sciendo

DOI: 10.2478/rjr-2020-0010

Romanian Journal of Rhinology, Volume 10, No. 38, April - June 2020

LITERATURE REVIEW

Extramedullary plasmacytoma with intranasal localization

Alexandru Pirvu[1], Codrut Sarafoleanu[1,2,3], Gabriela Musat[1,2,3]

[1]ENT&HNS Department, "Sfanta Maria" Hospital, Bucharest, Romania

[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

[3]CESITO, "Sfanta Maria" Hospital, Bucharest, Romania

ABSTRACT

Plasmacytoma is a rare, non-epithelial, malignant tumor, affecting soft or bony tissues, which can have a unique location (solitary or extramedullary solitary plasmacytoma), or multiple (multiple myeloma). In the ENT sphere, it is most commonly encountered in its extramedullary form, which develops in the region of the head and neck, at the level of the submucosa. Most commonly, it affects the elderly, who have cardinal symptoms such as unilateral nasal obstruction, nasal or facial swelling, tissue necrosis or mucosal ulcerations, perforation of the nasal septum with dysmorphia of the nasal pyramid, recurrent unilateral epistaxis. Radiotherapy is the treatment of choice for extramedullary plasmacytoma. The prognosis is a reserved one, the risk of recurrence or conversion to multiple myeloma also existing 15 years after treatment.

KEYWORDS: extramedullary plasmacytoma, radiotherapy, recurrence.

INTRODUCTION

Plasmacytoma belongs to the category of lymphoproliferative neoplasms. It represents a rare malignant rhinosinusal tumor, along with the esthesioneuroblastoma (tumor originating from the olfactory epithelium in the upper part of the nasal cavity, the ethmoid riddled blade and the medial surface of the superior nasal concha), Ewing's sarcoma, malignant melanoma of the rhinosinusal mucosa, hemangiopericytoma (mesenchymal tumor originating from extravascular cells surrounding small blood vessels – Zimmermann's Pericytes)[1].

Lymphoproliferative neoplasms are the most common non-epithelial malignancies found in the nasal cavity, maxillary sinus and rhinopharynx, and the main types are Hodgkin and non-Hodgkin lymphomas. Lymphomas account for 3% to 5% of all rhinosinusal malignancies, 60% of them being non-Hodgkin's lymphomas[2].

Plasmacytoma is a B-cell lymphoproliferative neoplasm, with uncontrollable multiplication, which develop the ability to invade normal tissue (cancer feature). We are talking about a rare, non-epithelial, malignant tumor, affecting soft or bony tissues, which can have a unique location (bony or extramedullary solitary plasmacytoma) or multiple (multiple myeloma).

In the upper respiratory tract, the plasmacytoma has exceptional intraosseous localization, the most common being the extramedullary form. Extramedullary plasmacytoma occurs in approximately 4% of non-epithelial tumors of the upper respiratory tract, with occasional localization in the gastrointestinal tract, skin or lungs, but 80-90% are found in the head and neck region[3,4].

Extramedullary plasmacytoma (EMP) represents less than 1% of all head and neck tumors and less than 0.5% of all the upper airway tumors[4-6]. In terms of location, depending on the frequency, EMP can be found in the submucosa of the nasal cavity, paranasal sinuses, oropharynx or larynx[4]. Regarding the rhinosinusal localization, the maxillary sinus is the most commonly involved. In 10 – 20% of the cases, it presents a multiple location[7].

It represents a rare rhinosinusal tumor with increased potential of conversion to multiple myeloma.

Corresponding author: Prof. Dr. Codrut Sarafoleanu, ENT&HNS Department, "Sfanta Maria" Hospital, 37-39 Ion Mihalache Blv., District 1, Bucharest, Romania

e-mail: csarafoleanu@gmail.com

Received for publication: January 6, 2020 / **Accepted:** January 23, 2020

INCIDENCE AND ETIOPATHOGENESIS

Extramedullary plasmacytoma was first described in 1905 by Schridde[8,9] and has a global incidence of about 1 case in 500,000 people[10,11].

