e-ISSN 2083–4640
ISSN 1507–1367

RESEARCH PAPER

Reports of Practical Oncology and Radiotherapy
2024, Volume 29, Number 2, pages: 197–203
DOI: 10.5603/rpor.99705
Submitted: 03.08.2023
Accepted: 07.03.2024

Esthesioneuroblastoma: 38 years of experience in an oncological center

Susana P.F. Costa[1], Eduardo Rocha[1], Jéssica Rodrigues[2, 3], André Soares[1], Diana Moreira[1], Cláudia Vieira[4]

[1]Department of Radiotherapy, IPO Porto, Porto, Portugal
[2]Cancer Epidemiology Group, IPO Porto Research Center, IPO Porto, Porto, Portugal
[3]Centre of Mathematics, University of Minho, Braga, Portugal
[4]Department of Medical Oncology, IPO Porto, Porto, Portugal

ABSTRACT

Background: Esthesioneuroblastoma (ENB) is an uncommon malignant sinonasal tumor. There are few data regarding ENB management, namely its treatment. We review our institute's experience in the treatment of ENB and evaluate survival outcomes.

Materials and methods: Retrospective study of patients with ENB treated between 1984–2022. A total of 20 patients were identified, 13 men and 7 women, aged between 20 and 76 years.

Results: Eleven patients were stage C of the modified Kadish staging system at initial presentation, 7 stage B, 1 stage A and 1 stage D. Seventeen patients underwent surgery alone or combined with adjuvant treatment (radiotherapy or chemoradiotherapy). The majority of the patients (71.4%) treated with surgery alone were stage B, whereas most of the patients (63.6%) that underwent surgery combined with adjuvant treatment were stage C. Five of the 7 patients treated with surgery alone had a locoregional recurrence. Two of the 10 patients treated with surgery followed by adjuvant treatment had relapsed, locoregionally and at a distance, respectively. One patient was treated with chemotherapy and 2 patients were treated with chemoradiotherapy and neoadjuvant chemotherapy followed by chemoradiotherapy, respectively. The recurrence and persistence rates were 35% and 15%, respectively. The median time from the end of the first treatment to recurrence was 20.9 months. Two- and 5-year overall survival rates were 83.9% and 77.9%; while progression-free survival rates were 76.7% and 61.0%, respectively.

Conclusions: Sixty percent of patients were treated with a multimodal approach, which appeared to be a favorable strategy for the majority of patients.

Key words: esthesioneuroblastoma; multimodal; chemotherapy; radiotherapy; surgery

Rep Pract Oncol Radiother 2024;29(2):197–203

Introduction

Esthesioneuroblastoma (ENB), also designated as olfactory neuroblastoma, is a rare malignant neoplasm of the sinonasal tract, originating from the olfactory neuroepithelium. ENB accounts for to 3–6% of nasal and paranasal sinus cancers [1, 2]. ENB affects individuals of all ages, with an apparent bimodal distribution, with peaks in the second and sixth decades of life [2]. It occurs in both genders and across ethnicities, with no apparent familial predisposition. As in other intranasal tu-

Address for correspondence: Susana P.F. Costa, Instituto Português de Oncologia do Porto Francisco Gentil, EPE. Rua Dr. António Bernardino de Almeida; 4200-072 Porto, Portugal, tel: +351 225084000, fax: +351 225084001; e-mail: susanpatricia88@hotmail.com

mors, initial symptoms are non-specific and include nasal obstruction, epistaxis, cephalgia, hyposmia, exophthalmos and amaurosis, depending on the extension of the tumor to paranasal sinuses, orbital region and/or anterior skull base [2, 3]. ENB has no specific radiological findings, requiring a biopsy of the lesion to confirm the diagnosis by histoimmunopathology [2]. The modified Kadish system [4, 5] is commonly used for staging ENB. In stage A, the tumor is limited to the nasal cavity; in stage B, the tumor extends into the paranasal sinuses; in stage C, the tumor invades beyond the nasal cavity and paranasal sinuses and in stage D, it presents with distant metastases. The international TNM system [6] is also used for the staging of disease. Given the rarity of the tumor, the majority of articles published regarding the disease are retrospective reports, most often case reports or small heterogenous series [3, 7-10]. Therefore, there are no standard guidelines regarding its treatment. The few available studies reported better outcomes with a multimodal approach [11–14].

