International Journal of Otolaryngology and Head & Neck Surgery, 2015, 4, 204-210
Published Online May 2015 in SciRes. http://www.scirp.org/journal/ijohns
http://dx.doi.org/10.4236/ijohns.2015.43034

Esthesioneuroblastoma, Thyroid Gland Carcinoma and Gastrointestinal Stromal Carcinoma

Plamen Nedev

Department of Neurosurgery and ENT Medical University Varna, Bulgaria and University Hospital, Clinic of Otorhinolaryngology "St. Marina", Varna, Bulgaria
Email: drnedev@avb.bg

Received 2 April 2015; accepted 20 April 2015; published 24 April 2015

Abstract

Olfactory neuroblastoma (esthesioneuroblastoma, ENB) is a rare tumor arising from the olfactory neuroepithelium. We report a case of ENB located in inferior nasal concha, combined with thyroid gland carcinoma and gastrointestinal stromal carcinoma in a 77-year-old man. The tumor was resected endonasally. When the final diagnosis of olfactory neuroblastoma was confirmed by histopathologic examination and immunohistochemical staining, the PET/CT examination was performed. The imaging revealed a small focus of a moderately increased cancer activity in the thyroid region. A gastrointestinal stromal carcinoma was detected one year after the resection of the thyroid gland. We discuss the clinical appearance of ENB, staging systems, diagnosis and management. During the endonasal surgery, ENB was removed entirely. Seven days after operation, in order to monitor the postoperative result, PET/CT was performed and a papillary thyroid cancer was detected. One year after the thyroid surgery, gastroendoscopy showed a neoplastic formation in the stomach. In conclusion, we state that when identified as aggressive tumors such as ENB, it is necessary to provide regular examinations in order to detect distant ENB metastases or other neoplastic localisations.

Keywords

Esthesioneuroblastoma, Olfactory Neuroblastoma, Thyroid Gland Carcinoma, Gastrointestinal Stromal Carcinoma (GIST)

1. Introduction

Olfactory neuroblastoma (esthesioneuroblastoma, ENB) is a tumor arising from the olfactory neuroepithelium.

How to cite this paper: Nedev, P. (2015) Esthesioneuroblastoma, Thyroid Gland Carcinoma and Gastrointestinal Stromal Carcinoma. *International Journal of Otolaryngology and Head & Neck Surgery*, **4**, 204-210.
http://dx.doi.org/10.4236/ijohns.2015.43034

Usually, the tumor mass originates from the superior nasal cavity meatus and it is presented as a nasal polyp that occupies superior turbinate, superior portion of nasal septum and cribriform plate. Its biological activity ranges from indolent growth to local recurrence and rapid widespread metastasis [1]. We report a rare case of olfactory neuroblastoma combined with thyroid gland carcinoma, treated successfully with surgical resections. One year after surgeries, the clinical examination of the patient showed gastrointestinal stromal carcinoma.

2. Case Report

2.1. History

A 77-year-old man has a history of obstruction in the left nasal cavity and recurrent hemorrhage. Those symptoms disturbed the patient for about 3 - 4 months. The patient does not report other symptoms as hypo- or anosmia, diplopia, facial pain, etc. In the previous examination an ENT specialist diagnosed a benign nasal polyposis and recommended operative treatment.

2.2. Physical Examination and Investigation

The anterior rhinoscopy examination confirmed a tumor mass obturating the left nasal cavity. The neoplasm had whitish-red color, smooth surface and soft consistency, resembling nasal polyposis. There were not neck lymphadenopathies. Coronal and axial CT scans examinations showed 5, 5 - 6 cm/4, 5 - 5 cm tumor mass in inferior and middle nasal meatus without lesions in the neighboring structures (**Figure 1**). The complete blood count was within normal limits.