Extramedullary plasmacytoma develops in the head and neck region at the level of the submucosa in over 90% of cases and it most commonly affects the elderly, the maximum incidence being in the 6th and 7th decades of life[8]. It seems to present a predisposition for males (male / female ratio = 3/1)[12,13]. In the literature, there are only 5 cases of EMP in young patients, under 15 years old[13-16].

Factors involved in the development of lymphomas, implicitly plasmacytoma, are Epstein-Barr virus and HTLV-1 (Human T-lymphotropic virus 1) or different inhaling irritants[13,17].

EXTRAMEDULLARY PLASMACYTOMA HISTOPATHOLOGY

From a histopathological point of view, these tumors are made up of a pure plasmacytic population (B lymphocytes in the final stage of maturation) that proliferates in cords, solid masses or strings, with nuclear atypia and mitotic activity. Approximately 20-30% of the cases of EMP can become multiple myeloma.

The component cells of this type of tumor have 3 degrees of differentiation: grade I (completely mature cells), grade II (intermediate cells) and grade III (poorly differentiated cells) (Figure 1).

CLINICAL SIGNS AND DIAGNOSIS OF EXTRAMEDULLARY PLASMACYTOMA

The symptomatology of this type of tumor has an insidious onset, which leads to late presentation to the specialist doctor, with the discovery of the tumor in advanced stages. The clinical and paraclinical presentation of the tumor is non-specific, the "gold standard" in its diagnosis being the histopathological examination.

The symptomatology depends primarily on the location of the tumor and less on its nature. These patients present as cardinal symptoms local edema (80% of cases), nasal obstruction (most commonly unilateral; 35% of cases), recurrent episodes of unilateral epistaxis (35% of cases), facial pain (20% of cases), proptosis (15%), rhinorrhea or adenopathy (10% of cases), tissue necrosis or mucosal ulceration, perforation of the nasal septum with dysmorphia of the nasal pyramid[5,18-20].

