CASE REPORT
PRIKAZ BOLESNIKA
DOI: https://doi.org/10.2298/SGS2003154M
UDC: 616.211-006.04

Primary intraosseous leiomyosarcoma of the nasal and paranasal cavities – a case report

Nikola Milošević, Suzana Stojanović-Rundić, Srđan Milanović, Marko Dožić

Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

SUMMARY

Leiomyosarcomas belong to one of the histological subtypes of soft tissue sarcomas. They most often occur in genital, gastrointestinal tract and extremities, and the appearance of these tumors in the bones (especially head and neck) is very rare. Clinically, leiomyosarcomas are aggressive tumors. Treatment is multidisciplinary and includes surgery, radiotherapy, and chemotherapy.

This case report presents a 61-year-old patient who was referred to a maxillofacial surgeon due to congestion of the right side of the nose, pain in the right eye, and occasional epistaxis. After complete examination, including biopsy with histopathology and immunohistochemistry, primary intraosseous leiomyosarcoma of the nose and paranasal cavities was diagnosed. Since the tumor lesion was assessed as inoperable, the treatment started with radiotherapy. Two and half years after the radiotherapy was completed, there was good local control of the disease and no dissemination. The case report illustrates the rarity of localization, challenges and difficulties in multimodal treatment, and contribution of radiotherapy to good treatment results.

Keywords: primary intraosseous leiomyosarcoma; nasal and paranasal cavities; radiotherapy

INTRODUCTION

Sarcomas are rare diseases that arise from malignantly transformed connective tissue cells. They are divided into the two major groups: soft tissue sarcomas and bone sarcomas.

Soft tissue sarcomas form a heterogeneous group of rare tumors that differ in anatomical location, histology, and biological behavior [1]. In adults, incidence of soft tissue sarcomas is less than 1% of all solid tumors, of which about 45% are localized in the extremities (mostly in the lower extremities in the femoral region), 38% are intra-abdominal and pelvic (mostly retroperitoneal), 10% are in the trunk (skin and subcutaneous tissue) and 5% in head and neck (mostly skin and subcutaneous tissue) [2]. There are over 50 histological subtypes of soft tissue sarcomas, and leiomyosarcomas make up about 10% [3]. Leiomyosarcomas are tumors of smooth muscle cells, and most often occur in genital and gastrointestinal tract and extremities, less often in head and neck, and rarely in the nasal and paranasal cavities [4].

Literature data show that it is a disease of the elderly population, usually after the age of 50 [5]. There is no clearly defined cause of these tumors, but there are certain risk factors: genetic (hereditary leiomyomatosis, hereditary retinoblastoma and Li-Fraumeni syndrome), lymphedema, trauma, previous exposure to radiotherapy and carcinogens (vinyl chloride, arsenic) [6]. The symptoms of these tumors are different, such as epistaxis, nasal congestion, sinus pain and pressure. At the time of diagnosis, more than 95% of patients have localized disease, and 5% have distant metastases. Patients with local and close regional disease (stages I-III) have a 5-year survival rate of about 55-65 %, while 5-year survival rate in patients with metastases is less than 1% [7]. Treatment is multimodal, individualized, and includes surgery, radiotherapy, and chemotherapy.

CASE REPORT

A 61-year-old female patient underwent a CT scan of the head and neck in March 2017 due to nasal congestion, right eye pain, and occasional epistaxis. Examination showed a 3x3x4cm tumor lesion in the right nasal space (in the projection of the middle and lower nasal concha with extension to ethmoidal sinuses), with an impression on the medial wall of the right orbit (without clear signs of orbit infiltration), with retention changes in the right maxillary sinus and hemorrhagic content in the right sphenoidal sinus without intracranial penetration (Figure 1). Chest and abdomen CT showed no dissemination of the disease. The patient had type II diabetes and high blood pressure as the comorbidities.