We aimed to review our institute's experience in the treatment of ENB over 38 years and assess the survival outcomes.

Materials and methods

We conducted a unicentric retrospective review of 20 patients with histologically confirmed ENB, treated in our Institution between 1984 and 2022. Medical records of all patients were reviewed. Patients' characteristics, clinical presentation of disease, staging and treatment were analyzed. The diagnosis of ENB was based on imaging findings and confirmed by histopathology. All patients were staged according to the modified Kadish system [4, 5] and the 8th edition of American Joint Committee on Cancer tumor–node–metastasis (AJCC/TNM) staging [6].

Overall survival (OS) and progression-free survival (PFS) were calculated from the time of diagnosis. The site of recurrence and salvage therapies were recorded. Statistical analysis for OS and PFS was estimated by the Kaplan-Meier method using R statistical software v4.1.0. The Institutional Ethics Committee approved this study. The ethical standards displayed in the Declaration of Helsinki (1964) and its later amendments were followed.

Results

The patients' characteristics and therapeutic approaches are described in Table 1. The median age was 51 years (20 to 76 years), with 40% of patients being over 60 years old at diagnosis. Sixty-five percent of patients were men. The most common symptoms at diagnosis were: nasal obstruction (78%), recurrent epistaxis (56%), headache (28%), rhinorrhea (28%), hyposmia (28%), proptosis (17%), facial/neck mass (17%), followed by dizziness (6%) and diplopia (6%).

According to the modified Kadish staging system, there were: 1 stage A patient (5%), 7 stage B patients (35%), 11 stage C patients (55%) and 1 stage D patient (5%). Regarding TNM staging, 3 patients presented early-stage disease (T1–2) and 17 advanced disease (T3–4), one of the latter had cervical metastasis (N3) at diagnosis. Seventeen patients underwent surgical resection, 10 of them received postoperative therapy [7 radiotherapy (RT) and 3 chemoradiotherapy (ChRT)]. The remaining 3 patients were treated with ChRT and chemotherapy (ChT), either alone or followed by ChRT. The ma-

Table 1. Patients' demographic characteristics, staging and initial treatment

Patients' characteristics	n = 20 (%)
Median age (years) [min-max]	51 [20–76]
> 60	40%
Sex	
Men	13 (65%)
Women	7 (35%)
Modified Kadish Staging	
A	1 (5%)
B	7 (35%)
C	11 (55%)
D	1 (5%)
TNM Staging (8th ed.)	
T1–2	3 (15%)
T3–4	17 (85%)
N+	1 (5%)
M+	0 (0%)
Initial treatment	
Surgery alone	7 (35%)
Surgery + Radiotherapy	7 (35%)
Surgery + Chemoradiotherapy	3 (15%)
Chemotherapy + Chemoradiotherapy	1 (5%)
Chemoradiotherapy	1 (5%)
Chemotherapy	1 (5%)

jority of the patients (71.4%) treated with surgery alone were stage B at diagnosis. The remaining 2 stage B patients received surgery followed by adjuvant treatment. Of the 11 stage C patients, 7 (63.6%) underwent surgery and adjuvant treatment, 2 (18.2%) surgery alone, 1 (9.09%) systemic treatment and 1 (9.09%) ChRT. The patient with stage A at diagnosis was treated with surgery followed by RT, while the patient with stage D received neoadjuvant chemotherapy, followed by ChRT.

RT was delivered to the tumor bed and local extension, in the dose of 50 to 70 Gy, at 1.8–2 Gy/day, 5 days a week. One patient was treated with Cobalt-60, in the dose of 80 Gy. Until 2011, a total of 4 patients were treated with 3-dimensional conformal radiation therapy (3DRT). Afterward, 8 patients were treated with intensity-modulated radiation therapy [1 IMRT and 7 with volumetric modulated arc therapy (VMAT)]. ChT consisted of the combination of cisplatin (100 mg/m^2) and etoposide (100 mg/m^2), with dose adjustment if needed.

