

Management and clinical outcome of sinonasal teratocarcinosarcoma: single institution experience

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Abstract

Purpose: To study the outcome of patients with sinonasal teratocarcinosarcoma treated at a single institution.

Methods: We reviewed the medical records of 22 patients with histopathologically proven sinonasal teratocarcinosarcoma diagnosed during the period 1993–2007. Treatment was completed in 16 patients.

Results: Fourteen patients underwent surgery (six received craniofacial resection, four open surgery and four endoscopic resection); this was followed by radiation therapy with or without chemotherapy in 11 patients. Two patients received chemoradiation as the definitive treatment. At median follow up in surviving patients of 34 months (range one to 180 months), only five were controlled. Disease recurred in 11 patients, with a median time to recurrence of seven months. The two-year disease-free survival rate and the overall survival rate were 28 and 46 per cent, respectively.

Conclusion: Sinonasal teratocarcinosarcoma appears to be an aggressive disease, with the majority of patients suffering locoregional failure. Multimodality treatment, in the form of a combination of surgery, radiation therapy and chemotherapy, appears to be the optimal approach.

Key words: Paranasal Sinus Neoplasms; Teratocarcinosarcoma; Radiation; Surgery

Introduction

Sinonasal teratocarcinosarcoma is an uncommon malignant tumour arising in the sinonasal tract, and consists of various components of teratoma, carcinoma and sarcoma supposedly arising from cells of embryonal origin.[1,2] The nomenclature of sinonasal teratocarcinosarcoma was established by Heffner and Hyams in 1984, before which such tumours were reported variously as teratoid carcinosarcoma, blastoma and malignant teratoma.[1] Currently, approximately 75 cases have been reported.[1–4] The majority of reports have focused on pathology and immunohistochemistry.[2,5,6]

Due to this tumour's rare presentation and varied combination of histopathological features, it is very difficult to choose a treatment strategy and to optimise outcomes, and there are currently no available management guidelines. These tumours arise in the sinonasal tract and become symptomatic when they invade the surrounding tissues, resulting in presentation at an advanced stage. Therefore, the overall prognosis in reported series has generally been poor.

In this report, we review our data for sinonasal teratocarcinosarcoma over a 15 year period; this represents one of the largest single institution series described.

Materials and methods

We reviewed the medical records of patients with histopathologically proven sinonasal teratocarcinosarcoma diagnosed during the period 1993–2007. The details of patient characteristics with respect to age, presenting features, investigations, treatment and follow up were obtained. We located 22 medical records containing a histopathology report of sinonasal teratocarcinosarcoma. As our institution is a large, comprehensive cancer treatment centre, three records were for patients referred only for a second opinion, and were therefore excluded from analysis. Of the remaining 19 patients, one progressed and died before treatment, and two others defaulted from further treatment. Hence, the study cohort consisted of 16 patients who had completed the planned treatment, in the form of surgery, radiation therapy and/or chemotherapy.

Pre-treatment investigation included baseline blood tests, chest X-ray, computed tomography (CT) scan of the paranasal sinuses and a biopsy. Central pathology review was done by our head and neck pathologist (SK) in all the patients.

Treatment was offered based on the extent of the disease and the patient's general condition. Surgery

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was considered as the primary modality if feasible. The surgical technique evolved over time: in the early years, open craniofacial resection was considered, while endoscopic resection was performed more recently. The aim of surgery was complete resection of the tumour. Adjuvant treatments, in the form of radiation therapy and chemotherapy, were considered as and when necessary.

Radiation therapy was given either as conventional two-dimensional planning or as three-dimensional conformal radiation therapy. In patients treated with the latter, a contrast-enhanced CT scan with 3–5 mm slices was taken after immobilisation using a thermoplastic mask. Target volume delineation was performed on all the slices using pretreatment imaging. Fields were placed using beam's eye view and normal structures were blocked using multileaf collimators. Three-four fields were considered in each patient. Appropriate beam-modifying devices were used as and when necessary. The final plan was approved based on the target volume coverage. Doses to critical structures, such as the eyeballs, optic nerves and optic chiasm, were evaluated, and the final dose was decided upon based on the tolerance of critical structures.

