EXPERT REVIEWS

Treatment outcomes for patients with synovial sarcoma of the head and neck

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Nancy Lee[†] and Edward Shin
[†]*Author for correspondence*
Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, NY, USA
Tel.: +1 212 639 3341
Fax: +1 212 639 2417
leen2@mskcc.org

Evaluation of: Harb WJ, Luna MA, Patel SR, Ballo MT, Roberts DB, Sturgis EM. Survival in patients with synovial sarcoma of the head and neck: association with tumor location, size, and extension. *Head Neck* 29, 731–740 (2007).

Synovial sarcoma of the head and neck occurs most commonly in males in their third decade of life. Synovial sarcoma of the head is rare, accounting for less than 10% of all head and neck sarcomas. Due to its rarity, there are very few publications on the treatment approach for these tumors. However, it is uniformly accepted that all head and neck synovial sarcomas should undergo complete surgical resection followed by postoperative radiation therapy in those at high risk for locoregional recurrence. In terms of chemotherapy, there are also emerging data on its effectiveness in the treatment of synovial sarcoma of the head and neck. The paper under evaluation reports a single institution's 36-year experience on the treatment of synovial sarcoma of the head and neck. This paper highlights the importance of a multidisciplinary approach in the treatment of this disease.

KEYWORDS: chemotherapy • radiation • surgery • synovial sarcoma

Summary of methods & results

Investigators from the MD Anderson Cancer Center (TX, USA) sought to analyze their institution's experience on synovial sarcoma of the head and neck via a retrospective review of patient charts from 1945 to 2004. Information recorded was: age, race and sex at diagnosis, exposure to radiation, presenting clinical symptoms, histologic subtype, treatment approach and treatment outcomes. The authors retrospectively determined the stage of the disease using either pathology and/or available imaging, as this information was not determined by the original treatment records. Histologic information that was extracted from the patient records included whether the tumor was monophasic or biphasic, presence of lymph nodal involvement and margin status at the time of the initial surgery. Treatment information including therapy prior to presentation at their institution was also recorded. Treatment outcomes including the type of first recurrence, time and cause of death, as well as the disease status at death were recorded.

The authors identified a total of 42 cases, which represented less than 5% of all sarcomas of the head and neck at their institution. Two patients had to be excluded due to a different pathologic diagnosis. Of the remaining 40 cases, 57% were designated as monophasic, 38% biphasic and 5% unclassified. The median age of this cohort of patient was 29 years (range: 5–55). There was almost a 3:1 male to female ratio. Most patients were non-Hispanic white with only one patient being African–American. The authors were not able to find any difference in demographic characteristics between patients with monophasic or biphasic tumors. Most tumors were located in the neck (60%), with the remainder in the upper aerodigestive tract or anterior skull base/sinonasal tract. The tumor location was also similar for patients whether they had monophasic or biphasic tumors. In terms of size, monophasic tumors tend to be 5 cm or smaller on presentation while biphasic tumors tend to be greater than 5 cm. Patients with biphasic tumors have a higher prevalence of bone invasion. No patients reported a history of prior radiation exposure.

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Monophasic tumors were more commonly treated with a multimodality approach when compared with biphasic tumors. Local recurrence tends to be the predominant failure pattern. It was more common to see local recurrence in patients older than 29 years of age and in females. Patients who were referred due to recurrent disease from an outside institution tended to have local recurrence only. Local recurrence also appeared to be associated with the biphasic subtype, skull base location, large size and positive margins, but was not statistically significant. There were significantly more local recurrences that occurred in patients with tumors that had bone involvement than those without ($p = 0.04$). There was a trend towards more local recurrence in patients with tumors of the skull base and those treated without any adjuvant therapy. Distant metastases were more common in patients younger than 29 years of age ($p = 0.09$), those with tumors in the paraspinal neck ($p = 0.038$), larger tumors ($p = 0.146$) and those with bone involvement ($p = 0.128$) than in the other patients. Overall, recurrence at any site was highest for females, those with biphasic or large tumors, those treated surgically without adjuvant therapy and those with bone involvement, but these were nonsignificant statistically. However, patients with skull base or paraspinal tumors were more likely to experience a recurrence than tumors of the nonparaspinal neck or upper aerodigestive tract ($p = 0.017$).

Approximately 50% of the patients died of synovial sarcoma while three patients died of other causes. With a median follow-up of 62 months, the 5-year disease-specific, overall survival rates were both 72%. All patients, except for one, who had metastatic disease died, while only 50% of those who experienced local recurrence died. Although there was no difference in disease-specific survival, patients with monophasic tumors had higher overall survival than those with biphasic tumors: this was statistically significant. Survival was poor with those who had skull base or paraspinal neck disease when compared with the upper aerodigestive tract. Patients with larger tumors had lower disease-specific and overall survival than those with smaller tumors. Patients whose initial treatment consisted of surgery followed by postoperative radiotherapy had the highest overall and disease-specific survival rates. Patients with tumor extending to the bone had significantly worse disease-specific and overall survival rates.

