Germinal Center- Like Diffuse Large B cell Lymphoma of the Frontal Sinus Misdiagnosed as a Pott’s Puffy Tumor

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Abstract

Non-Hodgkin’s Lymphoma (NHL) of the frontal sinus is very rare and early diagnosis is usually made with some delay because of the non-specificity of the clinical presentation and overlapping with other diseases. We report herein the story of a 40-year-old man who presented to the outpatient clinic with pain and swelling of the forehead. The first diagnosis was a sub-acute rhinosinusitis mimicking a Pott’s puffy tumor. On the CT scan, there was a partial opacity of the left frontal sinus with osteomyelitis of the anterior and posterior tables of the frontal sinuses. He received broad-spectrum antibiotics and systemic glucocorticosteroids. He responded well to the treatment but the symptoms and signs relapsed at the completion of the treatment.

A second CT scan was performed but no significant improvement was found compared with the first CT scan. As there was no pus coming from the middle meatus we decided to take specimen for bacteriological and histopathological examination during a therapeutic window. This was done via a supraciliary incision and frontal trephine. The final diagnosis was a diffuse large B cell lymphoma, germinal center B cell subtype. He underwent 6 cycles of chemoimmunotherapy with R-CHOP and central nervous system prophylaxis via intrathecal methotrexate. 2 years after the initiation of the treatment the patient is still free of symptom and disease confirmed by serial PET scans.

Keywords: B Cell Lymphoma; DLBCL; Frontal Sinus; GCB; NHLS; Pott’s Puffy Tumor; Swelling of the Forehead

Introduction

Malignancies of the paranasal sinuses are commonly of epithelial origin. The most frequent are squamous cell carcinoma, adenocarcinoma and adenoid cystic carcinoma [1]. Malignant lymphomas are the most common non-epithelial head and neck malignancies. They are divided into Hodgkin’s disease and Non-Hodgkin’s Lymphomas (NHLs). The majority of NHLs are of B-cell subtypes in European countries and North America [2-4]. Primary Paranasal Sinus Lymphomas (PPSL) are rare. The most common type of lymphoma is the diffuse large B cell lymphoma followed by follicular lymphoma, Peripheral T Cell Lymphoma (PTCL), T/NK nasal type, Burkitt lymphoma and others [4-12]. The median age at presentation is the sixth decade. (Range: 27-97 years).

The maxillary sinus is by far the most commonly involved, followed by the ethmoid sinus and the nasal cavity [4-12]. The clinical presentation of PPSL is nonspecific at the early stage and can be misconfused with other “benign” diseases leading to a protracted time between the onset of the disease, its dignosis and the initiation of the treatment [9-11]. We report herein a unique case of a Diffuse Large B-Cell lymphoma, germinal center B cell subtype, of the frontal sinus misdiagnosed with a Pott’s puffy tumor. We report the medical history, the imaging, the modality of treatment and review the pertinent literature.
Clinical Case

A 40-year-old man presented to the outpatient clinic with 4 weeks history of pain and forehead swelling, which was smooth with no tenderness. The medical history was unremarkable except a story of previous “rhinosinusitis”. There was no sign of fever, nocturnal sweating or body weight loss. On examination, he had a 2 cm non-tender soft tissue swelling on the median side of his forehead (Figure 1a and 1b). The sensitivity in the frontal region was preserved. There was no lymphadenopathy. Anterior rhinoscopy and nasal fiberoscopy were normal with no purulent discharge coming from the middle meatus. Initial Computed Tomography (CT) scan of the paranasal sinuses revealed a central opacity of the left frontal sinus with a subcutaneous soft tissue swelling and lytic bone changes compatible with osteomyelitis in the anterior and posterior tables of the frontal bone.

Figure 1: visualization of the swelling of the forehead without any inflammatory sign.

The other paranasal sinus cavities were free of disease (Figure 2a-d). A presumptive diagnosis of Pott’s puffy tumor was made. Broad-spectrum antibiotics and systemic steroids were administered. The patient responded well to this therapy but the swelling relapsed at the completion of the medical treatment. A second CT scan was then performed. It confirmed the recurrence of the swelling. However, there were no significant changes compared with the first CT scan. Therefore, we decided to do a therapeutic window and to take specimens for histopathological and bacteriological evaluation. This was done under general anesthesia via a supraciliary incision. We associated the biopsies with a trephine of the frontal sinuses. On gross examination, the subcutaneous tissue was edematous and hyperplastic. There were some bony defects in the anterior table of the frontal bone but no pus was found. The culture did not yield any pathogen.