2.3. Surgery 1

On the endoscopic examinations, polypoid-like mass with bleeding tendency was observed in the left inferior meatus. The tumor lesion arised from inferior nasal conchae. The formation had well defined margins. Other soft tissues and bone structures were not engaged. During surgery the neoplasm's consistency seems to be much easier to tear apart than a bening polyp. The hole tumor mass was removed completely. The diagnosis of esthesioneuroblastoma was determined byhystological analysis (**Figure 2**) and by use of special stains such as immunohistochemistry (**Figure 3**).

2.4. Postoperative Period

The postoperative period was normal; the patient was stable, with restored nasal breathing, without hemorrhage. Seven days after surgery, in order to monitor the postoperative result PET/CT was performed (**Figure 4** and **Figure 5**). The staging FDG PET/CT after the removal of the esthesioneuroblastoma in the nasal cavity revealed that there are no hypermetabolic lesions, indicative of local recurrence/residual tumor or distant metastases. There were not pathological activities in the lungs, axiles, abdominal organs and spine. However a small focus of moderately increased activity is noted in the thyroid region. This finding could be considered as second malignancy

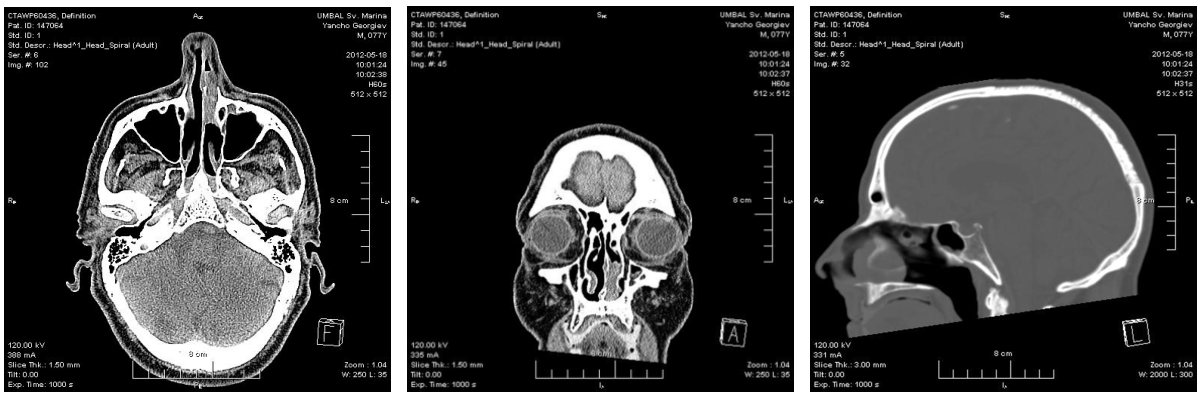

Figure 1. Axial, coronal and sagital CT scans showed 5, 5 - 6 cm/4, 5 - 5 cm tumor mass in left inferior and middle nasal meatus without lesions in the neighboring structures.