Regardless of the stage at which the tumor is dis-

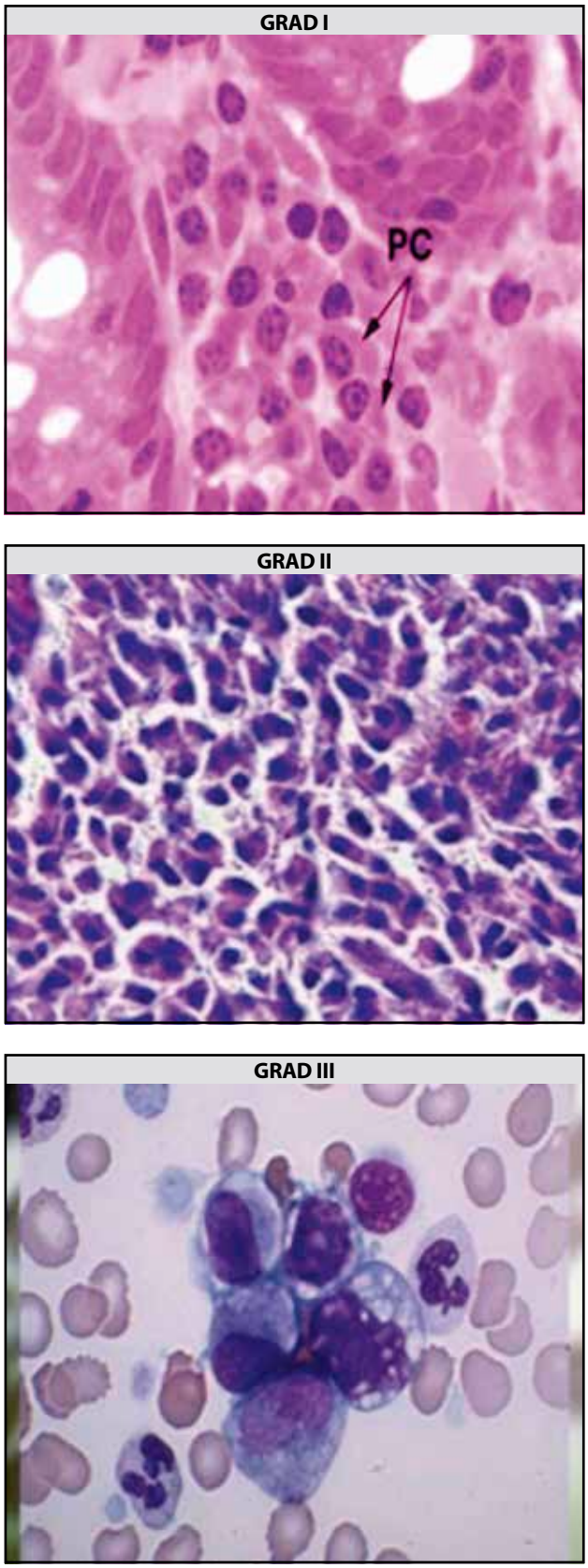

Figure 1. The degrees of cellular differentiation of the extramedullary plasmacytoma – histopathological aspect.

covered, the plasmacytoma has a non-specific macroscopic appearance, like a well-delimited polypoid mass, replacing space at the level of the rhinosinusal anatomical segment involved, with a sessile or pedicled implantation base, the colour ranging from yellowish-grey to dark red, often slightly bleeding at instrumental palpation.

EMP has a non-characteristic imaging appearance. At the MRI examination, the slightly non-homogeneous signal can be hyperintense on T2 and intermediate on T1, but varying degrees of intensity can also be observed on the craniofacial CT examination after administration of contrast substance[21].

The positive diagnosis of the extramedullary plasmacytoma is based on the histopathological examination and it is recommended to perform bone marrow biopsy (less than 10% of atypical plasma cells), bone scintigraphy to exclude bone damage[1], as well as laboratory serological tests (absence of anemia, immunoglobulin electrophoresis within normal limits)[5,10].

Differential diagnosis of extramedullary plasmacytoma with nasal localization can be made with pathologies in which there is a rich plasmacytic infiltrate, namely with olfactory neuroblastoma, rhinoscleroma, plasma cell granuloma, malignant melanoma, adenoma of the pituitary gland. From a histopathological point of view, it is the most difficult to differentiate between an EMP and a multiple myeloma. The absence of bone lysis, the immunoglobulin electrophoresis within normal limits, as well as the absence of anemia can be essential in differentiating the two types of tumors[4].

THERAPEUTIC STRATEGY

The treatment strategy of extramedullary plasmacytoma with nasal localization involves the implementation of a therapeutic plan together with a multidisciplinary oncology, and it must be individualized according to the histological type of the tumor, tumor stage, the feasibility of complete tumor resection, the patient's medical conditions, treatment risks and comorbidities, the experience of the team of surgeons in preventing or treating possible intraoperative complications, patient's personal preference and reconstructive options.

The solitary plasmacytoma is a radiosensitive tumor, the main therapeutic methods being represented by radiotherapy (indicated in the early stages) and chemotherapy (reserved for advanced stages and tumors with poorly differentiated cells); however, one can also opt for surgical techniques (if the tumor is completely resectable) or polymodal techniques (wide surgical resection and postoperative radiotherapy). Polymodal treatment (radiotherapy / chemotherapy and surgery) provides the most effective therapeutic results[9,22].

Radiotherapy is the treatment of choice for extramedullary plasmacytoma, presenting a local control rate of 90-100%[23,24]. There is no consensus regarding the recommended optimal dose; doses with an optimal control rate can range from 35 to 80 Gy for a period between 3 and 6 weeks[4,12,25-27]. Typically, plasmacytomas smaller than 5 cm in size responded favourably to 30-40 Gy, while larger tumors require higher radiation doses (40-50 Gy)[19]. Intensity-modulated radiotherapy (IMRT) is a safe treatment that protects surrounding structures such as the skin, orbit, brain or salivary glands.

Chemotherapy has a weaker response in non-Hodgkin lymphomas with sinonasal involvement, than in other anatomical locations and is indicated for tumors larger than 5 cm, refractory to other therapies, or in case of disease progression or relapse[12,18]. Preoperative induction chemotherapy followed by surgery and postoperative radio-chemotherapy represents a multimodal treatment that resulted in increased survival of patients with rhinosinusal neoplasm in advanced stages[9]. Cisplatin and 5-FU have been shown to enhance the effect of radiation therapy on tumor cells.