After the first line of treatment, the recurrence rate was 35% (locoregional recurrence in 6 patients and distance disease in 1 patient). The median time from the end of the first treatment to recurrence was 20.9 months. Five of the 7 patients treated with surgery alone had locoregional recurrence (Tab. 2). Two of these patients performed surgical re-excision, one without evidence of disease for 267 months after the second surgery and the other with disease progression and death 4.3 months afterwards. One of the patients received surgery and radiotherapy and remained alive without disease. One patient performed various surgical re-excisions and radiotherapy, dying with disease 127 months after the first surgery. One of the 5 patients who underwent surgery alone, received RT after relapse and stayed alive without evidence of disease 74 months after RT. Two patients treated with surgery combined with RT also relapsed, locoregionally and at a distance, respectively. Both died with evidence of disease more than 100 months after the first treatment. Three patients (15%) had persistence of disease after the initial treatment, one patient died 2 months later and the other 2 patients received additional treatment, surgery and radiotherapy, respectively. These patients remained alive, without evidence of disease and with stable disease, respectively, with a follow-up of 224 and 41 months.

After a median follow-up of 59.7 months (1.8 to 287 months), 8 patients had died, 1 patient was alive with evidence of disease and 11 patients were alive and free of disease. Median OS was 11 years, with a survival rate of 83.9% and 77.9% at two and five years of follow-up (Fig. 1). Two and five-year PFS rates were 76.7% and 61.0%, respectively (Fig. 2).

Discussion

ENB is a rare intranasal malignant tumor with origin in the olfactory neuroepithelium [1, 2]. The symptoms are nonspecific and associated with the site of invasion. Magnetic resonance imaging (MRI) and computed tomography (CT) are commonly used to assess the extension of disease [15]. The diagnosis is confirmed by histology and immunohistochemical tests, allowing the differential diagnosis from other tumors such as lymphoma, Ewing's sarcoma, melanoma, rhabdomyosarcoma, extracranial meningioma, pituitary adenoma or undifferentiated nasosinusal carcinoma [16]. Histologically, the cells are small, with a round nucleus and scarce cytoplasm, surrounded by neurofibrillar matter and exhibiting pseudorosette or rosette arrangement in up to 50% of the samples [17].

There are no standard guidelines regarding the staging and the treatment of ENB, since the published articles on this theme are frequently retrospective studies, with small sampling [3, 7–10]. Most of the available data reported good outcomes with a multimodal approach, namely surgery, pre or postoperative radiotherapy and/or (neo)adjuvant chemotherapy [11–14]. Various retrospective studies and two meta-analyses demonstrated that a combined treatment improves the survival outcomes, especially in advanced stages [11–13, 18–20]. Open craniofacial resection used to be the gold standard surgical procedure, although, in the last years, endoscopic endonasal approaches have been preferred, mainly in the early stages [21]. Regarding RT, the literature recommends preoperative doses of 45 Gy and postoperative doses of 50 to 60 Gy, according to surgical margins. Doses of 65 to 70 Gy have been proposed for radical radiotherapy [12, 22]. Chemotherapy combined with radiotherapy has been described in some cases with more advanced stages and/or unresectable tumors [23–25]. The combination of cisplatin and etoposide is one of the most widely