Figure 2: Computed tomography showing on cut A & C a swelling of the forehead and in front of the nasal bones. Cut B shows area of osteomyelitis in the anterior and posterior walls of the frontal sinus. Cut D shows a partial opacity of the left frontal sinus.

The pathologist used immunohistochemistry staining to make the diagnosis. This one was a diffuse Large B-cell Lymphoma, germinal center B cell like subtype, (GCB) DLBCL (Figure 3a and 3b). The patient was referred to the hematologists for staging and chemotherapy. Whole body Positron Emission Tomography (PET) scan showed a hypermetabolic lesion involving the frontal sinus but no significant lymphadenopathy. Bone marrow aspiration was negative for malignant infiltrate. The disease was classified as stage 1E according to the Ann Arbor Staging system. The patient underwent 6 cycles of chemotherapy with Rituimab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP), and central nervous system prophylaxis via intrathecal methotrexate. He did not receive radiotherapy. 24 months after completion of therapy, he is still free of disease based on serial positron emission tomography and computed tomography scanning.
Figure 3A: Diffuse large B-cell lymphoma. The tumor exhibited a diffuse and polymorphic proliferation of large lymphoid cells with vesicular and irregular nuclei containing central or membrane-bound nucleoli. There are numerous apoptotic bodies. Hematoxylin and eosin stain: X10 & X 40.

Figure 3B: Immunohistochemistry: B. Immunohistochemistry demonstrated positivity of the tumor cells for CD20, CD10 and Bcl6. The Ki-67 proliferation index was high.
Discussion

This case illustrates perfectly well the difficulty to make the correct diagnosis in case of a swelling of the forehead. This is explained by the fact that the clinical presentation overlaps with many other diseases such as hematoma or abscess of the forehead, Pott’s puffy tumor, frontal mucocele, osteoma, fibrous dysplasia, primary sinus malignancies or metastasis to the frontal sinus (from primary sites: kidney, prostate, lung, breast...). Clinical examination particularly the tumor consistency can give some information to orientate the diagnosis but this is highly subjective. Therefore, imaging remains the additional investigation to make the differential diagnosis. In the present case, 2 diagnoses were specifically considered: a Pott’s puffy tumor and an expanding process of the frontal sinus.

Pott’s Puffy Tumor (PPT) is a rare but serious clinical entity seen as a complication of an acute or subacute frontal sinusitis [13-17]. It is described as a subperiosteal or subgaleal abscess in the frontal bone secondary to frontal osteomyelitis. The swelling concerns the forehead or the scalp. It is usually well circumscribed, overlying the area of frontal osteomyelitis. Fever, headache, frontal sinus tenderness, nasal discharge and in some cases nausea, vomiting and photophobia can be present. PPT can be complicated by preseptal and orbital cellulitis and intracranial infection (with venous thrombosis, epidural abscess, subdural empyema, and brain abscess). PPT is mostly found in adolescents but may occur in adults [15, 16]. PPT must be treated promptly with broad-spectrum antibiotics for 4 to 6 weeks. Surgical intervention is necessary for removal of osteomyelitic bone.

In the present case, the first diagnosis of PPT was wrong. Even if the patient responded well to antibiotics and mostly to the systemic steroids the swelling of the forehead relapsed at the completion of the treatment. Therefore, a revision of the diagnosis was required and led to the definitive diagnosis of a diffuse large B cell lymphoma germinal center like subtype, of the frontal sinus. Non-Hodgkin’s Lymphomas (NHL) involving the paranasal sinuses are rare. Primary involvement of the frontal sinus is exceptional with less than 20 cases published in the worldwide literature. This represents only 0.17%-1.63% of all lymphomas [18, 19]. Table 1 summarizes some case reports published in the worldwide literature. There are also some cases included in case series [3, 9-11]. This disease affects mostly the middle aged and the elderly (40-80 yrs) patient with a slight male predominance. Our patient was a 40-year-old man. However, one case has been reported in the pediatric population [20].