Surgical treatment brings similar results with radiotherapy and is indicated if the tumor is completely resectable[9,19,28], and the resection of the tumor mass can be performed by endoscopic or external approach, depending on the degree of its extension. In the case of the external approach, to minimize intraoperative bleeding, a preoperative selective embolization may be effective, but it is not routinely indicated. The type of surgical approach is chosen following the analysis of CT or MRI sections, which are adapted to tumor localization and staging, but it can be modified by the intraoperative findings of the lesions. Intranasal extramedullary plasmacytoma resection by endoscopic approach is indicated in the stages: T1 (tumor limited to the nasal cavity or ethmoid sinus with or without bone invasion) and T2 (the tumor invades the nasal cavity or the ethmoid with or without bone invasion)[1]. There are also major contraindication criteria for endoscopic rhinosinusal surgery, namely the tumor invasion of the lacrimal duct, hard palate, posterior wall of the sphenoid sinus or all the walls of the maxillary sinus (except for the medial wall).

The ablation of tumor mass by external approach is recommended in stages: T3 (the tumor invades the posterior wall of the maxilla, the subcutaneous facial tissue, the floor or medial wall of the orbit, the pterygopalatine fossa, the palate or the riddled blade of the ethmoid); T4a (the tumor invades the

orbital contents, the skin of the nose and / or cheek; minimal extension to the anterior cranial fossa, pterygoid lamellae, the infratemporal fossa, sphenoid or frontal sinus); T4b (the tumor invades the orbital apex, dura, brain, middle cranial fossa, cranial nerves except the maxillary nerve, rhinopharynx, clivus)[1].

Regarding the effectiveness of the different types of treatments in case of intranasal extramedullary plasmacytoma, the specialized literature reports a 21% relapse rate in the case of radiotherapy, 20% for surgery and up to 46% for chemotherapy[4,6].

NATURAL EVOLUTION AND PROGNOSTIC

The natural evolution of EMP has been described by Batsakis as having five stages[4,29]:

- Stage I: localized disease; unique; controlled by surgery, radiotherapy or combined; without relapse; or disseminated.
- Stage II: disease with local relapse controlled by additional treatment.
- Stage III: aggressive, persistent or recurrent disease; exitus through uncontrollable local dissemination.
- Stage IV: localized disease with regional lymphatic "metastases" without obvious remote dissemination.
- Stage V: localized, recurrent or disseminated disease and the appearance of another neoplasm originating in plasma cells and / or multiple myeloma.

In the literature, a high risk of conversion of intranasal extramedullary plasmacytoma into malignant melanoma is described, this risk being higher in the first two years[30,31].

Considering all these aspects, it is recommended that the patient be followed postoperatively for a long period. Periodic follow-ups will be performed at 6 weeks, then every 3 months in the first and second years after treatment, at 6 months in the third year and annually thereafter[1,30]. From the otorhinolaryngologist's point of view, at each follow-up the patient will be clinically examined in the ENT department and a sinonasal endoscopy will be performed. At 3 months postoperatively, the patient will perform contrast-enhanced craniofacial MRI / CT scan and cervical MRI to exclude lymph nodes metastases; afterwards, a craniofacial MRI will be performed annually[1].

Given the increased risk of transformation into multiple myeloma, Myeloma Guidelines by the Italian Association of Medical Oncology (AIOM) recommend performing a serological check-up 45 to 60 days after the completion of the radiotherapy treatment, then every 3 months in the first year and, subsequently, every six months by serological analysis, radiologically and by spine biopsy[32].