Table 2. Patients' data, treatment and outcomes

No.	Age (y)	Sex	Kadish Stage	TNM Stage	Initial treatment	Site of relapse	Time to relapse (months)	2nd line of treatment	FUP (months)	Outcome
1	33	M	C	T3N0M0	S + RT	Persistence	NA	No	1.94	DED
2	49	F	B	T1N0M0	S	Locoregional	45.6	S	312	AND
3	28	F	B	T3N0M0	S + RT	NA	NA	NA	287	AND
4	52	M	B	T2N0M0	S + RT	Distance	103	NI	111	DED
5	42	M	C	T4N0M0	S + RT	Persistence	NA	S	224	AND
6	71	F	B	T3N0M0	S	Locoregional	11.7	S + RT	127	DED
7	75	M	C	T4N0M0	S + RT	NA	NA	NA	155	DND
8	64	F	C	T4N0M0	S	Locoregional	30.0	RT	106	DED
9	46	M	A	T1N0M0	S + RT	NA	NA	NA	112	AND
10	65	M	B	T4N0M0	S	NA	NA	NA	25.8	DND
11	68	M	B	T4N0M0	S	Locoregional	20.9	S + RT	104	AND
12	50	F	B	T3N0M0	S	NA	NA	NA	67.6	AND
13	52	M	C	T4N0M0	S + RT	Locoregional	5.3	S + ChT	8.00	DED
14	27	F	D	T4N3M0	ChT + ChRT	NA	NA	NA	51.8	AND
15	62	M	C	T4N0M0	ChT	Persistence	NA	RT	41.3	AED
16	20	F	C	T4N0M0	ChTRT	NA	NA	NA	35.7	AND
17	36	M	C	T4N0M0	S + ChTRT	NA	NA	NA	17.6	AND
18	76	M	C	T4N0M0	S	Locoregional	1.4	S	5.70	DED
19	71	M	C	T4N0M0	S + ChTRT	NA	NA	NA	4.40	AND
20	44	M	C	T4N0M0	S + ChTRT	NA	NA	NA	1.80	AND

S — surgery; RT — radiotherapy; NA — not applicable; DED — dead with evidence of disease; AND — alive with no evidence of disease; AED — alive with evidence of disease; NI — no information; DND — dead no evidence of disease; ChTRT — chemoradiotherapy; FUP — follow-up

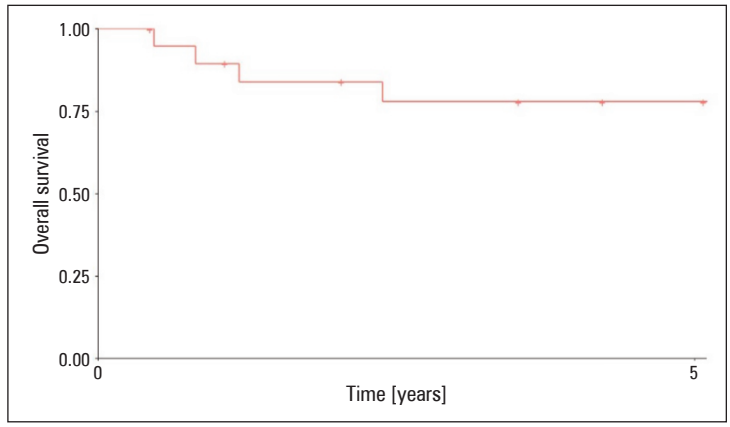

Figure 1. Overall survival for 20 patients with esthesioneuroblastoma using Kaplan-Meier analysis

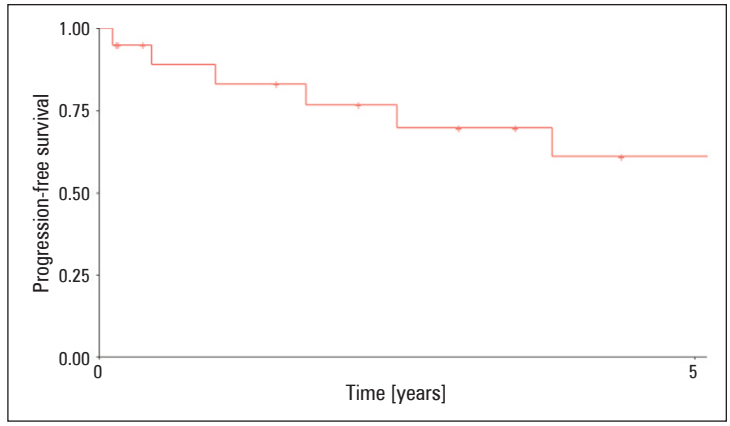

Figure 2. Progression-free survival using Kaplan-Meier analysis

used in the treatment of ENB. Other agents include adriamycin, cyclophosphamide, vincristine, 5-fluorouracil and doxorubicin [23].

