

Lymphoid lesions of Oral & Maxillofacial Region

Rare disease

Classification:

1. Reactive:

a. Lymphoid Hyperplasia.

b. ALHE

• 2. Developmental :

a. Oral Lymphoepithelial cyst

b. Cervical Lymphoepithelial cyst

• 3. Neoplastic:

a. Lymphoma:

i. Hodgkins lymphoma

ii. Non-Hodgkin's lymphoma

• b. Myeloma/ Plasmacytoma

CASE REPORT

Primary non-Hodgkin's lymphoma of the tongue: a diagnostic dilemma of unusual case presentation

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SUMMARY

Primary non-Hodgkin's lymphoma of the tongue is extremely uncommon, which makes its diagnosis quite challenging. A panel of 11 markers is used based on morphological differential diagnosis to elucidate the lymphoma subtype. A case of 43-year-old Egyptian man suffering from nodular mass on the right side of the tongue of 4 months duration is presented. No cervical lymphadenopathy was detected. No abdominal organomegaly was noted. The histological evaluation of incisional biopsy revealed a sheet of pleomorphic lymphoid cells with abnormal mitotic figures. A large number of histiocytes were infiltrating the lymphoid cellular sheet. The results of immunophenotyping were extranodal T-cell lymphoma. A proper immunohistochemical workup is crucial for the correct diagnosis and proper management.

The oral lesion presented as a 3×3 cm nodular mass involving the middle portion of the right side of the tongue. The deep central groove of the tongue separates the mass from the rest of the tongue (**figure 1**). The movement of the tongue was normal. The right pharyngeal wall and the tonsils were normal. No cervical lymphadenopathy was detected. No abdominal organomegaly was noted on CT scan. The patient underwent surgery for an incisional biopsy. The histological evaluation revealed a sheet of pleomorphic lymphoid cells and abnormal mitotic figures. A large number of histiocytes were infiltrating the lymphoid cellular sheet (**figure 2**).

INVESTIGATIONS

To differentiate between lymphoma subtypes, immunohistochemistry was performed for proliferation (Ki67), PAN-T (CD3), B-cell antigen (CD20), leucosialin (CD43), granzyme B, CD68, CD4, CD8, CD30, CD56 and ALK to confirm the diagnosis which was extranodal T-cell lymphoma. **Figure 3A-F** revealed strong to mild expression against Ki67, CD3, CD20, CD43, granzyme B and CD68. However, **figure 4A-E** demonstrates weak to negative expression against CD4, CD8, CD30, CD56 and ALK1 (CD246).



Figure 1 The 3×3 cm nodular mass is seen at presentation.



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BMJ

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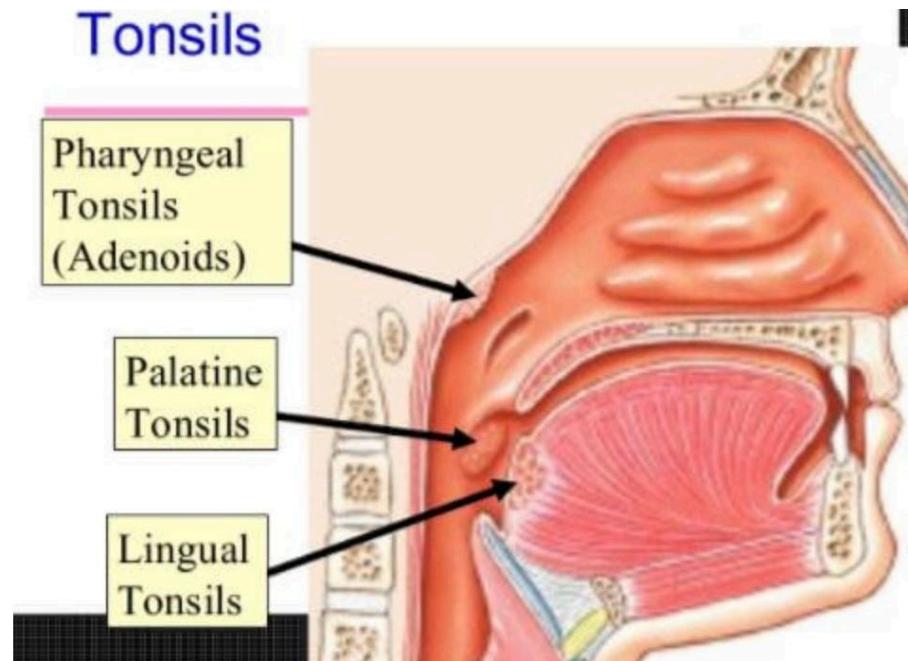
CASE PRESENTATION