After completion of treatment, patients were advised to attend follow up at regular intervals, and earlier if symptomatic. Patients were evaluated clinically for locoregional disease, and radiological investigations were carried out if required. Tumour marker evaluation was not routinely performed in our patients. Persistent local disease was defined as the presence of disease more than six weeks after completion of treatment. Local recurrence was defined as reappearance of the disease after its complete resolution following treatment. Regional recurrence was defined as the appearance of disease in the regional nodes. Distant metastasis was defined as disease in distant regions, including the bones, lung, liver and brain.

Statistical analysis was done using the Statistical Package for the Social Sciences for Windows software. Disease-free and overall survival was calculated using the Kaplan–Meier method.

Results

The median patient age at presentation was 44 years (range, 10–82 years) (Table I). There were 15 males and one female. Computed tomography showed involvement of a single sinus in eight patients; the remaining patients had involvement of two to three sinuses. The ethmoid sinus was the most common site of involvement, this being seen in 14 patients. Bone involvement and intracranial extension was observed in seven patients. One patient had nodal metastases at presentation to ipsilateral level I and II nodes.

Fourteen patients were treated with surgery and two with chemoradiation. Seven patients received adjuvant radiation therapy and four received adjuvant chemoradiation.

Surgery was in the form of craniofacial resection in six patients, endoscopic resection in four and open techniques in four. Open surgery involved total maxillectomy in one patient, lateral rhinotomy and excision of the mass in two, and Cadwell–Luc surgery in one.

TABLE I

DEMOGRAPHICS, TREATMENT CHARACTERISTICS AND OUTCOMES IN PATIENTS DIAGNOSED WITH SINONASAL TERATOCARCINOSARCOMA

Characteristics	*n*
Total patients	22
Second opinion & outside treatment	3
Defaulted	2
Died before treatment initiation	1
Evaluable for analysis	16
Male/female	15/1
Median age (yrs; range)	44 (10–82)
Treatment mode	
Surgery	14
Chemoradiation	2
Adjuvant chemoradiation	4
Adjuvant radiation therapy	7
Surgical procedure	
Endoscopic resection	4
Open	4
Craniofacial resection	6
Follow up	
Median follow up of survivors (mths)	34
Median time to recurrence (mths)	7
Disease outcome	
No evidence of disease	5
Recurrent disease	11
Site of recurrence	
Persistent primary disease	3
Primary disease + nodes	3
Primary disease	1
Nodes	2
Distant metastases	2
Status at last follow up	
Alive without disease	6
Alive with disease	2
Died of disease	8

Yrs = years; mths = months

Of the 13 patients who received radiation therapy, irradiation of the primary was considered in all patients. In one patient who presented with neck node metastases, post-operative radiation therapy to the neck was also considered. Other than this, elective nodal irradiation was not performed in our series. Six patients received radiation with three dimensional conformal radiation therapy technique while remaining patients received conventional radiotherapy. Radiation was delivered in conventional fractionation of 200 cGy, with a total dose ranging from 46 to 60 Gy. The median radiation therapy dose was 54 Gy.

The median follow up of surviving patients was 34 months (range, one to 180 months). Only five patients were controlled at their last follow-up. Disease had recurred in the remaining 11 patients, with a median recurrence time of seven months. Three patients had persistent primary disease and were advised to undergo symptomatic treatment only. One patient developed recurrence at the primary site six years after the initial surgery and was salvaged successfully; he developed a second recurrence seven years later, and was again salvaged. One patient developed nodal recurrence and was salvaged with neck dissection followed by radiation therapy; this patient later developed local recurrence

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and was considered for salvage surgery. Another patient developed nodal recurrence and was salvaged with surgery and radiation therapy; unfortunately, he developed lung metastases and eventually died of disease. Three patients developed recurrence at the primary site as well as regional nodes; two had extensive disease and were advised to undergo palliative care only, while the third was considered for radiation but progressed during therapy and eventually died. Two patients developed distant metastases, one of whom had lung metastases and was treated with palliative intent. Another patient had bony metastases and was treated with radiation therapy; he was alive with disease at last follow up.

Six patients were alive and disease-free at their last follow up: five were locoregionally controlled, while one had local recurrence but was successfully salvaged. One patient with bony metastases was alive with disease at final follow up. Another patient with nodal recurrence after salvage neck surgery developed local recurrence and was considered for local surgery. All the remaining eight patients died of disease.