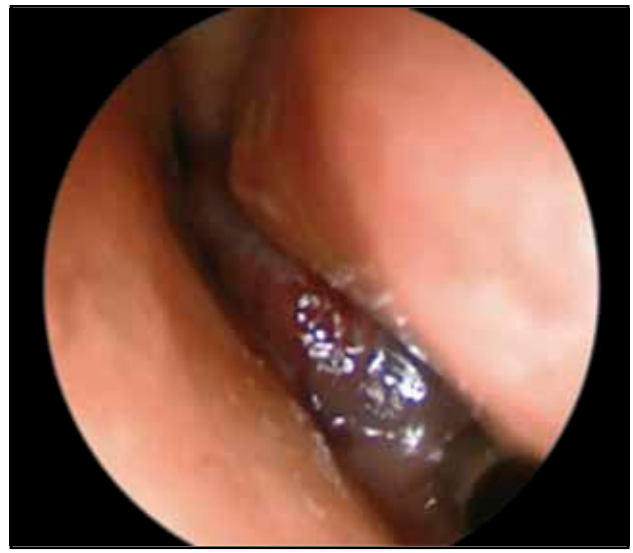

Figure 2. EMP with nasal localization – nasal endoscopic examination appearance.

The prognosis of extramedullary plasmacytoma with intranasal localization is a reserved one. With a low incidence in the upper respiratory tract, it is difficult to assess the outcome of the treatment and the prognosis of the disease. The risk of relapse or conversion to multiple myeloma also exists 15 years after treatment[31].

The elements of negative prognosis in the evolution of the disease are represented by the presence of bone lesions, large primary tumor, relapse, tumor located in the sphenoid and maxillary sinus or at the laryngeal level[6].

The survival rate can be about 70% at 10 years[9,13,30].

OUR EXPERIENCE

We present the case of a 79-year-old female patient, without significant personal pathological background, who was diagnosed in March 2018 with a tumor mass in the left nasal fossa. The symptomatology of the patient, which started 2 years before the presentation to the doctor, included progressive left nasal obstruction and repeated episodes of left unilateral epistaxis at minimal effort.

On clinical ENT examination and nasal endoscopy, a sessile, reddish, polypoid-like tumor mass was detected, originating in the middle third of the left nostril floor and the inferior part of the nasal septum, slightly bleeding at instrumental palpation (Figure 2).

The native CT scan (Figure 3) of paranasal sinuses revealed a space-occupying lesion in the left

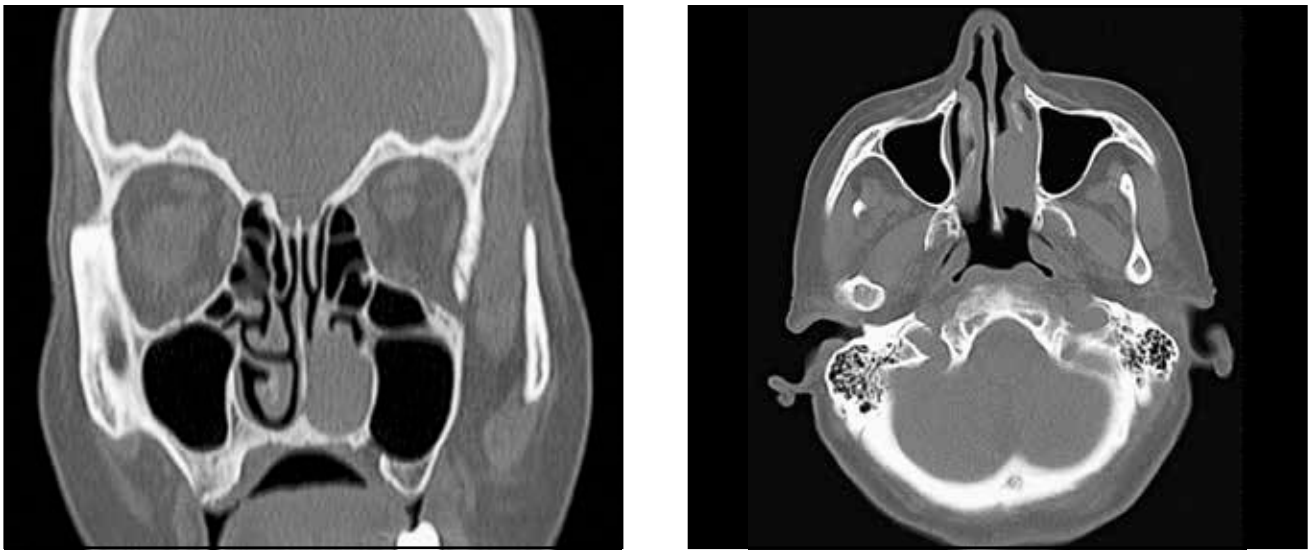

Figure 3. Native craniofacial CT scan, coronal and axial slices - a space-occupying lesion in the left nasal fossa.

nasal fossa, with apparent origin at the level of the left inferior turbinate which it encompasses, without invasion of the nasal septum, nasal cavity floor or left maxillary sinus.