Besides treatment modality, other major prognostic factors influencing the ENB outcomes include the Hyams grade [26–28], presence of positive lymph nodes [18, 29–30] and/or distant metastases [14], staging [14, 18, 30] and extension of surgical resection (R0 or R1) [30]. Age at diagnosis [18], orbital invasion [29], intracranial extension [28], and dural involvement [31] were also described as prognostic factors for ENB.

In our study, 85% of patients underwent surgical resection alone or combined with adjuvant RT/ChRT. Most of the patients (5/7) submitted to surgery alone presented locoregional recurrence. From 10 patients treated with surgery combined with adjuvant treatment, only 1 patient presented locoregional recurrence and 1 recurrence at distance. After the first line of treatment, the persistence and recurrence rates were 15% and 35%, respectively. Our data is in accordance with the literature regarding local recurrence (30%) [10, 11, 14], and slightly lower for distance metastases (5%) compared with other studies [11, 14]. In the Dulguerov et al. [11] meta-analysis, local, regional, and distant recurrence rates were 29%, 16%, and 17%, respectively. In a recent study of a series of 187 patients treated for ENB, local recurrence was documented in 26% of patients, nodal recurrence in 14.5%, and distant recurrence in 25.5% [14]. In our series, OS was 83.9% and 77.9% at 2 and 5 years of follow-up, respectively. Two and 5-year PFS rates were 76.7% and 61.0%. The OS and DFS obtained in our study are in accordance with those described in the literature: 45–90% and 41-65% at 5 years, respectively [11, 12, 18, 32].

Conclusion

ENB is a rare intranasal malignant tumor, with no guidelines regarding its management. The different approaches of our institute in the treatment of ENB followed the progressive scientific understanding of the disease. We consider that a multimodal approach could be a good strategy for most patients, while unimodal treatment may be an option for very well selected patients. The retrospective design and the small number of patients were the main limitations of this study, making it challenging to perform reliable and, therefore, meaningful comparisons between different therapeutic approaches. Given the rarity of this entity, further studies, ideally prospective randomized studies, are needed to optimize the management of patients with ENB.

Conflict of interests

The authors declare no potential conflict of interest.

Funding

This publication was prepared without any external source of funding.

