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Brief Communication

# An attempt to define the type of biopsy in a sinonasal lesion showing bony erosion

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**Abstract**

*Objectives* To present a case of sino-nasal destructive mass initially diagnosed as an inflammatory lesion following punch biopsy from the lesion however the post surgical histopathology was diagnostic of Grade 2 angiocentric immunoproliferative lesion (AIL). The reasons for the initial misdiagnosis are analyzed.

*Materials and methods* A 76-year-old male patient presenting with progressive bilateral nasal obstruction for 1 year. Repeated punch biopsies from the mass were suggestive of an inflammatory lesion.

*Result* The patient underwent surgical exenteration of the mass and the final histopathology report suggested AIL Grade 2. The patient was thereafter treated with chemotherapy and radiotherapy.

*Conclusion* Initial superficial punch biopsies lead to incorrect diagnosis leading to an unnecessary surgical exenteration. The explanations for the initial misdiagnosis are given below and appropriate diagnostic protocols, mode and depth of biopsy are suggested based on the case study.

**Keywords** Angiocentric immunoproliferative lesion · Incisional biopsy · Angiocentricity

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## Introduction

The nasal mucosa is affected by a variety of tumor and tumor like lesions. The most enigmatic are the hemato-lymphoid tumors. This is due to a variety of inflammatory cell infiltrates that appear in both neoplastic as well as non-neoplastic conditions. Radiologic investigations and initial superficial biopsies are known to have their limitations.

Angiocentric immunoproliferative lesions (AIL) are a group of extranodal lymphoproliferative disorders that share histological, immunophenotypic and clinical features. They are graded into three grades according to their cellular morphology and atypia. AIL, Grade 3 or angiocentric lymphoma is the end point in this sequence of grading [1]. We describe one such case of AIL Grade 2 and discuss the need to evaluate polymorphous cell infiltrate in superficial nasal mucosal biopsies. The definitive diagnosis was made by histopathological examination following surgical exenteration. The report is presented along with recommendations for appropriate biopsy modality and depth so that unnecessary surgeries can be avoided.

## Case report

A 76-year-old man presented with progressive bilateral nasal obstruction for 1 year, starting from the right side and then progressing to involve the left side also. He also had recurrent episodes of severe frontal headache and persistent watering from his right eye during this period. There was no history of bleeding from nose or pain.

On examination there was a firm mass in the right nasal cavity covered by foul smelling slough and discharge. The mass was not sensitive to touch and the probe could be insinuated all around the mass. There was broadening of the right naso-facial groove and pitting edema of the right lower eyelid along with proptosis of the right eyeball. There were palpable bilateral multiple discrete, non-tender, mobile level I lymph nodes, each <1cm in maximum diameter.

A 3 mm punch biopsy was taken from the nasal mass using endoscopic optical biopsy forceps, after a short course of oral antimicrobial agents. The biopsy report was suggestive of an inflammatory lesion. The CT scan images Fig. 1 showed a soft tissue mass involving the right nasal cavity extending into the nasopharynx, ethmoidal and sphenoidal sinuses ipsilaterally. The medial wall of the orbit appeared to be eroded and the mass extended into the orbit causing proptosis. The nasal septum was pushed to the contralateral side. The mass also had pushed the lateral wall of the nose laterally. Since the mass appeared neoplastic and possibly not inflammatory on CT scan the punch biopsy was repeated. The microscopy revealed a lesion lined by stratified squamous epithelium and small foci of pseudostratified columnar epithelium. The stroma was extensively infiltrated by neutrophils and lymphocytes along with a few macrophages. Foci of lymphoid aggregates, poorly formed clusters of epitheloid cells and necrosis were present. No specific evidence of malignancy could be determined in the given specimen. Thus only a diagnosis of acute on chronic inflammatory lesion could be rendered.