A 43-year-old Egyptian man attended oral medicine clinic at College of Dental Medicine, University of Sharjah, UAE, with 4 months history of slow growth of nodular mass on the right side of the tongue. The patient was heavy smoker and regular alcohol drinker. He had negative history of neck mass, febrile illnesses, weight loss and night sweats.

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Normal Lymphoid Tissue in and around oral cavity:

- Pharyngeal tonsils
- Lingual tonsils
- Palatine tonsils
- regional lymph nodes & lymphoid tissue



Lymphoid Hyperplasia:

- Proliferation of lymphocytes without cellular atypia.
- Mitotic figures restricted to germinal center.
- Occasionally mimic starry sky appearance.

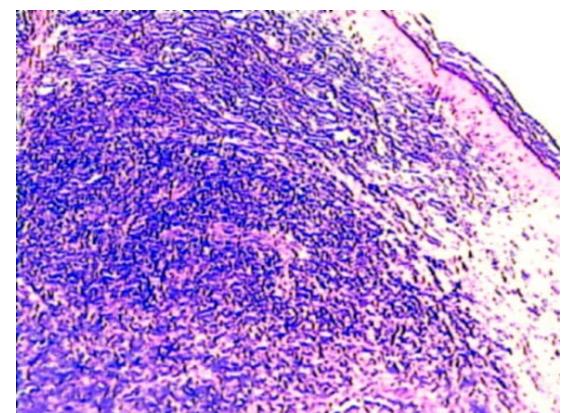
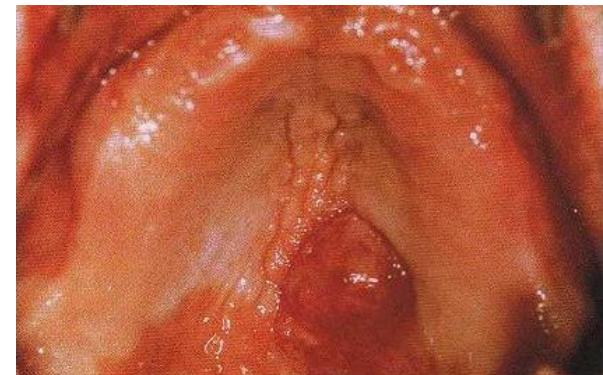
Difficult to distinguish from neoplastic lymphoblastic proliferation.

Site: Postero- lateral portion of the tongue, anterior floor of mouth, **anterior tonsillar pillar** & posterior part of soft palate.

- *Aggregations of lymphoid tissue are part of the foliate papillae or lingual tonsil.*
- Sometimes these papillae become inflamed or irritated with associated enlargement and tenderness.