References

1. Broich G, Pagliari A, Ottaviani F. Esthesioneuroblastoma: a general review of the cases published since the discovery of the tumour in 1924. Anticancer Res. 1997; 17(4A): 2683–2706, indexed in Pubmed: 9252701.
2. Fiani B, Quadri SA, Cathel A, et al. Esthesioneuroblastoma: A Comprehensive Review of Diagnosis, Management, and Current Treatment Options. World Neurosurg. 2019; 126: 194–211, doi: 10.1016/j.wneu.2019.03.014, indexed in Pubmed: 30862589.
3. Toader C, Stroi M, Kozma A, et al. Esthesioneuroblastoma: the complete picture - case report and review of the literature. Rom J Morphol Embryol. 2018; 59(4): 1211–1218, indexed in Pubmed: 30845303.
4. Kadish S, Goodman M, Wang CC. Olfactory neuroblastoma—A clinical analysis of 17 cases. Cancer. 1976; 37(3): 1571–1576, doi: 10.1002/1097-0142(197603)37:3<1571::aid-cncr2820370347>3.0.co;2-l, indexed in Pubmed: 1260676.
5. Morita A, Ebersold MJ, Olsen KD, et al. Esthesioneuroblastoma: prognosis and management. Neurosurgery. 1993; 32(5): 706–14; discussion 714, doi: 10.1227/00006123-199305000-00002, indexed in Pubmed: 8492845.
6. American Joint Committee on Cancer. AJCC Cancer Staging Manual. AJCC Cancer Staging Form Supplement. 8th ed . AJCC , Chicago 2018: 46–51.
7. Costa S, Soares A, Vieira C. Esthesioneuroblastoma: a brief review of literature in the context of a case report. Rev Portug Oncol. 2022; 5(1): 26–29.
8. Cunha ML, Oliveira RR, César D, et al. Esthesioneuroblastoma: case reports and literature review. Brazi Neurosur. 2015; 34(2): 153–156, doi: 10.1055/s-0035-1554048.
9. Alami Z, Farhane FZ, Bouziane A, et al. Management of Esthesioneuroblastoma: A Retrospective Study of 6 Cases and Literature Review. Case Rep Oncol. 2022; 15(1): 176–186, doi: 10.1159/000521736, indexed in Pubmed: 35431860.
10. Bachar G, Goldstein DP, Shah M, et al. Esthesioneuroblastoma: The Princess Margaret Hospital experience. Head Neck. 2008; 30(12): 1607–1614, doi: 10.1002/hed.20920, indexed in Pubmed: 18798301.
11. Dulguerov P, Allal AS, Calcaterra TC. Esthesioneuroblastoma: a meta-analysis and review. Lancet Oncol. 2001; 2(11): 683–690, doi: 10.1016/S1470-2045(01)00558-7, indexed in Pubmed: 11902539.
12. Dias FL, Sa GM, Lima RA, et al. Patterns of failure and outcome in esthesioneuroblastoma. Arch Otolaryngol Head Neck Surg. 2003; 129(11): 1186–1192, doi: 10.1001/archotol.129.11.1186, indexed in Pubmed: 14623748.
13. Eich HT, Hero B, Staar S, et al. Multimodality therapy including radiotherapy and chemotherapy improves event-free survival in stage C esthesioneuroblastoma. Strahlenther Onkol. 2003; 179(4): 233–240, doi: 10.1007/s00066-003-1089-x, indexed in Pubmed: 12707712.
14. Xiong Le, Zeng XL, Guo CK, et al. Optimal treatment and prognostic factors for esthesioneuroblastoma: retrospective analysis of 187 Chinese patients. BMC Cancer. 2017; 17(1): 254, doi: 10.1186/s12885-017-3247-z, indexed in Pubmed: 28399835.
15. Pickuth D, Heywang-Köbrunner SH, Spielmann RP. Computed tomography and magnetic resonance imaging features of olfactory neuroblastoma: an analysis of 22 cases. Clin Otolaryngol Allied Sci. 1999; 24(5): 457–461, doi: 10.1046/j.1365-2273.1999.00295.x, indexed in Pubmed: 10542931.
16. Bak M, Wein RO. Esthesioneuroblastoma: a contemporary review of diagnosis and management. Hematol Oncol Clin North Am. 2012; 26(6): 1185–1207, doi: 10.1016/j.hoc.2012.08.005, indexed in Pubmed: 23116576.
17. Barnes L, Eveson JW, Reichart P, Sidransky D. Pathology and genetics of head and neck tumours. World Health Organization Classification of tumours. IARC Press, Lyon 2005: 66–70.
18. Jethanamest D, Morris LG, Sikora AG, et al. Esthesioneuroblastoma: a population-based analysis of survival and prognostic factors. Arch Otolaryngol Head Neck Surg. 2007; 133(3): 276–280, doi: 10.1001/archotol.133.3.276, indexed in Pubmed: 17372086.
19. Marinelli JP, Janus JR, Van Gompel JJ, et al. Esthesioneuroblastoma with distant metastases: Systematic review & meta-analysis. Head Neck. 2018; 40(10): 2295–2303, doi: 10.1002/hed.25209, indexed in Pubmed: 29756250.
20. Platek ME, Merzianu M, Mashtare TL, et al. Improved survival following surgery and radiation therapy for olfactory neuroblastoma: analysis of the SEER database. Radiat Oncol. 2011; 6: 41, doi: 10.1186/1748-717X-6-41, indexed in Pubmed: 21518449.
21. Tosoni A, Di Nunno V, Gatto L, et al. Olfactory neuroblastoma: diagnosis, management, and current treatment options. Front Oncol. 2023; 13: 1242453, doi: 10.3389/fonc.2023.1242453, indexed in Pubmed: 37909011.