| Author | year | Patient/Age | Signs | Treatment | Follow-up |
|--------|------|-------------|-------|-----------|-----------|
| [20]   | 2019 | M/11        | Orbital / sinus ant cranial fossa | DLBC Frontal sinus Cranialisation Orbital and skull bas Reconstruction CTx | Free of disease at 12 months |
| [21]   | 1984 | F/43        | Frontal headache/persistent nasal drainage/ Frontal sinus & Intracranial extension | DLBCL Frontal sinus obliteration CTx (CHOP) | Free of disease at 20 months |
| [22]   | 2000 | M/58        | T diagnosis: acute rhinosinusitis with orbital cellulitis/medica treat FES/ relapse:biops1sMedial canthus edema & erythema, frontal headaches, rhinorrhea, PND, epistaxis, nasal obstruction, hyposmia | B CELL NHL (high grade) I E CTx (CHOP) CNS prophylaxis Sinus surgery | Free of disease at 3 months |
| [23]   | 2004 | M/83        | Pain, nasal discharge, headache, nasal bleeding | III E DLBCL CTx (CHOP) RTx | NA |
| [4]    | 2005 | M/43        | Frontal headache, frontal bulding involving the upper eyelid/pain/orbit | DLBCL High grade Steroids RXT | Death at 1 month |
| [24]   | 2005 | M/84        | Orbital invasion | DLBC Steroids RXt | Death at 9 months |
| [25]   | 2007 | M/55        | Osteomyelitis frontal sinus | II E External frontotomy / chionio/radiot/CNS prophylaxis | Free of disease at 18 months |
| [26]   | 2015 | M/69        | History of sinusitis/2 previous endoscopic surgeries | DLBC/Pott’s puffy Craniotomy/ CHimiot/RXT | Free of disease at3 years |
| [27]   | 2011 | M/42        | Frontal sinus and cranial nerve palsy | IV E R-CHOP CNS prophylaxis RXT | Free of disease at 50 months |
Symptoms and signs are vague and non-specific particularly at the early stage of the disease. Actually, the patient may report nasal obstruction, nosebleeds, rhinorrhea, post nasal dripping, frontal pressure, headache, fever, weight loss and nocturnal sweating. In later stage he may present with a swelling of the forehead, exophthalmos, diplopia, meningitis, neuralgia and cranial nerve palsies [18-26]. Moreover, it is not so rare that the patient reports a story of “rhinosinusitis”. In our case the initial diagnosis was a Pott’s puffy tumour. This error has also been published by el Hakim, Nemet, Chain, Khan and Wong [22, 24, 25, 26, 28]. This rhinosinusitis usually responds well to the medical treatment particularly to systemic steroids leaving the clinician with a false sense of security and delaying diagnosis and treatment. The patient could even have undergone FESS before the definitive diagnosis was made [8].

In 2012, Yen et al published a series of 32 patients who presented with a paranasalsinus lymphoma. In 20 patients (62.5%), the first impression was benign or malignant nasal neoplasm, but in the other 12 patients (37.5%) the first diagnosis was a rhinitis or rhinosinusitis [29]. Imaging of the paranasal sinuses is mandatory to assess a sinus disease. In case of lymphoma of the frontal sinus a variety of images can be found: partial or complete opacity of the frontal sinuses, signs of osteomyelitis of the anterior and posterior walls of the frontal sinus with osteolytic bone, and in later stages orbital or intracranial extension. The definitive diagnosis is based on histology. Large specimens are required and must be taken as soon as possible. In our case the final diagnosis was A Diffuse Large B Cell Lymphoma (DLBCL), germinal center like B cell subtype. DLBCL is the most common type of NHLs in Western countries. It represents a heterogeneous group of diseases [30-32].

There are different classifications. WHO classifications are certainly the references; There are different editions published in 2001, 2008 and 2016. However, these classifications are very large and complex. In 2016, a classification was published on the basis of GEP (gene expression profiles) studies [32]. These studies propose a molecular classification of DLBCL. Actually they are 3 main subtypes of DLBC; Germinat Center B Cell (GCB), Activated B Cell (ABC) and Primary Mediastinal B-Cell Lymphoma (PMBLCL). These subtypes arise from different stages of B-cell differentiation. They are associated with distinct genetic abnormalities and different oncologic outcomes. GCB-DLBC has a better response to Chemoimmunotherapy (CI) compared to patients with ABC-DLBC. Because GEP studies need substantial time, technological expertise and resources, pathologists prefer to use IHC (immunohistochemistry) staining method performed on Tissue Microarrays (TMAs).