Our patients' one-year disease-free survival rate was 47 per cent, and their two-year disease-free survival rate was 28 per cent (Figure 1). Our patients' one-year overall survival rate was 56 per cent, while their two-year overall survival rate was 46 per cent (Figure 2).

Discussion

Our patient series represents one of the largest series of sinonasal teratocarcinosarcoma patients from a single institution. Histopathologically, we have seen 22 cases of sinonasal teratocarcinosarcoma. However three of these were referred only for a second opinion, one patient died before any treatment was initiated and two others defaulted from treatment. Hence, the present report includes 16 patients who received the planned treatment.

Heffner and Hyams in 1984 defined this pathological entity as sinonasal teratocarcinosarcoma.[1] Prior to this, such tumours were reported using varied

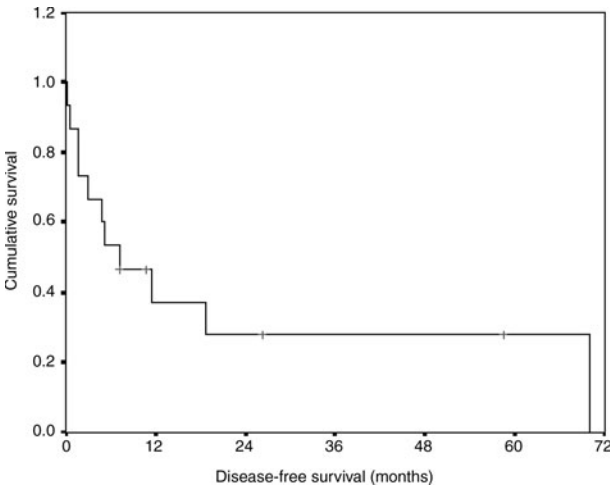

FIG. 1

Disease-free survival in patients treated for sinonasal teratocarcinosarcoma.

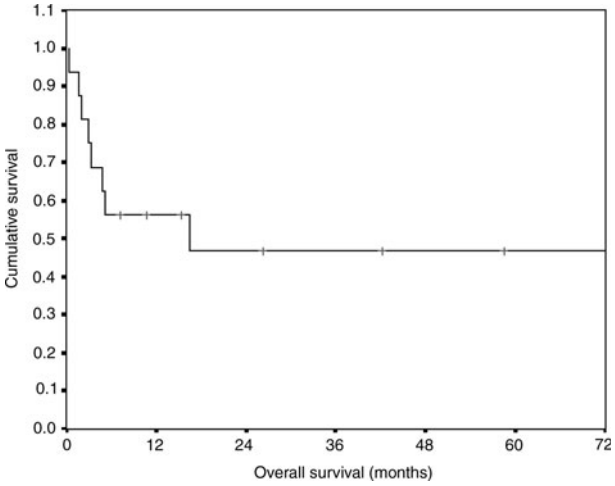

FIG. 2

Overall survival in patients treated for sinonasal teratocarcinosarcoma.

nomenclature, such as teratoid carcinosarcoma, blastoma and malignant teratoma.[7–11] The majority of the literature on sinonasal teratocarcinosarcoma is in the form of case series.[1–4,12] Two larger series have been published: one report of 20 patients by Heffner and Hyams, and a recent report of 10 patients from the M D Anderson cancer centre.[1,4] The data of Heffner and Hyams is based on cases selected from registry of otolaryngic pathology which has multiple contributors. To date, approximately 75 cases of sinonasal teratocarcinosarcoma have been reported, excluding our series.

This tumour is more common in males, as observed in the majority of reports. In our series, there was only one female. In a series reported by Smith *et al.*, all the patients were male.[4] In our series, the median age at presentation was 44 years. This disease appears to be of young adults; the majority of reported patients have been over 35 years of age, with only four patients aged less than 20 years being reported. In our series there was only one patient who was a 10 year old boy and had disease involving sphenoid sinus with bone erosion and neck node. This patient appears to represent one of the youngest reported cases of sinonasal teratocarcinosarcoma to date.