22. Foote RL, Morita A, Ebersold MJ, et al. Esthesioneuroblastoma: the role of adjuvant radiation therapy. Int J Radiat Oncol Biol Phys. 1993; 27(4): 835–842, doi: 10.1016/0360-3016(93)90457-7, indexed in Pubmed: 8244813.
23. Mishima Y, Nagasaki E, Terui Y, et al. Combination chemotherapy (cyclophosphamide, doxorubicin, and vincristine with continuous-infusion cisplatin and etoposide) and radiotherapy with stem cell support can be beneficial for adolescents and adults with esthesioneuroblastoma. Cancer. 2004; 101(6): 1437–1444, doi: 10.1002/cncr.20471, indexed in Pubmed: 15368332.
24. Bhattacharyya N, Thornton AF, Joseph MP, et al. Successful treatment of esthesioneuroblastoma and neuroendocrine carcinoma with combined chemotherapy and proton radiation. Results in 9 cases. Arch Otolaryngol Head Neck Surg. 1997; 123(1): 34–40, doi: 10.1001/archotol.1997.01900010038005, indexed in Pubmed: 9006501.
25. Patil VM, Joshi A, Noronha V, et al. Neoadjuvant Chemotherapy in Locally Advanced and Borderline Resectable Nonsquamous Sinonasal Tumors (Esthesioneuroblastoma and Sinonasal Tumor with Neuroendocrine Differentiation). Int J Surg Oncol. 2016; 2016: 6923730, doi: 10.1155/2016/6923730, indexed in Pubmed: 26955484.
26. Goshtasbi K, Abiri A, Abouzari M, et al. Hyams grading as a predictor of metastasis and overall survival in esthesioneuroblastoma: a meta-analysis. Int Forum Allergy Rhinol. 2019; 9(9): 1054–1062, doi: 10.1002/alr.22373, indexed in Pubmed: 31251848.
27. Malouf GG, Casiraghi O, Deutsch E, et al. Low- and high-grade esthesioneuroblastomas display a distinct natural history and outcome. Eur J Cancer. 2013; 49(6): 1324–1334, doi: 10.1016/j.ejca.2012.12.008, indexed in Pubmed: 23312882.
28. Zeng Q, Tian Y, He Y, et al. Long-Term Survival Outcomes and Treatment Experience of 64 Patients With Esthesioneuroblastoma. Front Oncol. 2021; 11: 624960, doi: 10.3389/fonc.2021.624960, indexed in Pubmed: 33747939.
29. Song X, Wang J, Wang S, et al. Prognostic factors and outcomes of multimodality treatment in olfactory neuroblastoma. Oral Oncol. 2020; 103: 104618, doi: 10.1016/j.oraloncology.2020.104618, indexed in Pubmed: 32126517.
30. Ozsahin M, Gruber G, Olszyk O, et al. Outcome and prognostic factors in olfactory neuroblastoma: a rare cancer network study. Int J Radiat Oncol Biol Phys. 2010; 78(4): 992–997, doi: 10.1016/j.ijrobp.2009.09.019, indexed in Pubmed: 20231062.
31. Harvey RJ, Nalavenkata S, Sacks R, et al. Survival outcomes for stage-matched endoscopic and open resection of olfactory neuroblastoma. Head Neck. 2017; 39(12): 2425–2432, doi: 10.1002/hed.24912, indexed in Pubmed: 28945299.
32. Shaaban SG, Caicedo-Granados E, Wilke C. Clinical Outcomes and Patterns of Failure in Esthesioneuroblatoma: A Single Institutional Experience. Indian J Otolaryngol Head Neck Surg. 2023; 75(1): 67–73, doi: 10.1007/s12070-022-03125-x, indexed in Pubmed: 37007884.