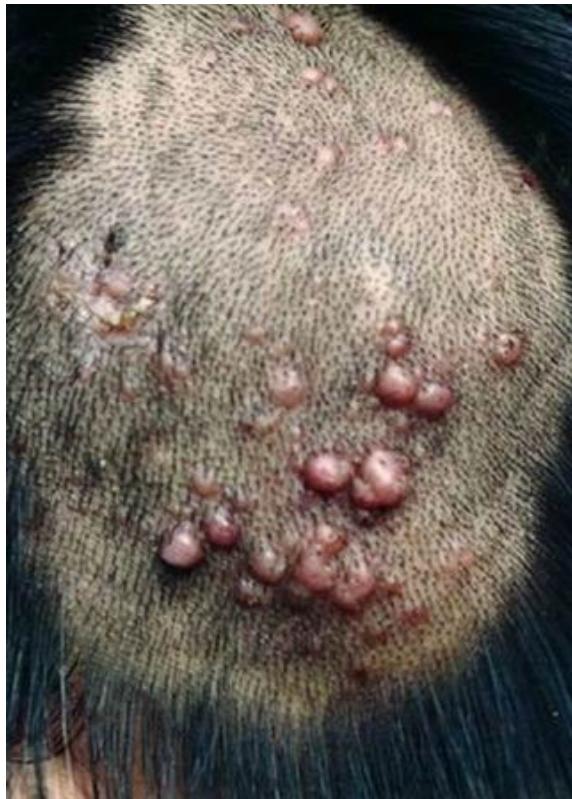
Histopathology:

- Reactive Lymphoid hyperplasia
(^{en}larged germinal center with mitosis & macrophages)



Angiolymphoid Hyperplasia with Eosinophilia (ALHE)

- Nodular subcutaneous benign diseases.
- Aggregates of lymphocytes and eosinophils.
- Blood eosinophilia.
- 85% in head & neck region, rare intra orally (lip).
- 1-2 cm. solitary or multiple, painless, mobile submucosal nodule which enlarge gradually



Histopathology:

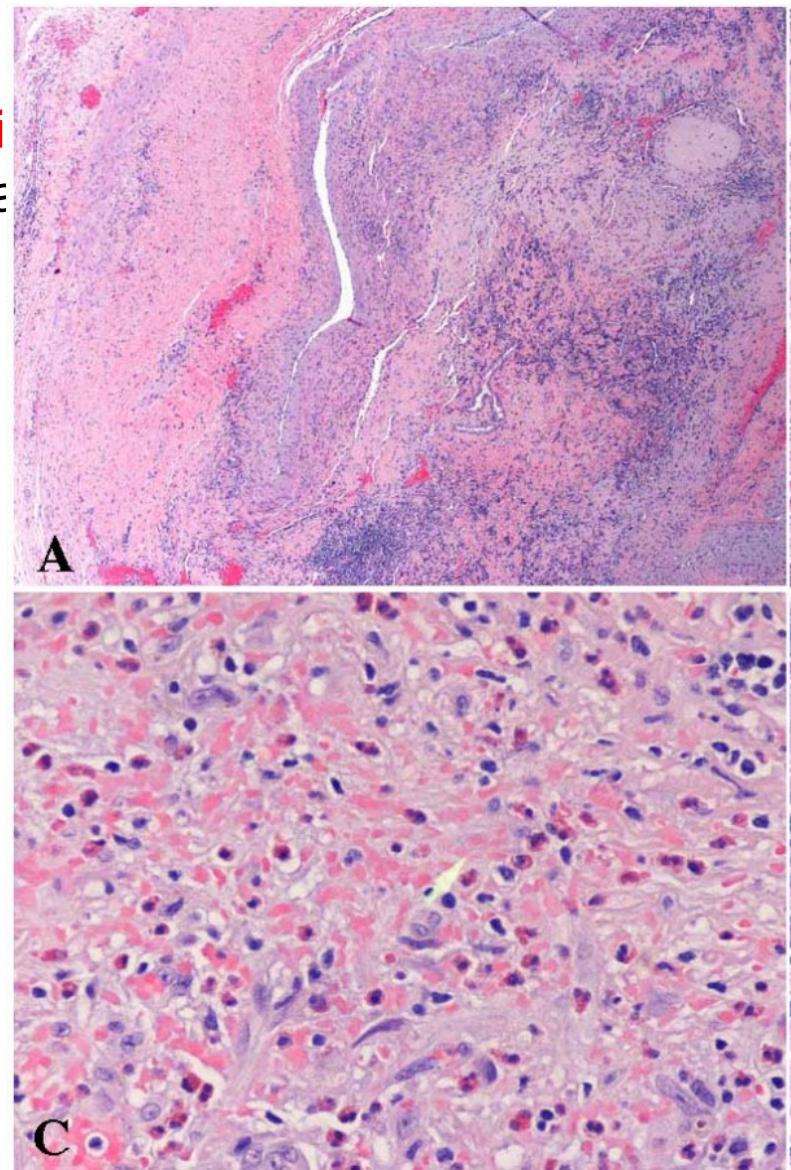
- Circumscribed lesion, **hyperplastic lymphoid tissue** (well developed follicle with germinal center).
- Eosinophilic infiltrate.
- Proliferating dilated capillaries.
- Intensive infiltration of lymphocytes & eosinophils.

