CASE REPORTS

Rare sinonasal lesions

CRISTIAN ANDREI SARĂU1), MĂRIOARA POENARU2), NICOLAE CONSTANTIN BALICA2), FLAVIA BADERCA3)

1)Department of Medical Semiology I, “Victor Babeș” University of Medicine and Pharmacy, Timișoara, Romania
2)Department of ENT, “Victor Babeș” University of Medicine and Pharmacy, Timișoara, Romania
3)Department of Microscopic Morphology, “Victor Babeș” University of Medicine and Pharmacy, Timișoara, Romania

Abstract
Rare naso-sinonasal lesions represent a diagnostic challenge for clinicians because of the paucity of the cases and similarities with other more frequently sinonasal pathologies. The aim of the study was to present five rare sinonasal lesions in order to emphasize their symptomatology, imaging aspects, histopathological features, algorithms of diagnosis, and strategies of treatment and importance of teamwork between clinicians, pathologists and radiologists for a correct and prompt diagnosis. Case presentations: The cases were represented by patients with nasal sarcoidosis, nasal primitive neuroectodermal tumors, sinonasal mucosal melanoma, sinonasal plasmacytomas and nasal-type extranodal natural killer (NK) T-cell lymphoma. All the patients were biopsied in the Department of ENT (Ear, Nose and Throat), “Victor Babeș” University of Medicine and Pharmacy, Timișoara, Romania, and the diagnosis was made using routine and immunohistochemical (IHC) stainings. The patients with sinonasal melanoma and the patient with extranodal NK T-cell lymphoma died in few months after diagnosis, despite treatment. Rare sinonasal lesions share similar symptomatology and imaging aspects with other, more frequently diagnosed entities. The cases reported in this paper showed the same pattern as those presented in other studies; the symptomatology, diagnosis, treatment and prognosis were the same. Clinical examination, imaging studies and routine and IHC markers guides us to the right diagnosis that should be prompt because of the prognosis of some tumors. The treatment has a few characteristics: surgery excision within safe margins, working with other specialties (oncology, radiotherapy, hematology, nephrology, pneumology), follow-up and correctly informing the patient being mandatory. Conclusions: In this paper, there were presented five interesting cases of rare sinonasal lesions, in order to highlight the importance of teamwork for a quick and correct diagnosis.

Keywords: rare nasosinusal tumors, nasal lymphoma, nasal sarcoidosis, nasal neuroectodermal tumors, sinonasal malignant melanoma, sinonasal plasmacytomas.

Introduction
A rare disease is estimated to affect from 1–2500 to 1–10 000 persons. The small number of patients, lack of adequate treatments or the severity of the disease may characterize these diseases. It implies diagnostically and treatment difficulties [1]. Due to studies absence, a rare disease may be neglected and new medical treatments or public health care programs may be expected [1, 2]. According to European Organization for Rare Diseases, 8% of the European population is affected (20–30 millions) [2].

These diseases represent a challenge for the ENT (Ear, Nose and Throat) doctors, being easily overlooked, neglected and insufficiently treated [1].

Sarcoidosis constitutes a granulomatous non-caseating disease of unknown etiology. It involves intrathoracic organs and upper respiratory tract [3–5]. It occurs mainly within the second and fourth decade. Granulomatous involvement of sinonasal mucosa and laryngopharynx is infrequent, isolated, or associated in multisystemic sarcoidosis [4]. Prognosis is relatively positive and it is not usually fatal, with the overall death rate remaining less than 5% without treatment [3, 5].

Primitive neuroectodermal tumors (PNETs) are a large family of tumors of neuroectodermal origin that belong to Ewing’s sarcoma family of tumors [6, 7]. The multi-modality treatment (surgical, chemotherapy, radiotherapy) is advocated to prevent metastatic or recurrent disease and to treat residual tumor after resection [6, 8, 9]. Patients with metastatic disease uniformly have poor outcome. The five years survival rates range from 0–25%, compared to 40–79% for those with localized disease [8, 10–12].

Sinonasal mucosal melanoma appears from the pigment-containing cells known as melanocytes. Sinonasal mucosal melanoma is a rare entity. It accounts for 1.7–3% of all melanomas and 8% of all head and neck melanomas [13, 14]. The five-year survival of sinonasal melanoma was found to be lower than 35% [14–16].