In April 2018, surgery was performed, achieving the "en block" resection of the tumor mass under endoscopic control (Figure 4).

The histopathological examination of the operative specimen established the diagnosis of extramedullary plasmacytoma with intermediate degree of differentiation.

Postoperatively, the patient underwent radiotherapy (40 Gy dose administration for 3 weeks) and also routine endoscopic follow-ups at 1 month and 3 months, with no signs of tumor remnants or relapse. The contrast-enhanced craniofacial CT examination performed at 3 months, respectively at 1 year postoperatively, did not show signs of tumor recurrence.

CONCLUSIONS

Extramedullary plasmacytoma is a malignant, non-epithelial, rare tumor, affecting soft or bony tissues, which can have unique or multiple location. Regarding the rhinosinusal localization, the maxillary sinus is the most commonly involved.

The symptomatology of this type of tumor has an insidious onset, which leads to late presentation to the specialist, with the diagnosis of the tumor in advanced stages.

Plasmacytoma is a radiosensitive tumor, the main

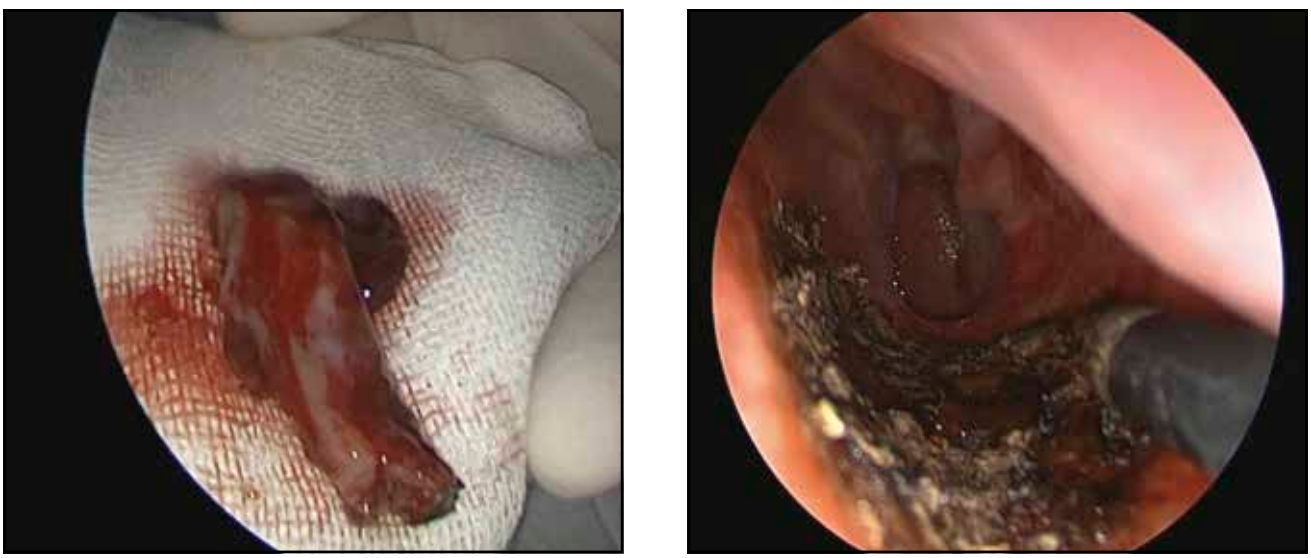

Figure 4. Intraoperatory view.

therapeutic methods being represented by radiotherapy (indicated in the early stages) and chemotherapy (reserved for advanced stages and tumors with poorly differentiated cells); however, one can also opt for surgical techniques (if the tumor is completely resectable) or polymodal techniques (wide surgical resection and postoperative radiotherapy).