She was referred to a competent maxillofacial surgeon who performed an endoscopic examination and biopsy of the tumor in April 2017. A definite pathohistological finding with additional immunohistochemical analysis showed spindle cell tumor, with the expression of a smooth muscle phenotype that infiltrates the bone. Necrosis was not present and the number of mitoses was large (10/10 HPF, high power fields). The tumor was positive for SMA (smooth muscle actin), PanActin, Vimentin, negative for

Address for correspondence: Nikola MILOŠEVIĆ, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia;
milosevicnikola43@gmail.com

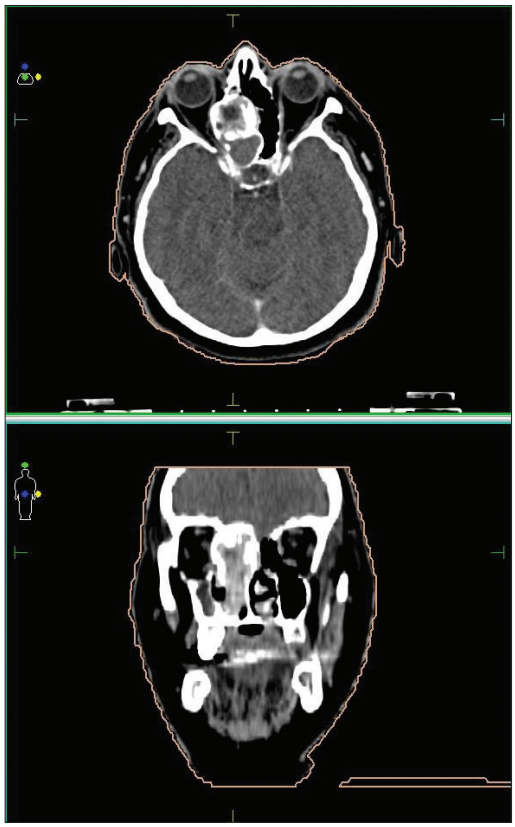

Figure 1. Tumor – Initial CT findings of the head and facial region
Slika 1. Tumor – Inicijalna KT endo- i splanhnokranijuma

EMA (epithelial membrane antigen), and S 100, with poor expression of estrogen and negative progesterone receptors, which corresponded most to the low-grade primary malignant mesenchymal tumor, intraosseous leiomyosarcoma type.

In May 2017, the patient was referred to the sarcoma board at the Institute for Oncology and Radiology of Serbia, and because the tumor was assessed as inoperable, radiation therapy was indicated. Radiation treatment was planned using 3D conformal technique, with standard fractionation schedule (2 Gy/day) with 60 Gy in 30 fractions of tumor (Figure 2). Radiotherapy was applied in August 2017, with good tolerance and local radiation mucositis grade I-II. Mucositis healed with enhanced local care.

Control CT examinations of the head and paranasal cavities and CT thorax (lungs) in January 2018 showed local partial response without dissemination of the disease, so the tumor board indicated regular follow-ups. At the checkup in January 2020, the patient was without symptoms, with stable local disease, without signs of dissemination, and without manifested toxicity two and a half years after the radiotherapy treatment was completed and three years after the diagnosis.

DISCUSSION

Leiomyosarcomas are rare diseases that are most common in the urogenital system (usually in uterus), gastrointestinal system (retroperitoneal) and extremities (mostly in