Plasmacytomas are malignant neoplasms of monoclonal B-cell proliferation, consisting of three types: multiple myeloma (MM), solitary bone plasmacytoma (SBP), and extramedullary plasmacytoma (EMP) [17, 18]. Treatment is polymodal, surgery followed by radiotherapy (40–50 Gy, 4–6 weeks) and adjuvant chemotherapy (tumor >5 cm) [17, 19]. Follow-up is at every six weeks for six months and tend to have favorable outcomes when compared to other plasma cell neoplasms. Overall survival rate at 10 years is estimated to be 70% [19].

Nasal-type extranodal natural killer (NK) T-cell lymphoma is a type of non-Hodgkin’s lymphoma. Out of all non-Hodgkin’s lymphomas, only 10% represent the NK/T-cell malignancies; nasal NK/T-cell lymphoma, also known as lethal midline granuloma, rarely manifests in the nose and paranasal sinus; it is very aggressive and carries a very poor prognosis [20]. Due to intrinsically aggressive nature of this type of lymphoma, treatment
The aim of the study was to describe five cases of rare nasosinusal lesions diagnosed and treated in the Department of ENT, Emergency City Hospital, Timișoara, Romania.

Case presentations

The authors present five patients with nasal sarcoidosis, sinonasal mucosal melanoma, sinonasal plasmacytomas nasal-type and extranodal NK T-cell lymphoma.

All the patients presented in the Department of ENT, “Victor Babeș” University of Medicine and Pharmacy from Emergency City Hospital, Timișoara, with nasosinusal lesions that were biopsied. The specimens were sent to the Service of Pathology of the same Hospital. The specimens were fixed in 4% (v/v) buffered formalin and processed with usual histological technique. Three μm sections were cut using a Leica Microtome, captured and applied on histological slides. The slides were stained with Hematoxylin and Eosin (HE), in order to obtain a diagnosis. In two cases, additional immunohistochemical (IHC) tests were done. All the antibodies used for immunohistochemistry were purchased from Novocastra. IHC tests were done. All the antibodies used for immunohistochemistry were purchased from Novocastra.

All the patients signed an informed consent to approve the participation in this study. The Ethics Committees of “Victor Babeș” University of Medicine and Pharmacy and of Emergency City Hospital, Timișoara, approved the study. For each patient, the authors obtained a Patient Informed Consent and the Consent of Ethics Committee from Emergency City Hospital, Timișoara.

Case No. 1: Nasal sarcoidosis

A 35-year-old female presented on September 27, 2014, in the Department of ENT, Emergency City Hospital, Timișoara, with mucopurulent rhinorrhea and chronic nasal obstruction. Nasal endoscopy showed hypertrophic, friable septal and middle turbinate nasal mucosa with an intense bluish color. Paraclinical exam comprised on: erythrocyte sedimentation rate (ESR) 15 mm in one hour, hemoglobin (Hb) 9.7 mg%, hematocrit (Ht) 31.1%, blood urea 15 mg%, serum creatinine 0.8 mg%, chest radiography – normal X-ray image, and anti-citrullinated peptide antibody (ACPA) test revealed a normal level of anti-cytoplasmic autoantibodies. Computed tomography (CT) scan of the paranasal sinuses showed signs of chronic sinus inflammation with mucosal thickening and opacification of both maxillary sinuses and left frontal and ethmoidal sinus.

No personal and heredo-collateral significant history it was obtained for the patient.

The biopsy revealed granulomatous reaction pattern characterized by multiple, small, non-confluent, predominantly epithelioid non-necrotizing granulomas surrounded by few lymphocytes (Figures 1 and 2). Rarely, the granulomas were centered by small area of necrosis (Figure 3). Langhans cells with many peripheral nuclei were also noted in the granulomas (Figure 4). The histopathological aspects were consistent with a granulomatous reaction. Clinically, there were no lymph nodes, skin and other organs involved. The differential between sarcoidosis and tuberculosis required additional tests. Polymerase chain reaction (PCR) test and culture for Mycobacterium were negative, excluding tuberculosis.

Despite these, high levels of angiotensin-converting enzyme (ACE) and hypercalcemia confirmed the diagnosis of sarcoidosis. She started treatment on 1 mg/body-kg/day Prednisolone.

Currently, the disease is stable, no other organ involvement being found.

Case No. 2: PNET sarcoma

A 26-year-old male patient was admitted on December 12, 2014, in the Department of ENT, Emergency City Hospital, Timișoara, with a chronic nasal obstruction, intermittent epistaxis and headache.