Presentation was advanced in all our patients, with five having intracranial extension. Metastasis to the neck at presentation is an uncommon feature in sinonasal teratocarcinosarcoma patients, and was observed in only one patient in our series. Neck metastases have been described in 17 per cent of reported patients.

Histopathologically, sinonasal teratocarcinosarcoma consists of varied amounts of epithelial and connective tissue. Immature cartilage, chondroid cells, smooth muscle cells, bone and neuronal tissue are also seen. Squamous epithelium resembling fetal oral mucosa is also seen in the majority of patients.

Sinonasal teratocarcinosarcomas are locally aggressive tumours, and locoregional control is therefore the main aim of treatment. Wherever feasible, surgery should be considered as the primary

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treatment modality, as it ensures complete resection of the tumour with adequate margins. Adjuvant treatment, in the form of radiation therapy and chemotherapy, should also be considered. The majority of patients require a combined modality approach, in the form of surgery, radiation therapy and chemotherapy. Of the 16 patients in our series, 14 underwent surgery, of whom six required craniofacial resection, four open surgery and four endoscopic resection.

Radiation therapy is an integral component of the management of sinonasal teratocarcinosarcoma, and the majority of patients require multimodality management due to advanced presentation. In our series, 13 patients required radiation therapy: two received chemoradiation alone, while radiation therapy was considered in the remainder as an adjuvant treatment. Only one patient, who presented with neck node metastases, was considered for radiation to the neck; in all other patients, prophylactic neck irradiation was not considered. Initially, a few of our patients were treated with conventional radiation to the primary site. However, more recently three-dimensional conformal radiation or intensity modulated radiation therapy was considered for tumours at such challenging sites. The doses required for adequate locoregional control of such tumours are not known, due to the scarcity of patients. In addition, due to the complex tumour shape and close proximity to critical structures, it is very challenging to deliver higher radiation doses to the target volume. In our series, doses ranged from 46 to 60 Gy in conventional fractionation.

As sinonasal teratocarcinosarcomas consist of different components like teratoma, carcinoma and sarcoma, it is extremely challenging to decide about the chemotherapeutic regimen in such patients. Therefore, it has been suggested that chemotherapy should be individualised for every patient, based on their tumour's histopathological characteristics.[13]

- **Sinonasal teratocarcinosarcoma is an uncommon malignant tumour arising in the sinonasal tract, and contains various components of teratoma, carcinoma and sarcoma**
- **Sinonasal teratocarcinosarcoma appears to be an aggressive disease, with the majority of patients suffering locoregional failure**
- **Multimodality treatment appears to be the optimal approach, in the form of a combination of surgery, radiation therapy and chemotherapy**

The overall outcome of these tumours was very poor in our series. Persistent disease or locoregional recurrence were the main modes of failure in our patients. Nodal metastases were observed in five patients (two with nodes alone and three with primary tumour plus nodes). This conflicts with the current belief that these tumours do not metastasise to regional or distant sites. In our series, two patients developed distant metastases: one had lung disease while the other developed bony metastases. The disease-free survival rate was 47 per cent after one year and only 28 per cent after two years. The median time to recurrence in our series was only seven months. Salvage surgery was considered in three patients. One patient had a long disease-free interval, six years, after which he developed local recurrence and was salvaged successfully. He subsequently developed another recurrence, after seven years, and was again salvaged. Two patients with neck node metastases underwent neck dissection and radiation therapy. One of them developed lung metastases and eventually died, while the other developed local recurrence and was considered for surgery. Our two-year overall survival rate was 46 per cent, similar to the 40 per cent rate reported by Heffner and Hyams; the average survival in their series was only 1.7 years. The rate of local recurrence following surgery alone is 43 per cent; hence, adjuvant treatment is recommended, in the form of radiation and chemotherapy.[6]

Conclusion

Sinonasal teratocarcinosarcoma appears to be an aggressive disease, with a two-year disease-free survival rate of 28 per cent and an overall survival rate of 46 per cent. The majority of patients suffer locoregional failure, while a small number also develop distant metastases. Multimodality treatment appears to be the optimal approach, in the form of a combination of surgery, radiation therapy and chemotherapy. However, the optimal radiation dose and chemotherapy regimen for this tumour remain unknown due to lack of data, and more work is needed in this regard.

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