Post-operative follow-up is essential, requiring periodic radiological examinations. The long-term prognosis is difficult to assess, because of the rarity of this condition; long-term follow-up is required, considering the possibility of late recurrences.

Contribution of authors: All contributors meet the criteria for authorship.

Conflict of interest: The authors have no conflict of interest.

Acknowledgements: None

REFERENCES

1. Sarafoleanu C. Patologia tumorala maligna nazo-sinusala. In: Popescu I, Ciuce C (eds); Sarafoleanu C (coord). Tratat de chirurgie. Editia a II-a. Vol I.: Otorinolaringologie si chirurgie cervico-faciala. Editura Academiei Romane, Bucuresti; 2012, p.231-55.
2. Quraishi MS, Bessell EM, Clark D, Jones NS, Bradley PJ. Non-Hodgkin's lymphoma of the sinonasal tract. Laryncoscope. 2000;110(9):1489-92.
3. Galieni P, Cavo M, Pulsoni A, Avvisati G, Bigazzi C, Neri S, et al. Clinical outcome of extramedullary plasmacytoma. Haematologica. 2000;85(1):47–51.
4. dos Anjos Corvo MA, Granato L, Ikeda F, de Prospero JD. Extramedullary nasal plasmacytoma: Literature review and a rare case report. Int Arch Otorhinolaryngol. 2013;17(2):213–7. DOI: 10.7162/S1809-97772013000200016.
5. Kuppersmith RB. Extramedullary plasmocytoma of the head and neck. [Internet]. Available from: http://www.bcm.edu/oto/grand/32896.
6. Wiltshaw E. The natural history of extramedullary plasmocitoma and its relation to solitary mieloma of bone and myelomatosis. Medicine (Baltimore). 1976;55(3):217-38.
7. Hidaka H, Ikeda K, Oshima T, Ohtani H, Suzuki H, Takasaka T. A case of extramedullary plasmocytoma arising from the nasal septum. J Laryngol Otol. 2000;114(1):53-5.
8. Ashraf MJ, Azarpira N, Khademi B, Abedi E, Hakimzadeh A, Valibeigi B. Extramedullary plasmocytoma of the nasal cavity report of three cases with review of the literature. Iran Red Cres Med J. 2013;15(4):363-6. DOI: 10.8512/ircmj.2209.
9. Soutar R, Lucraft H, Jackson G, Reece A, Bird J, Low E, et al. Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. Clin Oncol (R Coll Radiol). 2004;16(6):405–13.
10. Fernandes AM, Podovani JA, Maniglia JP. Plasmocitoma extramedular de nasofaringe: relato de un caso e revisao da literatura. Rev Bras Otorrinolaringol. 1998;64(3):296-8.
11. Sousa RMA, Costa EG, Takahashi GM, Butugan O, Miniti A. Mieloma multiplo e manifestacoes raras dentro da otorrinolaringologia. Rev Bras Otorrinolaringol. 1993;59(4):284-8.
12. Susnerwala SS, Shanks JH, Banerjee SS, Scarffe JH, Farrington WT, Slevin NJ. Extramedullary plasmacytoma of the head and neck region: clinicopathological correlation in 25 cases. Br J Cancer. 1977;75(6):921-7. DOI: 10.1038/bjc.1997.162.
13. Chang YL, Chen PY, Hung SH. Extramedullary plasmacytoma of the nasopharynx: A case report and review of the literature. Oncol Lett. 2014;7(2):458–60. DOI: 10.3892/ol.2013.1712.
14. Mann G, Trebo MM, Minkov M, Simonitsch I, Chott A, Gadner H. Extramedullary plasmacytoma of the adenoids. Pediatr Blood Cancer. 2007;48(3):361-2.
15. Nagasaka T, Lai R, Kuno K, Nakashima N, Nakashima N. Localized amyloidosis and extramedullary plasmocytoma involving the larynx of a child. Hum Pathol. 2001;32(1):132-4.