The patient described a history of nasal tumor that was excised in 2009, the biopsy revealing a hemangio-pericytoma. In six years, between 2009 and 2014, the patient presented seven recurrences. The patient presented no heredo-collateral important history. Blood analysis and chest X-ray revealed normal values and exams. Nasal endoscopy showed an exophytic tumor, with a reddish color, localized at the inferior turbinate in the left nasal fossa, extending through the middle meatus and reaching the left choana. CT scan with enhancement of the paranasal sinuses showed left paranasal sinuses (maxillary and anterior ethmoid) and left nasal cavity tumor involvement. No regional and distant metastases were identified. An open technique was employed in order to excise the entire tumor (medial maxillectomy via midfacial degloving approach).

Histology study revealed a well-differentiated primitive peripheral neuroectodermal tumor composed of small cells with big nuclei and small quantity of cytoplasm, positive for S100 protein and negative for CD34, the mitotic index being 20% (Figures 5–9). The patient was addressed to radiotherapy (45 Gy in four weeks) associated with chemotherapy.

Three years after surgery at nasal endoscopy and CT exam, there are no signs of loco-regional relapse (Figure 10). The sinonasal cavity was covered by crusts and granulation tissue with intermittent mucous and sanguinolent rhinorrhea.

Case No. 3: Sinonasal mucosal melanoma

A 68-year-old male patient presented on January 10, 2016, in the same Department of ENT with weight loss and chronic nasal obstruction on the left side. Nasal endoscopy revealed a 3/3 cm exophytic dark colored tumor on the left middle turbinate. Blood exams revealed: Hb 14 g/dL, Ht 49%, glycosylated Hb 7.2%, mean corpuscular volume (MCV) 95 fl, red blood cell distribution width (RDW) 11.9%, mean corpuscular hemoglobin (MCH) 0.5 fmol/cell, mean corpuscular hemoglobin concentration (MCHC) 35 g/dL, reticulocytes 1.3%, white blood cell (WBC) count 8×10^3/L, neutrophils 7×10^3/L, bands <1×10^3/L, lymphocytes 3×10^3/L, monocytes 0.6×10^3/L, eosinophils <0.5×10^3/L, platelets 350×10^3/L, prothrombin time 14 s, International Normalized Ratio (INR) 1.1, activated partial thromboplastin time (aPTT) 30 s, fibrinogen 3.8 g/L, bleeding time 8 min, glucose level 6.5 mmol/L (127 mg/dL). The patient was diagnosed with a type II diabetes mellitus in 2013, being treated with oral antidiabetic drugs (biguanides – Metformin). No heredo-collateral history was obtained for the patient.
An open technique, radical excision of the tumor was performed. Biopsy revealed foci of epithelioid malignant melanocytes in the nasal mucosa, with high pleomorphism, vesicular nuclei and big eosinophilic nucleoli. The cytoplasm contained small quantity of melanin (Figures 11 and 12). Histopathological aspects were consisted with mucosal melanoma. IHC reaction for S100 protein confirmed the diagnosis (not shown). In differential diagnosis of sinonasal mucosal melanoma were taken into consideration carcinoma, lymphoma, sarcoma and olfactory neuroblastoma. In order to identify any regional or distant metastases, there were performed a head and thorax CT scan and neck, abdominal and pelvis magnetic resonance imaging (MRI). There were no signs of regional and distant metastases.

The patient was addressed to oncology and started treatment with immunochemotherapy, but died a few months later.

Figure 1 – Epithelioid granulomas surrounded by small lymphocytes (HE staining, ×100).
Figure 2 – Granulomas composed of epithelioid macrophages surrounded by lymphocytes (HE staining, ×400).
Figure 3 – Small areas of necrosis centered few granulomas, composed of epithelioid macrophages and Langhans cells (HE staining, ×400).
Figure 4 – Granulomas composed of epithelioid cells and few Langhans cells (HE staining, ×400).
Figure 5 – Small cells with big nuclei and pulverulent chromatin (HE staining, ×400).
Figure 6 – Islands of tumor cells and extravasated erythrocytes (HE staining, ×400).
Case No. 4: Extramedullary plasmacytoma

A 64-year-old male patient was evaluated in the Department of ENT, Emergency City Hospital, Timișoara, on May 7, 2014, with unilateral nasal obstruction on the left side, headache, facial fullness and progressive hearing loss in the left ear. The symptoms lasted for two years. From the patient personal data, we noticed an ischemic cardiomyopathy diagnosed in 2009, a high blood pressure (hypertension) diagnosed in 2010 and chronic type B viral hepatitis diagnosed in 2012. Blood analysis revealed:
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Hb 11 g/dL, Ht 39%, MCV 87 fL, reticulocytes 1.1%, WBC 7×10^9/L, neutrophils 6×10^9/L, bands <1×10^9/L, lymphocytes 3×10^9/L, monocytes 0.7×10^9/L, eosinophils <0.5×10^9/L, platelets 370×10^9/L, prothrombin time 17 s, INR 1.3, aPTT 40 s, fibrinogen 4.5 g/L, bleeding time 9 min, glucose level 5.5 mmol/L (101 mg/dL), glutamate-oxaloacetate transaminase (GOT) 68 U/L, glutamate-pyruvate transaminase (GPT) 71 U/L, surface antigen of hepatitis B virus (HBsAg) >12 mIU, hepatitis B “e” antigen (HBeAg) 15 000 IU/mL. The patient is under Lamivudine treatment. The patient presented no heredo-collateral important history.