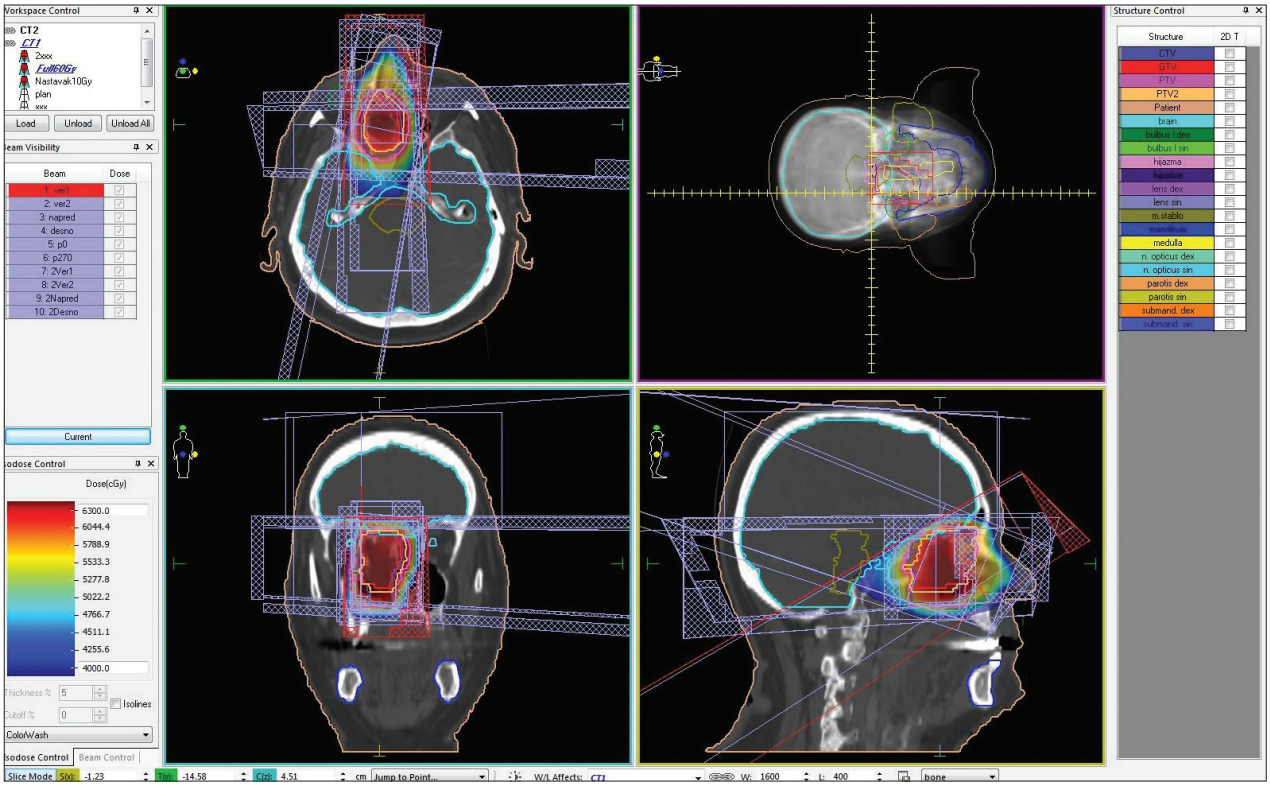

Figure 2. Treated volume, dose distribution and radiation fields arrangement
Slika 2. Tretirani volumen, dozna distribucija i raspored zračnih polja

the femoral region), while occurrence in head and neck is very rare (mainly in the skin and subcutaneous tissue) making about 3% of all leiomyosarcomas.

Leiomyosarcomas of the nose and paranasal cavities are very rare tumors that appear in population over 53 years [8], and more often occur in men [7].

These tumors are manifested by epistaxis, nasal congestion, pressure and sinus pain, which can lead to a clinical diagnostic dilemma because these symptoms can also be attributed to benign diseases such as chronic sinusitis, sinonasal polyposis, and allergic rhinitis. Appropriate time referral to a maxillofacial surgeon contributes to quick diagnosis and the beginning of treatment.

Pathohistological examination is necessary for the definitive diagnosis of leiomyosarcoma, but its differentiation from rhabdomyosarcoma, fibrosarcoma, malignant schwannoma, or spindle cell tumors is difficult using only standard pathohistological staining. Therefore additional immunohistochemical staining is used. Immunohistochemical markers that are useful in making a definitive diagnosis are smooth muscle actin (SMA) that is positive in 95%, muscle-specific actin (MSA) positive in 88%, desmin in 73% and myosin in 64% of cases. There is also expression of estrogen (ER) and progesterone (PR) receptors in almost all leiomyosarcomas except bone [9].

Treatment is multimodal, individualized, and includes surgery, radiotherapy, and chemotherapy, but the ideal treatment modality for these tumors can be a therapeutic challenge. The primary choice of treatment is usually radical surgical resection, and the maximum possible resection is also desirable. Often, due to the localization of the tumor, surgical resection is not feasible, and when surgical resection is without an appropriate safety margin, then recurrence occurs in about half of patients within the first year [10]. Leiomyosarcomas are not radiosensitive, but radiation treatment applies as an adjuvant, rarely as radical, and very rare as neoadjuvant treatment.

Radiotherapy contributes to reduction of local recurrence and better local control of the disease. Chemotherapy is used for metastatic disease, effective chemotherapy is not standardized, and various agents such as doxorubicin and ifosfamide are used. Among head and neck sarcomas, leiomyosarcomas do not have poor prognosis, probably due to the possibility of an earlier diagnosis, as nasal obstruction quickly leads to the appearance of symptoms. The five-year survival of patients with local and regional disease (stage I-III) is about 55-65% [7]. They rarely metastasize to the lymph nodes of the neck. The prognosis is affected by a number of factors such as tumor localization and extension (as the most important), tumor size, grade, and resection edges [9].

Primary intraosseous leiomyosarcoma in the region of the head and neck rarely occurs, and this case report indicates that maxillofacial surgeons play an important role in the early diagnosis of this disease, and thus can contribute to better treatment results. Although not considered radiosensitive, this case report suggests that radiotherapy may play a significant role in the local control of the disease.