Differential Diagnosis:

- Minor Salivary gland reactive or neoplastic lesions
- Lipoma or Schwannoma
- Eosinophilic Granuloma

Treatment:

- Surgical excision
- Intra lesional steroid injections



Neoplasms:

Hodgkin's Lymphoma:

Characteristics:

- Affect bone or soft tissue.
- Painless enlargement of lymph nodes
- Rarely affect oral cavity
- Within oral cavity: **Unilateral tonsillar enlargement** (early phase).
- Extranodal: **Submucosal swelling with mucosal ulceration.**



Staging:

Importance of staging:

- Determine the type & intensity of therapy.
- Overall prognosis
- Potential complication

Ann Arbor Staging System:

- **Stage I** : Involvement of a **single** lymph node region or of a single extranodal site or organ.
- **Stage II** : Involvement of **2** or more lymph nodes region on the same side of diaphragm or localized involvement of an extra nodal site or organ and one or more lymph node.
- **Stage III** : Involvement of lymph node regions of **both sides of the diaphragm**, which may also be accompanied by localized involvement of an extra nodal organ or site IIIE or spleen IIIS or both IIISE.
- **Stage IV** : Diffuse or disseminated involvement of one or more distant extra nodal organ.

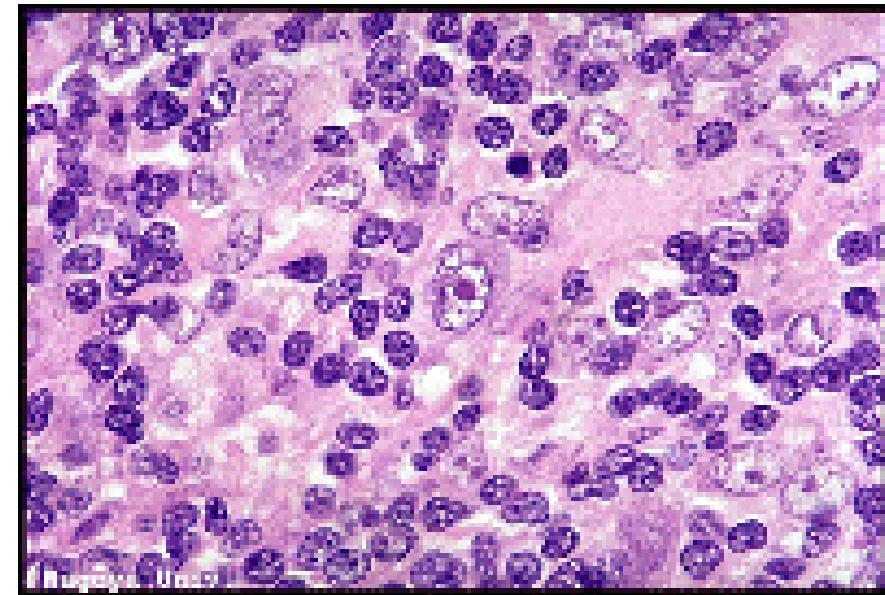
Sub classification:

- **A**: Without Symptoms
- **B**: With systemic symptoms: Unexplained fever $> 38^{\circ} \text{ C}$, unexplained weight loss $> 10\%$ of body weight in past 6 months, night sweats.