Nasal endoscopy revealed a rhino-pharyngeal tumor with a sessile aspect with peritubar extension and covered by sero-mucous secretions. Effusion of the left middle ear appeared on otoscopy. At audiogram, a moderate mixed hearing loss appeared on the left ear. The tympanogram was type B on the same ear. The MRI exam revealed a tumor with a 19 mm transverse diameter, 22 mm cranio-caudal and 23 mm anteroposterior dimensions, localized in the left part of the rhinopharynx, homogeneous, well delimited, with medial captation, reaching the inferior turbinate.

The tumor was partially excised endoscopically. Histological and IHC exams (tumor and bone marrow biopsy) revealed an extramedullary plasmacytoma. Other tests performed were X-rays, MRIs and CT scans.

The differential diagnostic evaluation was difficult due to extramedullary plasmacytoma histological appearance similarity to other tumors (lymphoma, undifferentiated carcinoma, esthesioneuroblastomas).

The patient was addressed to radiotherapy (40 Gy in four weeks). The patient is free of disease at three years from diagnosis.

Case No. 5: Nasal-type extranodal NK T-cell lymphoma

A 47-year-old female was admitted in the same Department of ENT on August 22, 2015, with the following symptoms: intermittent epistaxis, nasal obstruction, faulty smell, headache. The symptoms and signs appeared seven months prior to hospital admission. Inspection revealed cellulitis in the periorbital region bilateral and on the dorsum nasi, palpebral edema and chemosis, frontal sinus fullness and poor general status. The patient presented no personal and heredo-collateral important history.

Nasal endoscopy was performed revealing ulceration of nasal septum (both cartilaginous and osseous part), partial destruction of the lateral walls of the nasal cavities, crusts in the nasopharynx and nasal cavities. The patient underwent a head CT scan with enhancement revealing a nasal tumor involving both nasal fossa, with septal (cartilaginous and osseous) destruction, paransal sinuses involvement (both maxillary, both anterior ethmoid and left frontal sinuses), and bilateral orbital invasion predominantly on the left side. An MRI was indicated, but no intracranial extension was identified. There were no regional or distant metastases. The biopsy was performed from septum, lateral nasal wall mucosa and lateral nasopharyngeal wall. The morpho logical and IHC aspects of nasal tumor indicated a NK T-cell non-Hodgkin’s lymphoma (Figures 13 and 14). There were made differential diagnosis with other lymphomas, such as: angio-immunoblastic T-cell lymphoma, systemic anaplastic large cell lymphoma, T-cell rich diffuse large B-cell lymphoma, nodular lymphocyte predominance Hodgkin’s lymphoma and classical Hodgkin’s lymphoma.

The patient was addressed to oncohematology for treatment [BEACOPP chemotherapy – Bleomycin, Etoposide, Adriamycin (Doxorubicin), Cyclophosphamide, Oncovin (Vincristine), Procarbazine, Prednisone – and radiotherapy]. The patient died within a month.

Figure 13 – Islands of atypical lymphocytes with big nuclei with fine granular chromatin and small amounts of cytoplasm (HE staining, ×400).

Figure 14 – Islands of tumor cells with little cytoplasm and fine granular chromatin (HE staining, ×400).

Discussion

Sarcoidosis is estimated to affect the nose in 1–4% of patients with both rhinitis and chronic obstruction [3–5]. Symptomatology is represented by fever, anorexia, dyspnea, chough, xerostomia and local symptoms like rhinorrhea, nasal obstruction and hyposmia [4, 5]. On clinical examination, it may appear cervical polyadenopathy and violaceous rash on the cheeks or nose, cranial nerve palsies and hyperplasia of the parotid gland [3–5].

Chest radiography or CT may identify enlarged hilar lymph nodes; blood exams revealed: ACE, serum amyloid A, KL-6 glycoprotein, hypercalcemia or hypercalciuria [5].
Treatment is debated, it may be employed endoscopic sinus surgery in combination with local intranasal or systemic corticosteroids, Methotrexate (MTX) being a successful alternative to prednisone, while Azathioprine is a second-line therapy [3–5].