REFERENCES

1. Halperin EC, Wazer DE, Perez CA, Brady LW. Perez and Brady's Principles and Practice of Radiation Oncology. 7th ed. Wolters Kluwer; 2019.
2. Devita VT, Lawrence TS, Rosenberg SA. DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology. 10th ed. Wolters Kluwer; 2015.
3. Ducimetiere F, Lurkin A, Ranchère-Vince D, Decouvelaere AV, Péoc'h M, Istier L, et al. Incidence of Sarcoma Histotypes and Molecular Subtypes in a Prospective Epidemiological Study with Central Pathology Review and Molecular Testing. PLoS One. 2011;6(8):e20294. [DOI: 10.1371/journal.pone.0020294] [PMID: 21826194]
4. Jha K, Pant I, Kumari R, Singh G, Chaturvedi S. Primary leiomyosarcoma of frontoethmoidal sinus. Astrocyte. 2016;3(2):100–3. [DOI: 10.4103/2349-0977.197215]
5. Patel K, French C, Khariwala SS, Rohrer M, Kademani D. Intraosseous Leiomyosarcoma of the Mandible: A Case Report. J Oral Maxillofac Surg. 2013;71(7):1209–16. [DOI: 10.1016/j.joms.2013.01.028] [PMID: 23540427]
6. Brady LW, Heilmann HP. Decision Making in Radiation Oncology. Volume 2. Springer-Verlag, 2011.
7. Gore MR. Treatment, outcomes, and demographics in sinonasal sarcoma: a systematic review of the literature. BMC Ear, Nose and Throat Disorders. 2018;18:4. [DOI: 10.1186/s12901-018-0052-5] [PMID: 29581706]
8. Kudo M, Suzaki H. Leiomyosarcoma arising in the nasal cavity. Grand Rounds. 2013;13:4–11. [DOI: 10.1102/1470-5206.2013.0002]
9. Carvalho JC, Thomas DG, Lucas DR. Cluster Analysis of Immunohistochemical Markers in Leiomyosarcoma Delineates Specific Anatomic and Gender Subgroups. Cancer. 2009;115(18):4186–95. [DOI: 10.1002/cncr.24486] [PMID: 19626649]
10. D'Adesky C, Duterme JP, Lejeune D, Mehta R, Chaikh A, Castadot P, et al. Leiomyosarcoma of the Inferior Nasal Concha: A Case Report and Literature Review. B-ENT. 2012;8(3):213–7. [PMID: 23113386]

Received: 7.5.2020 • Accepted: 23.7.2020

Primarni intraosealni lejomiosarkom nosnih i paranazalnih šupljina – prikaz bolesnika

Nikola Milošević, Suzana Stojanović-Rundić, Srđan Milanović, Marko Dožić

Institut za onkologiju i radiologiju Srbije, Beograd, Srbija

KRATAK SADRŽAJ

Lejomiosarkomi spadaju u jedan od histoloških podtipova sarkoma mekih tkiva. Najčešće se javljaju u genitalnom, gastrointestinalnom traktu i ekstremitetima, a pojava ovih tumora u kostima (posebno glave i vrata) vrlo je retka. Klinički lejomiosarkomi su agresivni tumori. Lečenje je multidisciplinarno i uključuje primenu hirurgije, radioterapije i hemoterapije. Prikaz bolesnika se odnosi na pacijentkinju staru 61 godinu koja je upućena maksilofacijalnom hirurgu zbog zapušenosti desne strane nosa, bola u predelu desnog oka i povremene epistakse. Posle kompletne dijagnostičke obrade, biopsije sa patohistologijom i imunohistohemijom dijagnostikovan je primarni intraosealni lejomiosarkom nosa i paranazalnih šupljina. Pošto je tumorska promena procenjena kao inoperabilna, lečenje je započeto radioterapijom. Posle dve i po godine od završene radioterapije postoji dobra lokalna kontrola bolesti i nema diseminacije. Prikaz bolesnika ukazuje na retkost lokalizacije, izazove i poteškoće u multimodalnom lečenju i doprinos radioterapije dobrim rezultatima lečenja.

Ključne reči: primarni intraosealni lejomiosarkom, nosne i paranazalne šupljine; radioterapija

UVOD

Sarkomi su retki tumori koji nastaju iz maligno transformisanih ćelija vezivnog tkiva. Dele se u dve velike grupe: sarkome mekih tkiva i sarkome kostiju.