Discussion & significance

The authors found that synovial sarcoma located in the paraspinal region and the skull base had the worst treatment outcome when compared with other head and neck sites. Higher disease-specific and overall survival rates were also associated with tumors that did not extend to the bone or tumors measuring 5 cm or smaller. Patients treated with surgery and adjuvant radiotherapy had higher survival and lower recurrence rates than those treated with surgery alone or surgery with chemoradiotherapy. However, the authors acknowledged that their results were confounded by a small sample size treated over a long time period. The authors concluded that treatment of this rare disease should be directed towards a complete surgical resection. The authors further concluded that, given the known sensitivity of synovial sarcoma to chemotherapy, a multimodality approach should be considered in the perioperative setting.

Expert commentary

Soft tissue sarcomas arising from the head and neck are rare and account for less than 1% of all tumors of all soft tissue sarcomas and 1% of head and neck sarcomas. The disease is more common in men than women with a 3:2 ratio [1–13]. The histology of sarcomas is complex and immunohistochemical analysis is often required to differentiate one subtype from another. Head and neck synovial sarcoma presents both diagnostic and treatment challenges. Therefore, a multidisciplinary team approach in establishing accurate diagnosis and treatment is necessary.

Synovial sarcoma has a characteristic biphasic histologic pattern; however, monophasic variants also exist but this can be very difficult to diagnose. Recent cytogenetic data have shown that synovial sarcoma harbors a specific chromosomal translocation, t(X:18)(p11.2; q11.2) and this can be a useful diagnostic tool, particularly when the diagnosis is equivocal [2]. The current paper under review by Harb *et al.* is a retrospective review of patient charts from a single institution over a 36-year period on synovial sarcoma [1]. A mixture of different patients were seen and treated at their institution. Patients were subdivided into those who were referred after biopsy of the lesion, those who had microscopic disease after surgical resection requiring adjuvant treatment and those who presented with recurrent disease. With the median follow-up of 62 months, the 5-year disease-specific and overall survival rates were both 72%. Approximately 50% of their patients died of synovial sarcoma. These data are comparable with other reported series where the reported survival rates are typically between 40 and 60% [1,3–13].

Due to the presence of multiple vital structures within the head and neck, complete surgical resection is often compromised, thus requiring planned postoperative radiotherapy. Adjuvant radiotherapy has been reported in this series to have higher survival and lower recurrence rates, although due to the small sample size, the authors were unable to show statistical significance [1]. Other series also reported the importance of postoperative radiotherapy. Typically, the postoperative radiation dose ranges from 60 to 66 Gy [3–13]. Conversely, the value of chemotherapy added as an adjuvant treatment modality is questionable. Lindberg *et al.* demonstrated that there was no improvement when comparing patients treated with postoperative radiotherapy alone than those receiving postoperative chemoradiotherapy. In this current series, the authors also could not demonstrate additional value with the addition of chemotherapy; however, the authors do acknowledge the small number of patients treated in each subgroup: surgery alone, surgery with radiotherapy and surgery with chemoradiotherapy. Although there currently seems to be no role for chemotherapy

in the treatment of this disease, this is based on limited data. Patients with synovial sarcoma of the head and neck are at high likelihood of having distant metastases and, therefore, more effective systemic therapy is needed. Therefore, chemotherapy should be considered in the perioperative setting in carefully selected cases to maximize cure.

In summary, synovial sarcoma of the head and neck is rare among the sarcoma family and is exceedingly rare in the head and neck region. An accurate pathologic diagnosis is needed to ensure accurate treatment and, when in doubt, cytogenetic testing can be performed to verify the diagnosis. The treatment approach should include a multidisciplinary team of physicians consisting of head and neck surgery, radiation oncology and medical oncology specialists. Achieving locoregional control is crucial as most of the patients will succumb to their disease when the disease recurs locally. Lastly, although there are insufficient data to support the use of chemotherapy, this may need to be individualized so that the maximum cure of this disease can be achieved.

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Key issues

- Synovial sarcoma of the head and neck is a rare entity and there is limited information regarding treatment for this disease.
- Prior to definitive treatment, ensuring an accurate pathologic diagnosis is crucial.
- Synovial sarcomas involving the bone, measuring more than 5 cm and located either in the paraspinal neck region or the skull base had worse disease-specific and overall survival.
- Local recurrence is more common in those with a positive margin after surgery.
- Approximately 50% of the patients who experienced local recurrence died of their disease.
- Given the high rates of death after local failure, complete surgical resection followed by postoperative radiation should be considered in all patients.
- A multidisciplinary team comprising a head and neck surgeon, a radiation oncologist and a medical oncologist is needed to ensure proper treatment.
- A multimodality treatment approach consisting of complete surgical resection followed by postoperative radiotherapy with or without chemotherapy should be used to ensure maximum cure for this rare disease.

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Affiliations

- Nancy Lee, MD
Memorial Sloan-Kettering Cancer Center, Department of Radiation Oncology, NY, USA
Tel.: +1 212 639 3341
Fax: +1 212 639 2417
leen2@mskcc.org
- Edward Shin, MD
The New York Eye and Ear Infirmary, Department of Otolaryngology – Head and Neck Surgery, NY, USA
Tel.: +1 212 343 8399
Fax: +1 212 343 1386
entshin@yahoo.com