Histology:

Reed Sternberg cells must be present for the diagnosis of HL.

- **RS cells**: lymphocytic origin cells, characterized by its large size & bilobed nucleus, each lobe contain a large amorphous or eosinophilic nucleolus.
- Non Neoplastic inflammatory cells infiltrate



Classic HL comprises 4 entities: (Likes - Bulter Histo. Classification)

- Lymphocytic –rich --- most favorable diagnosis.
- Nodular Sclerosis---- most common form (50%) [collagen fibers penetrate into LN subdividing it into islands of tumors]
- Mixed cellularity --- contains combination of lymphocytes, many RS cells, PMNs, plasma cells & macrophages.
- Lymphocytic depletion --- least favorable prognosis.

Treatment:

- External Radiotherapy
- Chemotherapy

Non Hodgkin's Lymphoma

Characteristics:

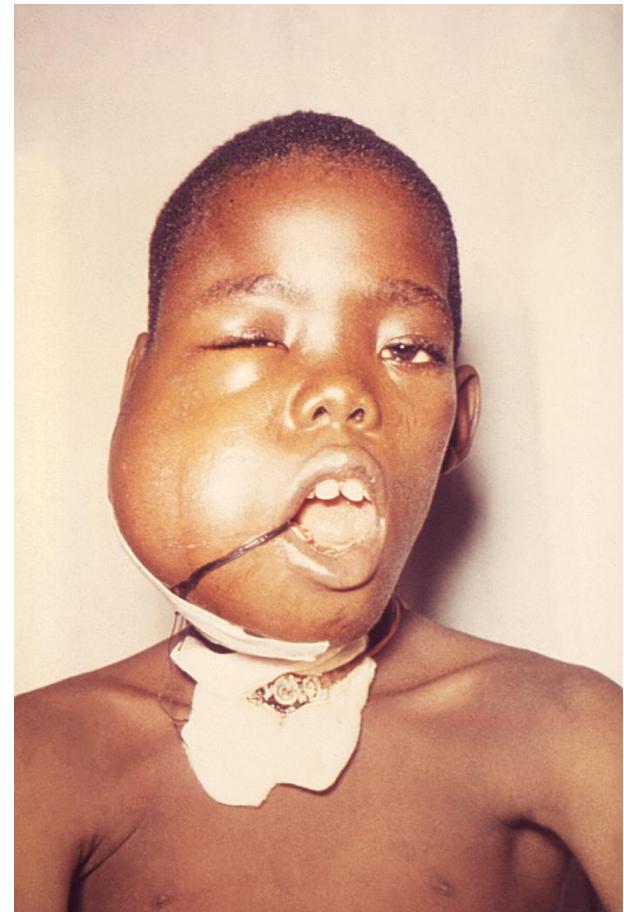
- Affect middle aged and elderly.
- Gradual, asymptomatic focal enlargement of lymph nodes.

Ann Arbor Classification:

- **Nodular lymphoma:**
 - Poorly differentiated
 - Mixed lymphocytic-histiocytic
 - Histiocytic (least favorable prognosis)
- **Diffuse Lymphoma:**
 - Lymphocytic (well differentiated or poorly differentiated)
 - Histiocytic
- **Mixed**

Non Hodgkins Lymphoma

- Arise in **nodal & extra** nodal sites
- Most common extra nodal site is **GIT**
- **Head & neck** is the **second** most common site (**Waldeyer's Ring**) (esp. in HIV infected patient)
- **B-cell Lymphoma** are the most common phenotype in extra nodal site.