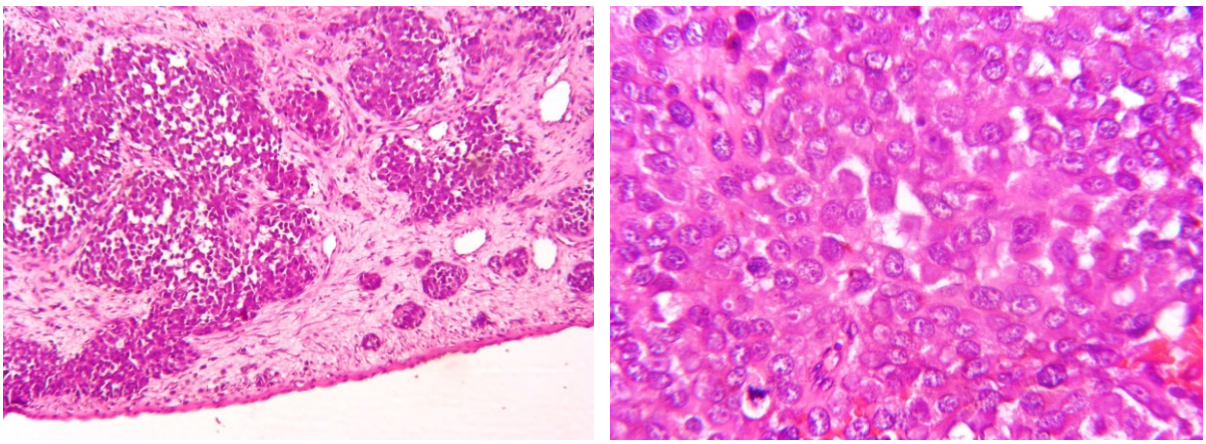

Figure 2. Hematoxylin and eosin stain showed proliferation of neoplastic cells containing uniform round nuclei and scant cytoplasm and cells with dispersed chromatin. Magnification times: 10 × 10 left hand photo; 40 × 10 right hand photo.

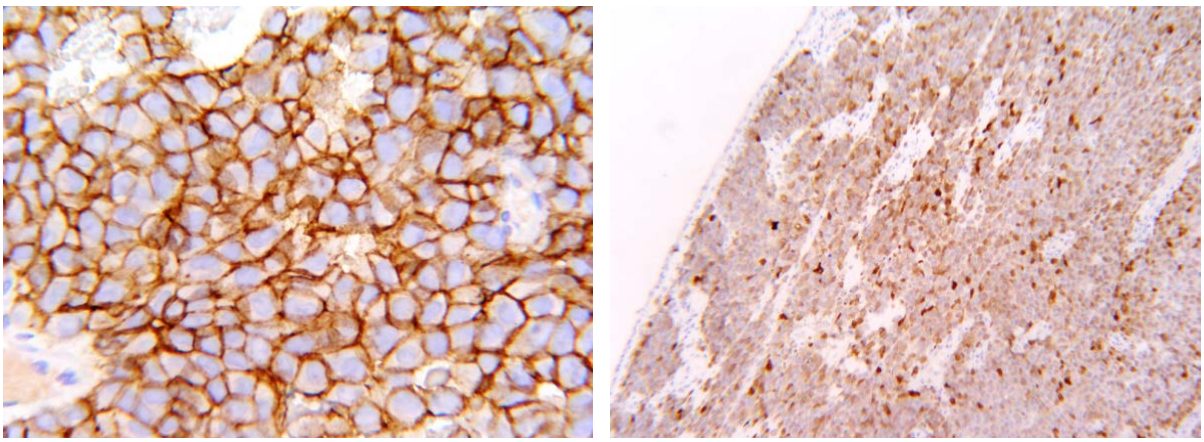

Figure 3. Immunohistochemisrty, hematoxylin and eosin stain 40 × 10, CD 56 (+); S-100 protein (+) GFAP, AE1/AE3 (−). Morphological diagnosis: esthesioneuroblastoma.

island in this patient. Further evaluation proved papillary thyroid cancer. The echographic examination visualized a node structure (5 - 8 mm), with irregular outlines.

2.5. Surgery 2

Second surgical procedure was performed. The intraoperative findings showed 8 mm node (SUV 3.3) in the right superior lobe of the thyroid gland. A partial thyroid resection was done. The histology confirmed papillary thyroid cancer (**Figure 6**).

2.6. Postoperative Care

The patient was discharged without additional courses of chemotherapy or radiation. Six months after the second surgery, the final histopathologic report showed no evidence of recurrent ENB. The echographic examination of the rest of the thyroid gland revealed no suspect formations and the imaging (PET/CT) showed no other cancer activities. One year later the patient had gastrointestinal complaints and the fibrogastroendoscopy showed a neoplasmic formation in the stomach. The histological results confirm gastrointestinal stromal tumor (**Figure 7**). The tumor was considered as inoperable and chemotherapy was recommended.