Several algorithms and methods have been published by (Hans[32], Muris[33], Choi[34] and Tally to categorize DLCL cases as GCB like or non-GCB- like DLBCL Hans’ algorithm utilizing staining for CD20, CD10, Bcl-6 and Mum1 was used for this clinical case [32-34]. Leading to the definitive diagnosis of a germinal center B cell lymphoma also called as GCB-like B-cell lymphoma. The prognostic depends on the histological subtype of lymphoma but also of the staging [35-37]; According to the Ann Arbor classification, our patient was on stageIIE as the tumor was localized in the frontal sinuses without any lymphadenopathy or intracerebral extension. NHL scan be managed by Chemotherapy (CHOP), immunotherapy, radiation therapy, and surgery in various combinations. Lymphomas are chemosensitive and radiosensitive pathologies. Adjunction of rituximab has dramatically improved the response to the chemotherapy [38, 39]. Because the lymphomas involving the paranasal sinus have a high propensity for CNS dissemination our patient received R-CHOP associated to injection of intrathecal methotrexate [40].

Surgery has limited indications. The role of surgery is primarily diagnostic [3]. The goal is to obtain specimen for histological evaluation. In our case it consists of performing biopsies only. In the literature extensive surgery has been done such as maxillectomy or cranialisation of the frontal sinus because the diagnosis was done at later stage.

Survival of paranasal non-Hodgkin lymphoma is not so poor if diagnosed early in the course of the disease. The 5- and
The patient agrees for the publication of his clinical story.

Inform Consent

The patient agrees for the publication of his clinical story.

Conclusion

Sinonasal NHLs of the paranasal sinuses are rare. Frontal localization is exceptional. Because of this rarity and the nonspecificity of the symptoms and signs at the early stages of the disease, the diagnosis may take some time and can be misconfused with other diseases such as Pott’s puffy tumour. Histological evaluation is necessary. Chemoimmunotherapy (R-CHOP) is the treatment of choice associated to CNS prophylaxis with methotrexate. Large surgery may be necessary in very advanced cases.