Histological Types involving head & neck region:

- Large B cell Lymphoma
 - Burkitt's Lymphoma)
- T-cell & NK Lymphoma (Midline Lethal Granuloma)
- Extra nodal Marginal Zone Lymphoma (Unique; arise in LN present in salivary glands)

Etiology:

- Genetic predisposition
- Immunodeficiency
- Chromosomal translocation

Clinical Features:

Three broad groups of NHL can be discerned on basis of biologic behavior:

- **Indolent**: Slow growth, wide dissemination, long natural history, relative incurability.
- **Aggressive**
- **Highly aggressive**

Both have rapid growth, localized presentation, short natural history

- Frequent responsiveness to chemotherapy

- Most lymphomas in **adults** are diffuse B-cell or **Follicular lymphoma**
- **Follicular lymphoma**: Predominant tumor of lymph nodes (**rare in oral cavity**).
- **T cell lymphoma** : less common at all sites , including oral cavity.
- In **Children**: **Aggressive and highly aggressive lymphoma** are the most common with **Burkitt's Lymphoma** (more than 40% of types)

Oral Presentation:

- Variable, account for < 5% of Oral malignancies.
- **Mass or ulcerated mass** resemble squamous cell carcinoma or salivary gland neoplasms (Waldayer's ring).
- **Burkitt's Lymphoma** show a striking predilection for primary involvement of **bone**.
- Bone loss & tooth mobility, swelling, pain & lip numbness.

Treatment:

- Radio & Chemotherapy



Large (Diffuse) B- cell lymphoma

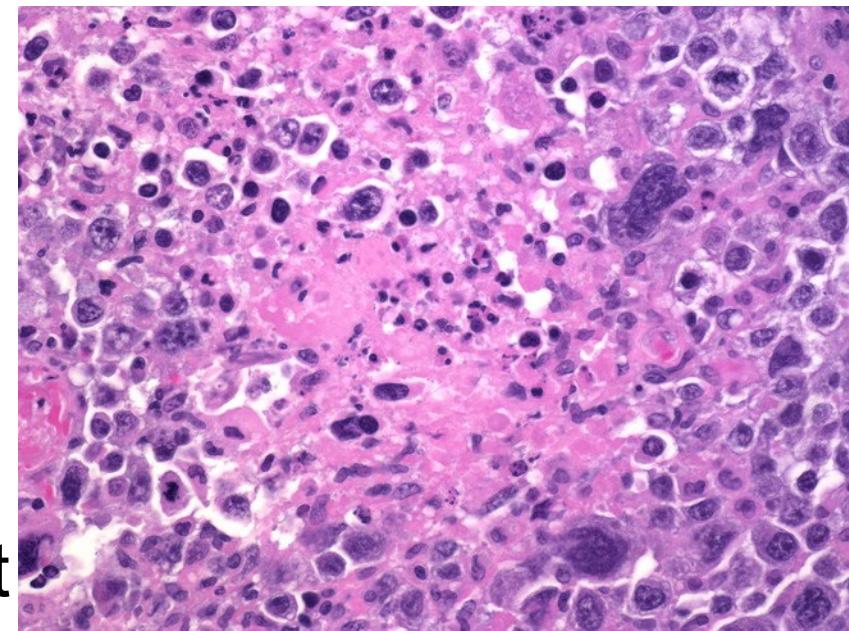
- Aggressive, rapidly growing neoplasm of large lymphoid cells.
- Arise *de novo* or as *transformation* of a lower grade lymphomas.

- Lymphadenopathy

- Extra nodal involvement:

Bone ----- Extensive destruction.

- **Histology:** Sheets of large lymphoid cells with abundant cytoplasm and reactive histiocytes.