3. Discussion

In the literature there are only few ENB casesarised from ectopic regions such as maxillary sinus, sphenoid sinus,

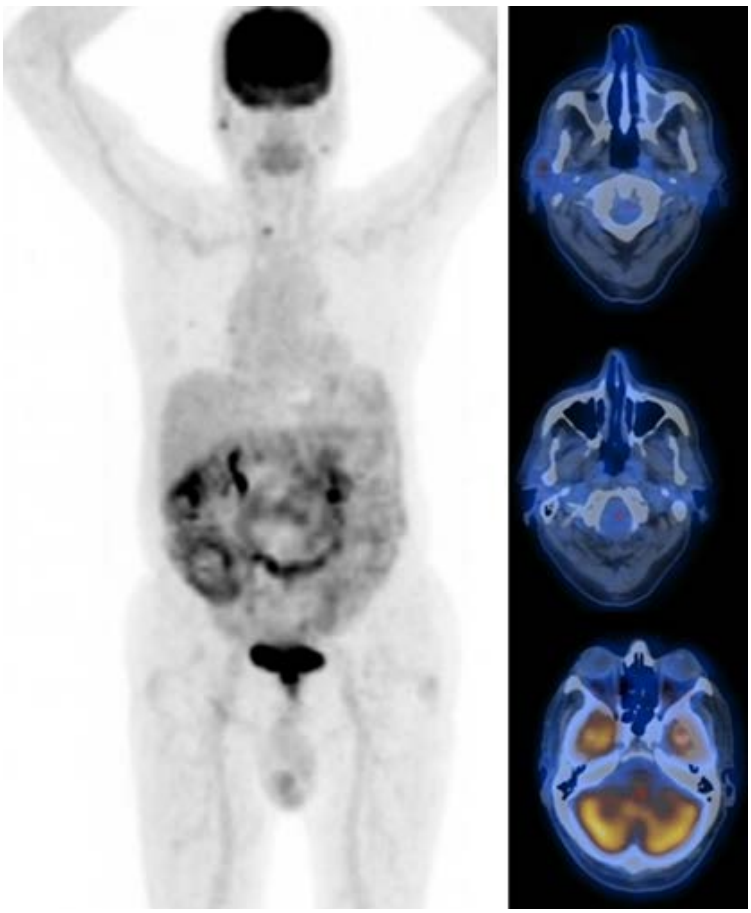

Figure 4. Staging FDG PET/CT performed after the removal of the ENB in the nasal cavity. There are no hypermetabolic lesions, indicative of local recurrence/residual tumors or distant metastases. A small focus of moderately increased activity is noted in the thyroid region.