References

1. Danesh-Sani SA, Sarafraz A, Chamani M, Derakhshandeh H (2016) Paranasal sinuses malignancies: A 12-year review of clinical characteristics. Med Oral Patol Oral Cir Bucal 21: e626-e630.
2. Amlot P (2002) Malignant Lymphomas. Br J Cancer 87: 372.
3. Duncavage JA, Campbell BH, Hanson GA, Kun LE, Hansen RM, et al. (1983) Diagnosis of malignant lymphomas of the nasal cavity, paranasal sinuses and nasopharynx. Laryngoscope 93: 1276-1280.
4. Neves MC, Lessa MM, Voegels RL, Butugan O (2005) Primary non-Hodgkin’s lymphoma of the frontal sinus: case report and review of the literature. Ear Nose throat j 84: 47-51.
5. Laskin JJ, Savage KJ, Voss N, Gascoyne RD, Connors JM (2005) Primary paranasal sinus lymphoma: natural history and improved outcome with central nervous system chemoprophylaxis. Leuk Lymphoma 46: 1721-1727.
6. Varillas AN, Eggerstedt M, Ganti A, Tajudeen BA (2019) Epidemiologic, prognostic, and treatment factors in sinonasal diffuse large B-cell lymphoma; Laryngoscope 129: 1259-1264.
7. NegarAzarpia, Mohammad J Ashraf, Ahmad Monabati, AlirezaMakarempour, BijanKhademi, et al. (2012) Primary Lymphoma of Nasal Cavity and Paranasal Sinuses, Laboratory Medicine 43: 294-299.
8. Su ZY, Zhang DS, Zhu MQ, Shi YX, Jiang WQ (2007) Primary non-Hodgkin’s lymphoma of the paranasal sinuses: a report of 14 cases. Acta Otolaryngol 126: 919-922.
9. Quraishi MS, Bessell EM, Clark D, Jones NS, Bradley PJ (2000) Non-Hodgkin’s lymphoma of the sinonasal tract. Laryngoscope 110: 1489-1492.
10. Peng KA, Kita AE, Suh JD, Bhuta SM, Wang MB (2014) Sinonasal lymphoma: case series and review of the literature. Int Forum Allergy Rhinol 4: 670-674.
11. Steele TO, Buniel MC, Mace JC, El Rassi E, Smith T (2016) Lymphoma of the nasal cavity and paranasal sinuses: A case series. Am J Rhinol Allergy 30: 335-339.
12. Shirazi N, Bist SS, Puri N, Harsh M, Ahmad S (2018) Primary sinonasal lymphoma in immunocompetent patients: A 10 years retrospective clinicopathological study. J Oral Maxillofac Pathol 22: 280-281.
13. Parida PK, Surianarayanan G, Ganesan S, Saxena SK (2012) Pott’s puffy tumor in pediatric age group: a retrospective study. Int J PediatrOtorhinolaryngol 76: 1274-1277.
14. Vanderveken OM, De Smet K, Dogan-Duyar S, Desimpelaere J, Duval ELI, et al. (2012) Pott’s puffy tumour in a 5-year old boy: the role of ultrasound and contrast-enhanced CT imaging; surgical case report. B-ENT 8: 127-129.
15. Ketenci I, Unli Y, Tucer B, Vural A (2011) The Pott’s puffy tumor: a dangerous sign for intracranial complications. Eur Arch Otorhinolaryngol 268: 1755-1763.
16. Collet S, Grulois V, Eloy P, Rombaux P, Bertrand B (2009) A Pott’s puffy tumour as a late complication of a frontal sinus reconstruction: case report and literature review. Rhinology 47: 470-475.
17. Şimşek H (2019) Patient presenting with frontal subperiosteal abscess and headache: a case of Pott’s puffy tumour. Br J Neurosurg 33: 275-277.
18. Nagafuji H, Yokoi H, Ohara A, Fujiwara M, Takayama N, et al. (2018) Primary diffuse large B-cell lymphoma of the frontal sinus: A case report and literature review. Radiol Case Rep 13: 635-639.
19. Wilder WH, Harner SG, Banks PM (1983) Lymphoma of the Nose and Paranasal Sinuses. Arch Otolaryngol 110: 310-312.
20. Knudson SA, Day KM, Harshbarger RJ (2019) Pediatric Diffuse Large B-Cell Lymphoma of the Frontal Sinus: A Case Report. CleftPalate Craniofac J 56: 1089-1095.
21. Burres SA, Crissman JD, McKenna J, Al-Sarraf M (1984) Lymphoma of the Frontal Sinus: Case Report and Review of Literature. Arch Otolaryngol 110: 270-273.
22. el-Hakim H, Ahsan F, Wills LC (2000) Primary non-Hodgkin’s lymphoma of the sinonasal tract. Oral Surg Oral Med Pathol Oral Radiol Endod 79: 738, 741-743.
23. Ajmal Masood, Ioannis Mouroumidis, Jaan Panesar (2007) Orbital eyelid/ acute rhinosinusitis/medical treatment than relapse biopsy external approach. Postgrad Med J 83: 402-408.
24. Shohat I, Berkowicz M, Dori S, Horowitz Z, Wolf M, et al. (2004) Primary non-Hodgkin’s lymphoma of the sinonasal tract. Oral Surg Oral Med Pathol Oral Radiol Endod 97: 328-331.
25. Nemet AY, Deckel Y, Kourt G (2006) Orbital invasion of frontal sinus lymphoma. Orbit 25: 149-151.
26. Chain JR and Kingdom TT (2007) Non-Hodgkin’s lymphoma of the frontal sinus presenting as osteomyelitis. Am J Otolaryngol 28: 42-45.
27. Khan NR, Lakicivic G, Callihan TR, Burrells G, Arnautovic K (2015) Diffuse large b-cell lymphoma of the frontal sinus presenting as a pott puffy tumour: case report. J NeurolSurg Rep 76: e23-e27.
28. Kim K, Kim MJ, Ahn S, Bae SY, Kim WS, et al. (2011) Frontal sinus lymphoma presenting as progressive multiple cranial nerve palsy. Yonsei Med J 52: 1044-1047.