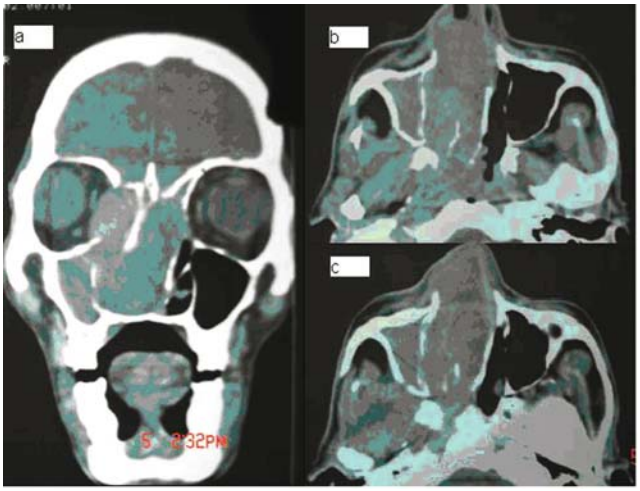


**Fig. 1a** CT Scan of the patient showing tumor mass occupying the right nasal cavity eroding the medial orbital wall, the lateral nasal wall and the nasal septum **(b and c).** Axial CT scan of the patient showing the tomor mass occupying the whole of the right nasal cavity extending into the nasopharynx

The patient was prepared for surgery and a lateral rhinotomy was done under general anesthesia. The mass was thereafter removed by blunt dissection. The mass was friable and partially necrotic especially the extensions into the ethmoidal sinuses and at its central area. The lamina papyraecea was eroded but the orbital periosteum appeared uninvolved. The nasal bones and the lateral margins of the pyriform aperture were eroded, demineralised and replaced by thick fibrotic tissue. The tumor extensions were carefully curetted out and sent for histopathological examination.

Grossly the specimen consisted of irregular fragments of tissue. The largest measuring 6.5 ×3 × 3 cm, while the smallest was 1cm across. Some were polypoidal in appearance. Cut surface showed a homogenous pale appearance with focal gelatinous areas. Microscopy revealed a lesion lined on one surface by pseudostratified epithelium and a few foci of squamous cells. The immediate underlying stroma showed extensive geographical necrosis with a polymorphous infiltrate of both acute and chronic inflammatory cells along with granulation tissue Fig. 2 i.e. the surface had the same appearance as the previous smaller biopsy. However the deeper areas of the stroma showed a lymphoplasmacytic infiltrate along with many large histiocyte like cells with moderate cytoplasm and oval vesicular nuclei. Some of these cells had a clearing around them and some had hyperchromatic nuclei. No significant mitoses were seen. The stains for microbes like PAS, Ziehl-Neilsen and Gram were negative. Reticulin stain (which stains the elastin of the vessel walls) showed disruption of vessel walls. In Grade 1, mostly mature lymphocytes are seen with sparse plasma cells or lymphoblasts. In Grade 2 polymorphous infiltrate with a few or rare atypical lymphocytes are seen. In Grade 3 there is an infiltrate of atypical cells with a cavitary lesion by the inifiltrating cells. Thus the findings described above matched with Grade 2 and the diagnosis of

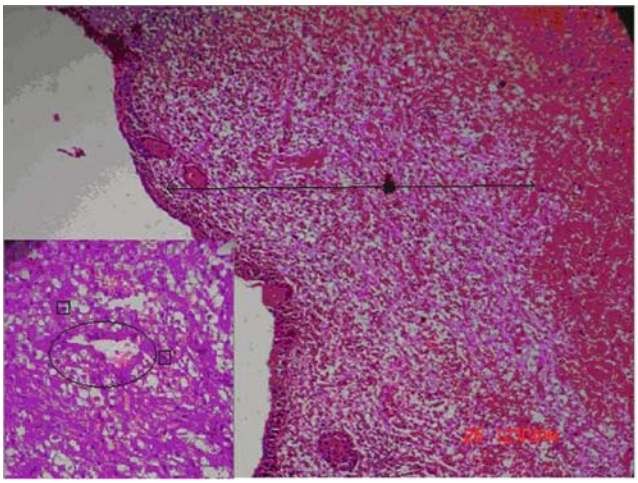

**Fig. 2** The stroma adjacent to the surface epithelium showing the mixed inflammatory infiltrate (Hematoxylin and eosin 5 × 10) **Inset:** Destruction of vessel wall encircled dotted line; dysplastic lymphocytic infiltrate open boxes (Hematoxylin and eosin 40 × 10)

a sinonasal angiocentric lymphoproliferative disorder was rendered [2].

Postoperative recovery was uneventful. The patient was sent for medical and radiation oncological consultation.

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## Discussion

This patient had a localized sinonasal destructive lesion histologically classified as AIL Grade 2 AIL are moderately aggressive (intermediate grade) lymphomatous lesions. They are a heterogeneous spectrum of hematolymphoid malignancies that share a particular histological characteristic, namely, an angiocentric or perivascular growth pattern. They include a variety of T-cell lymphomas, B-cell lymphomas, and natural killer-cell derived lymphomas (NK/T-cell lymphomas).