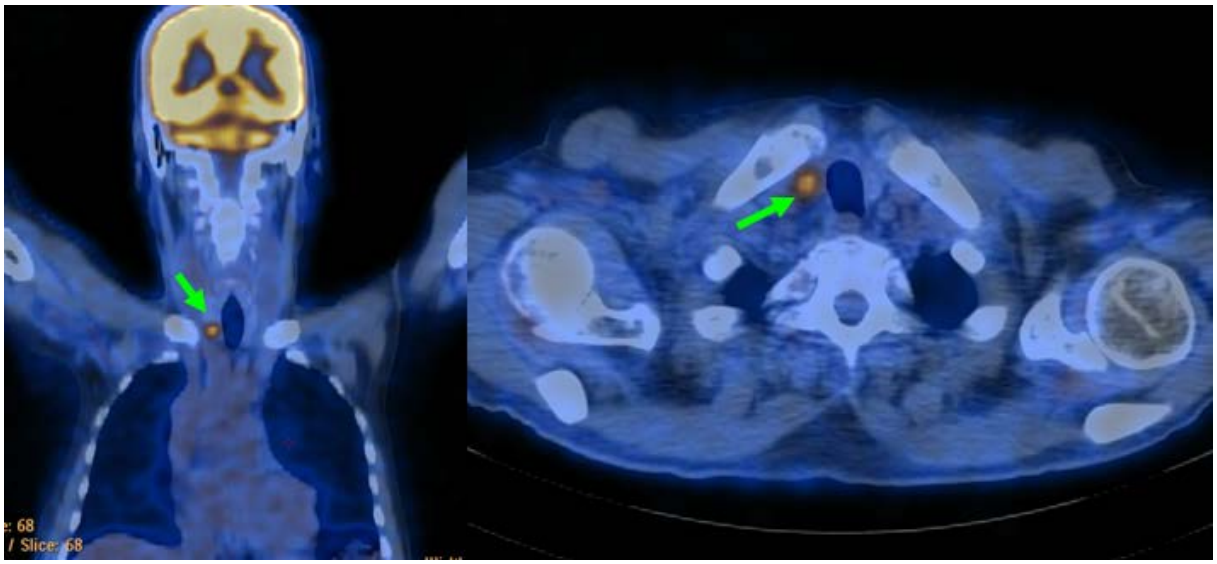

Figure 5. The noted focal uptake on FDG PET/CT is located in the right thyroid lobe. Due to the known high prevalence of malignancy in PET positive thyroid nodules the patient was referred for further evaluation which proved papillary thyroid cancer as a second malignancy in this patient.

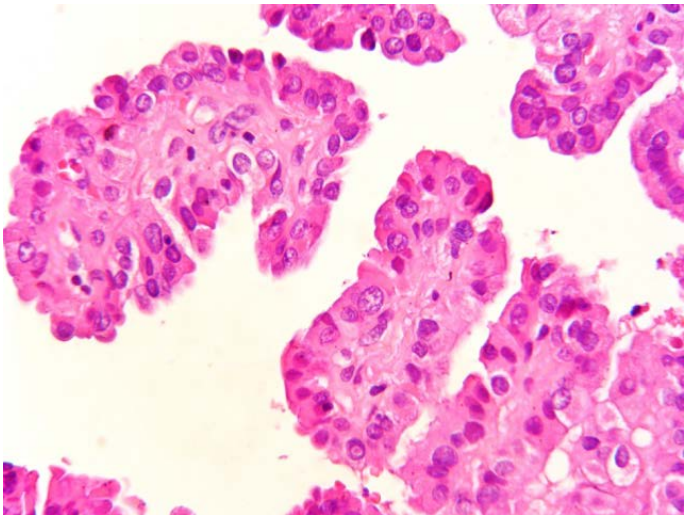

Figure 6. Hematoxylin and eosin stain 40 × 10. Papillary carcinoma of the thyroid gland.

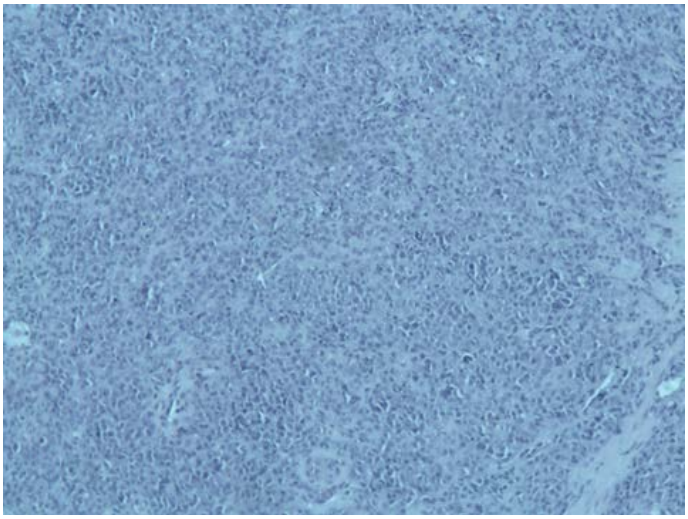

Figure 7. Hematoxylin and eosin stain showed proliferation of epitheloid monotonous cells with high N/C ratio, hyperchromatic nuclei, moderate nuclear and cellular polymorphism; high mitotic activity. Morphological diagnosis: gastrointestinal stromal carcinoma. Magnification times: 10 × 10.

etc. In 2007, Lee and Kim reported a primary olfactory neuroblastoma originating from the inferior meatus of the nasal cavity [2]. So far, we have not found reported case of ENB combined with thyroid gland carcinoma and GIST.