PNETs are rare tumors representing only 1% of the total sarcomas [7, 8]. The most common location in the head and neck region is the orbit followed by the neck and the parotid gland [6–8].

Structures involved are the orbit, the parotid gland, the mandible and the pharynx. The implication of maxillary and ethmoid sinus remains exceptional. Because of the aggressive nature and poor prognosis, meticulous surgical and medical treatment is needed [7–10].

The diagnostic is based on clinical, such as fever, fatigue, weight loss, nasal obstruction, epistaxis, purulent rhinorrhea, hyposmia, exophthalmos, neck masses, tumor in the sinonasal cavities, nose and facial swelling, pathologically bone fractures, IHC studies (gold standard), and laboratory tests as elevated C-reactive protein (CRP) and ESR, anemia, cytophagic studies translocation that involves the Ewing sarcoma (EWS) gene (22q12) and Friend leukemia integration-1 (FLI-1) (11q24) [6–12]. CT scan, MRI and bone marrow biopsy are essential in determining the limits of tumor involvement and ruling out metastatic disease (excluding metastatic disease) [6–9].

Sinonasal mucosal melanoma occurs mainly between the fourth and seventh decades [13–15].

These tumors show high local recurrence rate and the majority of recurrences are reported to be observed within one to two years after treatment [13, 16].

Symptomatology is represented by epistaxis, weight loss, faulty smell, nasal/facial deformity, enlarged cervical lymph nodes, dark exophytic hyperplastic growing mass [13–17].

CT/MRI are indicated in order to exclude any metastasis. Biopsies represent the gold standard by identification of intracellular melanin and IHC markers, such as S100 protein, human melanoma black-45 (HMB-45) and Melan-A [14–17].

Treatment includes surgical resection or any other open technique followed by immunochemotherapy [13–17].

In plasmacytomas, the incidence is 0.04 to three cases per 100 000; and it appears in 1% of all head and neck tumors, being four times more common in men and tends to affect the elderly [18].

The diagnostic is based on clinical symptoms like nasal obstruction, epistaxis, purulent rhinorrhea, sore throat, hoarseness, dysphonia, dysphagia, bone destruction with saddle nose, facial swelling, cervical lymph nodes and histological examination of tumor biopsy revealing a mononuclear plasma cell histology and on bone marrow biopsy less than 5% plasma cells without evidence of clonality [18, 19, 22].

It benefits from a poly-modal treatment limited surgery and radiotherapy [19, 22].

Extranodal NK T-cell lymphoma, nasal-type, accounts for 1% of non-Hodgkin’s lymphomas in Europe and North America [20].

Symptomatology is represented by rhinorrhea, nasal obstruction, epistaxis, skin lesions, weight loss and a poor general status [20, 21]. On clinical examination, it may be encountered facial and nasal deformity, cervical lymphadenopathy and destruction of nasal structures [21].

CT may reveal a hypervascular tumor and the immunohistochemistry shows T-lymphocytes positive for CD3 and CD56 [20, 21].

Although the etiology of the lymphoma is unknown, findings of the Epstein–Barr virus are almost constant using Epstein–Barr-encoded small RNAs [21].

Treatment is based on radiotherapy for localized disease, being usually combined with chemotherapy [20, 21].

Conclusions

The positive diagnosis is established on biopsy, using morphological and IHC studies. Nasal non-Hodgkin’s lymphoma with T-cells, nasosinusal Ewing’s sarcoma, nasosinusal melanoma and nasosinusal plasmacytoma are tumors rarely found in the sinonasal cavity. These case reports have the same pattern as those from other studies regarding the symptomatology, diagnosis, treatment and prognosis. Clinical examination, biopsy, immunohistochemistry, tumor markers, antibodies, imaging studies [CT, MRI, positron emission tomography (PET)-CT] allowed an accurate diagnosis.

Conflict of interests

The authors declare that they have no conflict of interests.

Acknowledgments

This work was supported by the Department of ENT, “Vitor Babeș” University of Medicine and Pharmacy, Timișoara, Romania.

References


Corresponding author
Nicolae Constantin Balica, Assistant Professor, MD, PhD, Department of ENT, “Victor Babeș” University of Medicine and Pharmacy, 6 Revoluţiei 1989 Avenue, 300024 Timișoara, Romania; Phone +40726–427 163, e-mail: balica@umft.ro

Received: March 10, 2017
Accepted: February 24, 2018