Sarkomi mekih tkiva sačinjavaju heterogenu grupu retkih tumora, koji se dosta razlikuju po anatomskoj lokaciji, histologiji i biološkom ponašanju [1]. Kod odraslih sarkomi mekih tkiva čine manje od 1% svih solidnih tumora, a od toga je oko 45% lokalizovano u ekstremitetima (najviše u donjem ekstremitetu i to najčešće u butini), 38% intraabdominalno i pelvično (najviše retroperitonealno), 10% u trupu (najviše u koži i potkožnom tkivu) i 5% u glavi i vratu (najviše u koži i potkoži) [2]. Postoji preko 50 histoloških podtipova sarkoma mekih tkiva, a lejomiosarkomi čine oko 10% njih [3]. Lejomiosarkomi su tumori glatkih mišića, a najčešće se javljaju u genitalnom i gastrointestinalnom traktu i ekstremitetima, ređe u glavi i vratu, a vrlo retko u nosnim i paranazalnim šupljinama [4].

Literaturni podaci govore da se radi o bolesti starije populacije, obično posle 50. godine života [5]. Ne postoji jasno definisan uzrok nastanka ovih tumora, ali postoje određeni faktori rizika: genetski (nasledna lejomiomatoza, nasledni retinoblastom i Li-Fraumenijev sindrom), limfedem, trauma, prethodna izloženost radioterapiji i karcinogeni (vinil-hlorid, arsen) [6].

Simptomi ovih tumora su različiti – epistaksa, zapušenost nosa, pritisak i bol u sinusima.

U trenutku dijagnostikovanja više od 95% pacijenata ima lokalizovanu bolest, a 5% ima udaljene metastaze. Pacijenati sa lokalnom i lokoregionalnom bolešću (stadijum I–III) imaju petogodišnje preživljavanje oko 55–65%, dok je kod bolesnika sa metastazama manje od 1% [7].

Lečenje je multimodalno i individualizovano, uključuje hirurgiju, radioterapiju i hemioterapiju.

PRIKAZ BOLESNIKA

Pacijentkinji staroj 61 godinu je u martu 2017. godine zbog zapušenosti desne strane nosa, bola u predelu desnog oka i povremene epistakse učinjena inicijalna KT endo- i splanhokranijuma, koja je pokazala tumorsku promenu nazalnog prostora desno (u projekciji srednje i donje nazalne konhe sa ekstenzijom prema etmoidalnim sinusima), sa impresijom na medijalni zid orbite desno (bez jasnih znakova njene infiltracije) dimenzija 3×3×4 cm, sa retencionim promenama u desnom maksilarnom sinusu i hemoragičnim sadržajem u desnom sfenoidalnom sinusu bez prodora intrakranijalno (Slika 1), dok inicijalna KT toraksa i abdomena nije pokazala diseminaciju bolesti. Od komorbiditeta pacijentkinja je imala dijabetes tip II i povišen krvni pritisak.

Potom je upućena nadležnom maksilofacijalnom hirurgu, koji je načinio endoskopski pregled i biopsiju tumorske promene aprila 2017. godine. Definitivni patohistološki nalaz sa dopunskom imunohistohemijskom analizom je pokazao da se radi o vretenastom ćelijskom tumoru sa ekspresijom glatko-mišićnog fenotipa koji infiltriše kost. Nekroza nije bila prisutna, a broj mitoza je bio veliki (10/10 HPF (*high power fields*, polja velikog uvećanja)). Tumor je bio pozitivan na SMA (*smooth muscle actin*, aktin glatkih mišića), PanAktin, Vimentin, negativan na EMA (*epithelial membrane antigen*, antigen epitelne membrane) i S 100, sa slabom eksprimacijom estrogenskih i negativnim progesteronskim receptorima, što je najviše odgovaralo niskogradusnom primarnom malignom mezenhimalnom tumoru tipa intraosealnog lejomiosarkoma.

Pacijentkinja je maja 2017. godine od strane nadležnog maksilofacijalnog hirurga upućena konzilijumu za sarkome Instituta za onkologiju i radiologiju Srbije, a s obzirom na to da je promena bila procenjena kao inoperabilna, indikovana je zračna terapija.

Zračna terapija je planirana 3D konformalnom tehnikom (3DCRT) standardnim režimom frakcionisanja 2 Gy/dnevno sa TD 60 Gy u 30 frakcija na tumorsku promenu (Slika 2). Radioterapija je sprovedena avgusta 2017. godine uz dobru subjektivnu toleranciju i razvoj radiomukozitisa gr I/II, koji su sanirani uz pojačanu lokalnu negu.