Esthesioneuroblastoma has been described by Berger and Luc in 1924 [3]. This neoplasm is relatively rare and it is known by various names: esthesioneuroepithelioma, esthesioneurocytoma, esthesioneuroblastoma, olfactory esthesioneuroma, intranasal neuroblastoma, and neural olfactory tumor [4]. The tumor can affect both children and adults, with a bimodal peak incidence between 11 and 20 years and between 51 and 60 years [5].

There are cases of 3-year-old [5] and 89-year-old man with ENB [2]. ENB is locally aggressive tumor that has an incidence of 3% to 6% of all intranasal tumors [6] and it metastasizes most commonly to cervical lymphnodes. Cervical lymph node metastasis (10% - 30%) and distant metastasis develop irrespective of tumour grade [7]. Distant metastases can be found in the lungs, the abdominal organs, thespinal cord or in the long bones.

The most common symptoms are nose bleeding, unilateral nasal obstruction, anosmia, facial pain and headache. Macroscopically ENB can be wrongly diagnosed as benign nasal polyp or malignant neoplasms such as: malignant lymphoma, sinonasal undifferentiated carcinoma, *etc*. Therefore any suspicious tissue should be subjected to histological analysis. One of the most important characteristics that can lead the surgeon to suspect a malignancy is the soft and easy to tear apart tumor mass tissue.

One of the most reliable histologic features is itslobular architecture. The circumscribed lobules or nests are made up of primitive neuroblastoma cells. They are usually located below an intact mucosa and in avascularized fibrous stroma. The tumor cells are small, round and blue [8]. The neoplastic cells form arosette- or pseudo-rosette-like pattern [9] [10]. The neoplastic ENB cells are characterized by uniform round nuclei, dispersed chromatin and scant cytoplasm. The final histopathological diagnosis can be established by light microscopy or by immunohistochemical staining and electron microscopy, depending on the tumor differentiation. The detailed analysis of ENB cytogenetic characterization is presented by Heidrun Holland *et al*. [11].

Thus, olfactory neuroblastomas can be detected, delineated and its characteristics suspected by CT and MRI, but definite diagnosis however is still based on histopathology [12]. Depending on the propagation of the tumor mass Dulgerov and Calcaterra [13] proposed a four-stage classification.

The clinical behavior of olfactory epithelium tumors depends on patient age and the clinical stage of the neoplasm. In this particular case the esthesioneuroblastoma was classified as Kadish stage A, because the tumor was confined to the nasal cavity and according TNM system the tumor was ranged as stage T1N0M0.

The treatment of ENB depends on the stage and the presence of metastases. It seems that so far the best results are obtained with a combination of surgical resection and radiotherapy, with or without chemotherapy [14].

Unfortunately, despite aggressive therapy, ENB has been noted to have a high local recurrence rate of 50% - 60% with 10% - 62% presenting as metastatic cases and 20% - 30% of those cases involving the CNS [15]. The patients with tumors of Kadish stage A have a 5-year survival rate ranging from 72% to 81% [5] [16] [17].