16. Sharma MC, Mahapatra AK, Gaikwad S, Biswal A. Primary extramedullary orbital plasmacytoma in a child. Childs Nerv Syst. 1996;12(8):470-2.
17. Sasaki S, Hashimoto K, Nakatsuka S, Hasegawa M, Nakano T, Nagata S, et al. Plasmablastic extramedullary plasmacytoma associated with Epstein-Barr virus arising in an immunocompetent patient with multiple myeloma. Intern Med. 2011;50(21):2615-20.
18. Kapadia SB, Desai U, Cheng VS. Extramedullary plasmocytoma of the head and neck. A clinicopathologic study of 20 cases. Medicine (Baltimore). 1982;61(5):317-29.
19. Bachar G, Goldstein D, Brown D, Tsang R, Lockwood G, Perez-Ordonez B, et al. Solitary extramedullary plasmacytoma of the head and neck–long-term outcome analysis of 68 cases. Head Neck. 2008;30(8):1012–9. DOI: 10.1002/hed.20821.
20. Kitamura A, Yamashita Y, Hasegawa Y, Kojima H, Nagasawa T, Mori N. Primary lymphoma arising in the nasal cavity among Japanese. Histopathology. 2005;47(5):523-32.
21. King AD, Lei KIK, Ahuja AT, Lam WWM, Metreweli C. MR imaging of nasal T-cell/natural killer cell lymphoma. AJR Am J Roentgenol, 2000;174(1):209-11. DOI: 10.2214/ajr.174.1.1740209.
22. Creach KM, Foote RL, Neben-Wittich MA, Kyle RA. Radiotherapy for extramedullary plasmacytoma of the head and neck. Int J Radiat Oncol Biol Phys. 2009;73(3):789–94. DOI: 10.1016/j.ijrobp.2008.04.077.
23. Chao MW, Gibbs P, Wirth A, Quong G, Guiney MJ, Liew KH. Radiotherapy in the management of solitary extramedullary plasmocytoma. Intern Med J. 2005;35(4):211-5.
24. Mendenhall WM, Thar TL, Million RR. Solitary plasmacytoma of bone and soft tissue. Int J Radiat Oncol Biol Phys. 1980;6(11):1497-501. DOI: 10.1016/0360-3016(80)90006-1.
25. Kotner LM, Wang CC. Plasmacytoma of the upper air and food passages. Cancer. 1972;30(2):414-8. DOI: 10.1002/1097-0142(197208)30:2<414::aid-cncr2820300217>3.0.co;2-z.
26. Woodruff RK, Whittle JM, Malpas JS. Solitary plasmacytoma. I: Extramedullary soft tissue plasmacytoma. Cancer. 1979;43(6):2340-3.
27. Petrovich Z, Fishkin B, Hittle RE, Acquarelli M, Barton R. Extramedullary plasmacytoma of the upper respiratory passages. Int J Radiat Oncol Biol Phys. 1977;2(7-8):723-30. DOI: 10.1016/0360-3016(77)90054-2.
28. Wax MK, Yun KJ, Omar RA. Extramedullary plasmocytomas of the head and neck. Otolatyngol Head Neck Surg. 1993;109(5):877-85.
29. Batsakis JG. Plasma cell tumors of the head and neck. Ann Otol Rhinol Laryngol. 1992;92(3):311–3.
30. D'Aguillo C, Soni RS, Gordhan C, Liu JK, Baredes S, Eloy JA. Sinonasal extramedullary plasmacytoma: a systematic review of 175 patients. Int Forum Allergy Rhinol. 2014;4(2):156–63. DOI: 10.1002/alr.21254.
31. Cantone E, Di Lullo AM, Marano L, Guadagno E, Mansueto G, Capriglione P, et al. Strategy for the treatment and follow-up of sinonasal solitary extramedullary plasmacytoma: a case series. J Med Case Rep. 2017;11(1):2019. DOI: 10.1186/s13256-017-1382-4.
32. Pinotti G, Proserpio I, Bringhen S, Chini C, Mangiacavalli S, Olivares C, et al. Linee guida Mieloma. Edizione 2017. Available from: http://media.aiom.it/userfiles/files/doc/LG/2017_LGAIOM_Mieloma.pdf.