Kontrolna KT endo- i splanhokranijuma i KT toraksa januara 2018. ukazale su na lokalni parcijalni odgovor bez diseminacije bolesti, te je konzilijum indikovao redovne kontrole.

Na kontroli januara 2020. pacijentkinja je bila bez tegoba, sa stabilnom bolešću lokalno i bez znakova diseminacije bolesti, bez ispoljene toksičnosti dve i po godine posle sprovedenog radioterapijskog lečenja i tri godine od postavljanja dijagnoze.

DISKUSIJA

Lejomiosarkomi su retki tumori koji se obično javljaju u genitalnom traktu (najčešće u uterusu), gastrointestinalnom traktu (najčešće u retroperitoneumu) i estremitetima (najčešće u femoralnoj regiji), dok je pojava u glavi i vratu vrlo retka (najčešće u koži i potkožnom tkivu; oko 3% svih lejomiosarkoma).

Lejomiosarkomi nosa i paranazalnih šupljina su vrlo retki tumori koji se najčešće javljaju u populaciji preko 53 godine [8], a oboljevaju češće muškarci [7].

Ovi tumori se manifestuju epistaksom, zapušenošću nosa, pritiskom i bolom u sinusima, što može dovesti do kliničko dijagnostičke dileme, jer se ovi simptomi mogu pripisati i benignim oboljenjima kao što su hronični sinuzitis, sinonazalna polipoza i alergijski rinitis. Pravovremeno upućivanje maksilofacijalnom hirurgu doprinosi brzom postavljanju dijagnoze i otpočinjanju lečenja.

Patohistološki pregled je neophodan za definitivnu dijagnozu lejomiosarkoma, ali njegovo razlikovanje od rabdomiosarkoma, fibrosarkoma, malignog švanoma ili tumora vretenastih ćelija je teško upotrebom samo standarnog patohistološkog bojenja, već se koristi dopunsko imunohistohemijsko bojenje. Imunohistohemijski markeri koji su vrlo korisni u postavljanju definitivne dijagnoze su aktin glatkih mišića, koji je pozitivan u 95% slučajeva, mišićno specifičan aktin, koji je pozitivan u 88% slučajeva, dezmin u 73% slučajeva i miozin u 64% slučajeva. Postoji ekspresija estrogenskih i progesteronskih receptora u skoro svim lejomiosarkomima osim u koštanim [9].

Lečenje je multimodalno i uključuje hirurgiju, radioterapiju i hemioterapiju, a idealni način lečenja ovih tumora može predstavljati terapijski izazov. Primarni izbor lečenja je obično radikalna hirurška resekcija, a poželjna je i maksimalno moguća resekcija. Često zbog same lokalizacije tumora hirurška resekcija nije izvodljiva, a kada je hirurška resekcija bez odgovarajuće sigurnosne margine, onda se recidiv javlja kod oko polovine pacijenata unutar prve godine [10]. Lejomiosarkomi nisu radiosenzitivni, ali se radioterapija primenjuje kao postoperativna, ređe kao radikalna, a najređe kao preoperativna. Radioterapija doprinosi smanjenju pojave lokalnog recidiva i boljoj lokalnoj kontroli bolesti. Hemioterapija se koristi kod metastatske bolesti, efikasna hemioterapija nije standardizovana, a koriste se razni agensi, kao što su doksorubicin i ifosfamid.

Među sarkomima glave i vrata lejomiosarkomi imaju ne tako lošu prognozu, verovatno zbog mogućnosti ranijeg postavljanja dijagnoze, zato što nosna opstrukcija brzo dovodi do pojave simptoma. Petogodišnje preživljavanje pacijenata sa lokalnom i lokoregionalnom bolešću (stadijum I–III) jeste oko 55–65% [7]. Oni retko metastaziraju u limfne čvorove vrata. Na prognozu utiču brojni faktori, kao što su lokalizacija i ekstenzija tumora (kao najznačajniji), veličina tumora, gradus i ivice resekcije [9].

Primarni intraosealni lejomiosarkom u regiji glave i vrata se retko javlja, a ovaj prikaz bolesnika ukazuje da maksilofacijalni hirurzi imaju izuzetno važnu ulogu u što ranijoj dijagnozi ove bolesti, a samim tim mogu doprineti boljim rezultatima lečenja. Iako se smatra da nisu radiosenzitivni, ovaj prikaz bolesnika ukazuje da radioterapija može da ima značajnu ulogu u lokalnoj kontroli bolesti.