Survival according to treatment modalities was 65% for surgery plus radiotherapy, 51% for radiotherapy and chemotherapy, 48% for surgery, 47% for surgery plus radiotherapy and chemotherapy, and 37% for radiotherapy alone [16]. The histopathological grading according to Hyams and the presence of cervical lymph-node metastases emerged as prognostic factors [16] [18]. The disease-free actuarial survival and overall survival rates were 77% and 61% at 5 years and 53% and 42% at 10 years, respectively [19]. In 2015, Petruzzelli *et al*. published a retrospective analysis of 32 patients, where the estimated overall rate of survival at 10 years was 78% based on Kadish and T stage [20]. Esthesioneuroblastoma is an uncommon malignancy of the head and neck for which there is no defined treatment protocol [20].

In this case study we demonstrate that in some cases the diagnosis ENB might be unexpected because the tumor mass arises from the anterior end of the inferior nasal concha. The combination of ENB with thyroid gland carcinoma and GIST isextraordinary and we defined it as extremely rare.

In this particular case we did not recommended course of radiotherapy/chemotherapy because of the early stage of the ENB, its radical removal and the lack of regional or distant metastases. The thyroid gland carcinoma was removed radically as well. The GIST was considered as inoperable. Regardless of the course of chemotherapy the outcome was lethal 6 months after the diagnosis of gastrointestinal stromal tumor.

4. Conclusions

We presented a rare case of ENB with thyroid gland carcinoma as a second finding of cancer activity. The early stage of the tumors allowed applying surgical treatments. The thyroid gland carcinoma was found by PET/CT examination, which was applied in order to detect the presence of ENB possible metastases.

We cannot determine with certainty whether the thyroid gland carcinoma and gastrointestinal stromal tumor (diagnosed one year later) are metastatic from the ENB or whether they are primary cancer activities.

When identified as aggressive tumors such as ENB, it is necessary to provide regular examinations in order to detect distant ENB metastases or other neoplastic localisations.

References

[1] Sampath, P., Park, M.C., Huang, D., Deville, C., Cortez, S. and Chougule, P. (2006) Esthesioneuroblastoma (Olfactory Neuroblastoma) with Hemorrhage: An Unusual Presentation. *Skull Base*, **16**, 169-173. http://dx.doi.org/10.1055/s-2006-939677

[2] Lee, J.Y. and Kim, H.K. (2007) Primary Olfactory Neuroblastoma Originating from the Inferior Meatus of the Nasal Cavity. *American Journal of Otolaryngology-Head and Neck Medicine and Surgery*, **28**, 196-200.

[3] Berger, L. and Luc, R. (1924) L'Estesioneuroepitheliome olfactif. *Buletin de L'Association francaise pour l'etudede de Cancer*, **13**, 410-421.

[4] Arnol, P.M., Habib, A., Newell, K. and Anderson, K.K. (2009) Esthesioneuroblastoma Metastatic to the Thoracic Intradural and Extradural Space. *The Spine Journal*, **9**, 1-5.

[5] de Santana Sarmento, D.J., *et al*. (2012) Aggressive Olfactory Neuroblastoma Invading the Oral Cavity: Report of a Rare Case and Review of the Literature. *Journal of Oral and Maxillofacial Surgery*, **70**, 252-257. http://dx.doi.org/10.1016/j.joms.2011.11.020

[6] Bak, M. and Wein, R.O. (2012) Esthesioneuroblastoma: A Contemporary Review of Diagnosis and Management. *Hematology/Oncology Clinics of North America*, **26**, 1185-1207. http://dx.doi.org/10.1016/j.hoc.2012.08.005

[7] Bragg, T.M., Scianna, J., Kassam, A., *et al*. (2009) Clinicopathological Review: Esthesioneuroblastoma. *Neurosurgery*, **64**, 764-770. http://dx.doi.org/10.1227/01.NEU.0000338948.47709.79

[8] Yu, T., Xu, Y.K., Li, L., Jia, F.G., Duan, G., Wu, Y.K., Li, H.Y., Yang, R.M., Feng, J., Ye, X.H. and Qiu, Y.W. (2009) Esthesioneuroblastoma Methods of Intracranial Extension: CT and MR Imaging Findings. *Neuroradiology*, **51**, 841-850. http://dx.doi.org/10.1007/s00234-009-0581-0