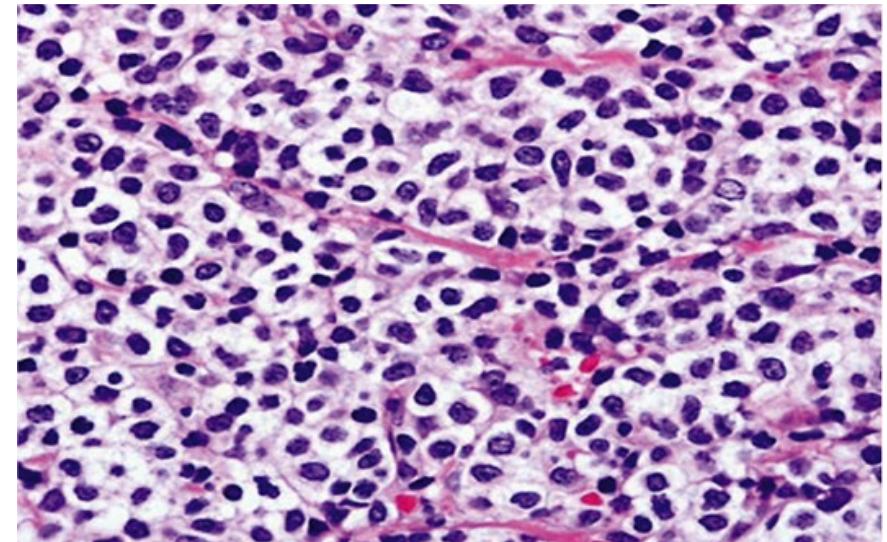


Extra Nodal Marginal Zone Lymphoma

- **Indolent** lymphoma occurring in mucosal sites or extra nodal tissue like: GIT, SG, Thyroid gland and skin.

- **Predisposing factors:**

- Hashimoto's thyroiditis
- Sjogren Syndrome
- H. P gastritis



Localized with protracted course before dissemination .

- **Histology:** **Centrocyte-like cells** (resemble a range from lymphocytes to monocytoid cells)

Burkitt's Lymphoma

- *Highly aggressive B-cell lymphoma.*
- Primarily affects *children and adolescents.*

Three forms:

- **Endemic** : In Africa
- **Sporadic**: In north America & Europe
- **Associated with immuno deficiency.**

Endemic BL:

- Diseases of children in Equatorial Africa, where endemic malaria may serve as pathogenetic co-factor.
- 95% associated with EBV infection.
- *Jaw bones involvement* is characteristic in up to 50% of cases.
- Other organs involved: *Kidney, liver, Retroperitoneum & gonads.*



Sporadic BL:

- Affect **young adults**
- As **abdominal mass** & bone marrow involvement.
- **Jaw lesions** are less common (**10%** of cases).

HIV associated BL:

- Tumor present in **lymph node** and at **extranodal sites** (CNS, bone marrow & GIT).

Radiographic Features:

- Poorly marginated radiolucency.
- Cortex: Expanded, eroded or perforated.