In this lesion the inflammatory out pouring of both the acute and chronic inflammatory cells was the cause of initial misdiagnosis as an inflammatory lesion. The damage to the vessel wall could not be ascertained due to the small and superficial biopsy sample, which only showed the inflammatory response and not the neoplastic process. To determine the depth at which this neoplastic lesion was evident a measurement was done using Vernier scale in the histological slide taken after exenteration. This was seen to range between 4 to 8 mm from the epithelial or ulcerated surface.

The issues discussed are (i) The failure to locate the putative cells in superficial biopsies, (ii) the problems related to grading angioimmunoblastic lymphoproliferative diseases and (iii) the criteria by which the diagnosis can be arrived at based on the hematoxylin and eosin sections. The angioimmunoblastic lymphoproliferative disease has an exuberant inflammatory reaction consisting of an intense infiltrate of a mixed population of both acute and chronic inflammatory cells probably related to the Epstein Barr virus infection with which it is invariably associated [3]. The fact that early lesions are misdiagnosed as benign process due to this mixed population of inflammatory cells has been documented [4].

The two most important diagnostic criteria used in histology are angiocentricity and atypical lymphocytes. The criteria for angiocentricity needed to be defined precisely. The angiocentricity is defined as presence of tumor cells around and within vascular spaces with infiltration and destruction of vessel wall. Perivascular localization is not sufficient for angiocentricity [5]. Presence of nuclear hyperchromasia and presence of nucleoli were used as criteria to determine atypia. Because of the necrosis and other inflammatory cells; these atypical cells are very difficult to be identified and most series report multiple biopsies [5]. We hypothesized that the difficulty may be related to the depth at which these vessels are situated. We searched ‘Medline’ and ‘Pubmed’ for any article related to depth and vessels in relation to the angiocentric lymphomas or AIL with no result. We therefore worked on the Vernier scale of the microscope to determine the depth at which such destructive vessels are detected. To identify the vessels with wall damage reticulin stain was used. Our results showed most of the vessels were at a depth of between 4 and 8 mm from the surface epithelium or ulceration. The tumor marker studies were done to determine whether they are T or B or NK cells. CD45 (also called leukocyte common antigen) is present in all leukocytes so it confirmed that the neoplastic elements were not epithelial cells. CD3 and CD20 are specific for T-cells and B-cells respectively. So the presence of CD3 marker confirmed a T-cell origin neoplasia. The message is that in cases of destructive sino-nasal lesions, if the superficial biopsy shows a mixed population of inflammatory cells it may be prudent to take a deeper biopsy. The question we have tried to answer is what should be the approximate required depth and modality of the biopsy to be taken. A single case report cannot obviously give a firm answer but it is indicative. Since the surrounding cuff of inflammatory tissue in our case was 4–8 mm thick, it is recommended that instead of a punch biopsy with an endoscopic optical biopsy forceps which gives a very superficial tissue sample (around 3 mm depth), a deeper incisional biopsy be performed of at least 10 mm depth so as to get enough tissue to visualize blood vessels in all cases of nasal masses which show evidence of bone destruction clinically and/or radiologically. The obvious risk of epistaxis is manageable and is anyway much less serious than those associated with full scale surgical intervention.

The look for atypia of the lymphocytes revealed only a few infrequent atypical cells. Presence of nuclear hyperchromasia and presence of nucleoli were used as criteria to determine atypia. However the presence of nucleoli was not a conspicuous finding. Thus a Grade 2 AIL could be ascertained.

## Conclusion

Angiocentric lymphoma like all angioimmunoproliferative lesions is an enigmatic condition which is likely to be misdiagnosed on routine surgical biopsy sampling due to its surrounding cuff of inflammatory tissue. In case of suspicion of a neoplastic lesion, a deeper incisional biopsy extending sufficiently beyond 10 mm from the surface is recommended in order to ensure a representative histopathological sample. This is especially pertinent for peripheral centers where facilities for detecting CD markers may be absent, but presence of sufficiently aware otorhinolaryngologist/head and neck surgeons and pathologists may prevent an unnecessary surgery alongwith the associated morbidity and initiate treatment on the correct lines. We learnt our lessons and would like to share it with others.

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