[9] Thompson, L.D. (2009) Olfactory Neuroblastoma. *Head and Neck Pathology*, **3**, 252-259. http://dx.doi.org/10.1007/s12105-009-0125-2

[10] Ferreira, M.C.F., Tonoli, C., Varoni, A.C.C., Gusmon, C.C., Alvarenga, M., Chagas, J.F. and Pascoal, M.B.N. (2007) Esthesioneuroblastoma. *Revista de Ciências Médicas Campinas*, **16**, 193-198.

[11] Holland, H., Koschny, R., Kruppd, W., Meixensberger, J., Bauer, M., Kirsten, H. and Ahnert, P. (2007) Comprehensive Cytogenetic Characterization of an Esthesioneuroblastoma. *Cancer Genetics and Cytogenetics*, **173**, 89-96. http://dx.doi.org/10.1016/j.cancergencyto.2006.09.024

[12] Gondim, J., Ramos Jr., F., Azevedo, J., Carrero Jr., F.P. and Tella Jr., O.I. (2002) Esthesioneuroblastoma: A Case Report. *Arquivos de Neuro-Psiquiatria*, **60**, 303-307. http://dx.doi.org/10.1590/S0004-282X2002000200024

[13] Dulguerov, P. and Calcaterra, T. (1992) Esthesioneuroblastoma: The UCLA Experience 1970-1990. *Laryngoscope*, **102**, 843-849. http://dx.doi.org/10.1288/00005537-199208000-00001

[14] Pickuth, D., Heywang-Kobrunner, S.H. and Spielmann, R.P. (1999) Computed Tomography and Magnetic Resonance Imaging Features of Olfactory Neuroblastoma: An Analysis of 22 Cases. *Clinical Otolaryngology*, **24**, 346-350. http://dx.doi.org/10.1046/j.1365-2273.1999.00295.x

[15] Shirzadi, A.S., Drazin, D.G., Strickland, A.S., Bannykh, S.I. and Patrick Johnson, J. (2013) Vertebral Column Metastases from an Esthesioneuroblastoma: Chemotherapy, Radiation, and Resection for Recurrence with 15-Year Follow-Up. *Case Reports in Surgery*, **2013**, 8 p.

[16] Dulguerov, P., Allal, A.S. and Calcaterra, T.C. (2001) Esthesioneuroblastoma: A Meta-Analysis and Review. *The Lancet Oncology*, **2**, 683-690. http://dx.doi.org/10.1016/S1470-2045(01)00558-7

[17] Kadish, S., Goodman, M. and Wang, C.C. (1976) Olfactory Neuroblastoma—A Clinical Analysis of 17 Cases. *Cancer*, **37**, 1571-1576. http://dx.doi.org/10.1002/1097-0142(197603)37:3<1571::AID-CNCR2820370347>3.0.CO;2-L

[18] Hyams, V.J. (1988) Olfactory Neuroblastoma. In: Hyams, V.J., Baksakis, J.G. and Michaels, L., Eds., *Tumors of the Upper Respiratory Tract and Ear*, Armed Forces Institute of Pathology, Washington DC, 240-248.

[19] Lund, V., Howard, D., Wei, W. and Spittle, M. (2003) Olfactory Neuroblastoma: Past, Present, and Future? *The Laryngoscope*, **113**, 502-507. http://dx.doi.org/10.1097/00005537-200303000-00020

[20] Petruzzelli, G.J., Howell, J.B., Pederson, A., Origitano, T.C., Byrne, R.W., Munoz, L., Emami, B. and Clark, J.I. (2015) Multidisciplinary Treatment of Olfactory Neuroblastoma: Patterns of Failure and Management of Recurrence. *American Journal of Otolaryngology*, in Press. http://dx.doi.org/10.1016/j.amjoto.2015.02.008