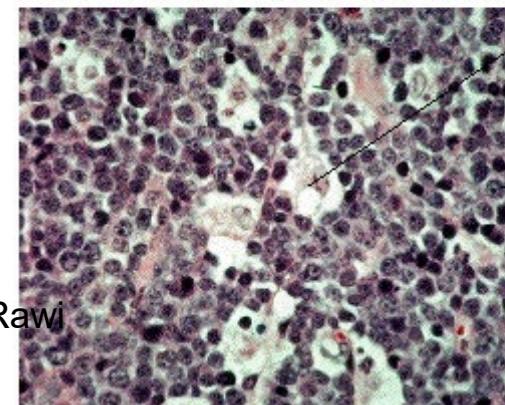
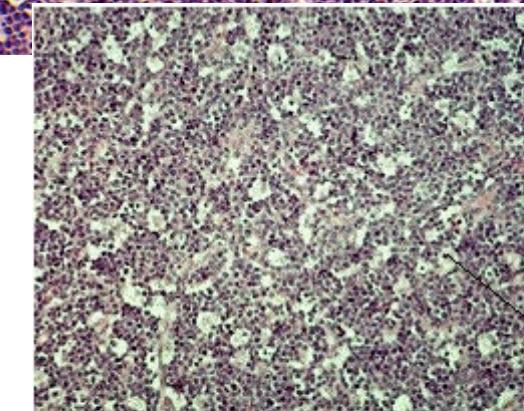
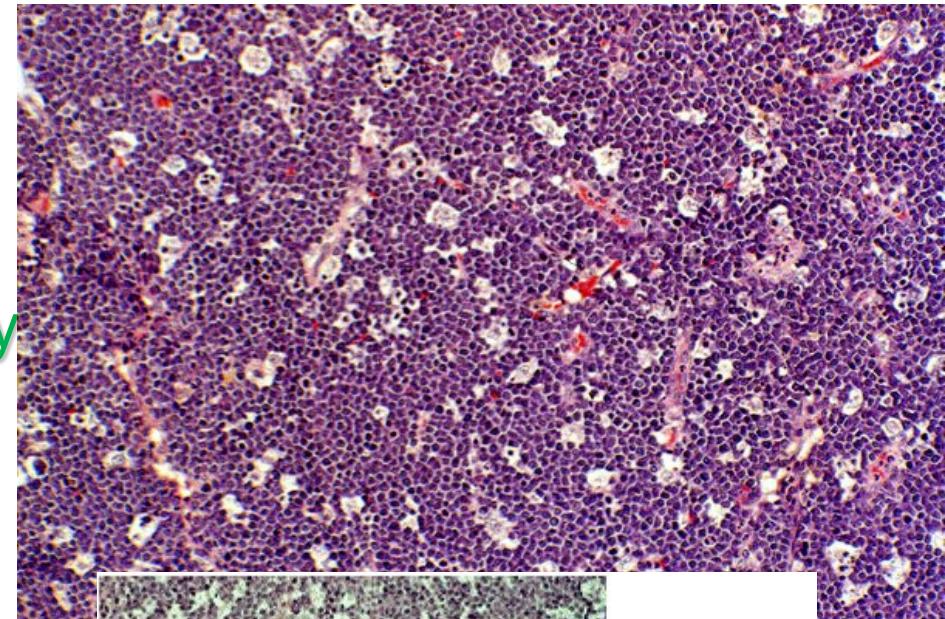
Histology:

All forms of BL share the same histological appearance.

- **Monomorphic** sheets of **densely packed, medium sized** neoplastic lymphocytes.
- Their cytoplasm is **deeply basophilic** with high mitotic rate (10 mitosis /HPF)
- Numerous **macrophages containing cellular debris** give the classic **Starry Sky** appearance to the tumor.

Treatment:

- Chemotherapy
- ²⁵ years survival



Macrophages

Tumor cells

BL	African	American
% of all childhood malignancy	50%	6-10%
Mean age	3-10	11 years
Race	100% black	77% white
Jaw bone involvement	Common	Rare
Association with EBV	90%	10%

Lymphoma Associated with HIV infection:

- ***Extra nodal*** (CNS, ano-rectal region and Oral cavity)
- **Orally:** **Fauces** or **gingiva** are the most commonly affected sites.
- **Rapidly growing mass & /or teeth mobility.**
- **Poor prognosis.**
- **B-cell** type predominate, although T-cell lymphoma are also seen.
- Most of B-cell type are **immunoblastic** or **Burkitt's like** lymphoma.



Nasofacial NK/T-cell Lymphoma (Midline Lethal Granuloma)

- Progressive, ulcerative destruction of the **palate**, nose & paranasal structures.
- **Epistaxis**
- **Swelling of soft and hard palate ---- Ulceration & destruction of palatal & nasal tissue---- Oroantral fistula.**
- MLG involve also **Wegner's granuloma**.

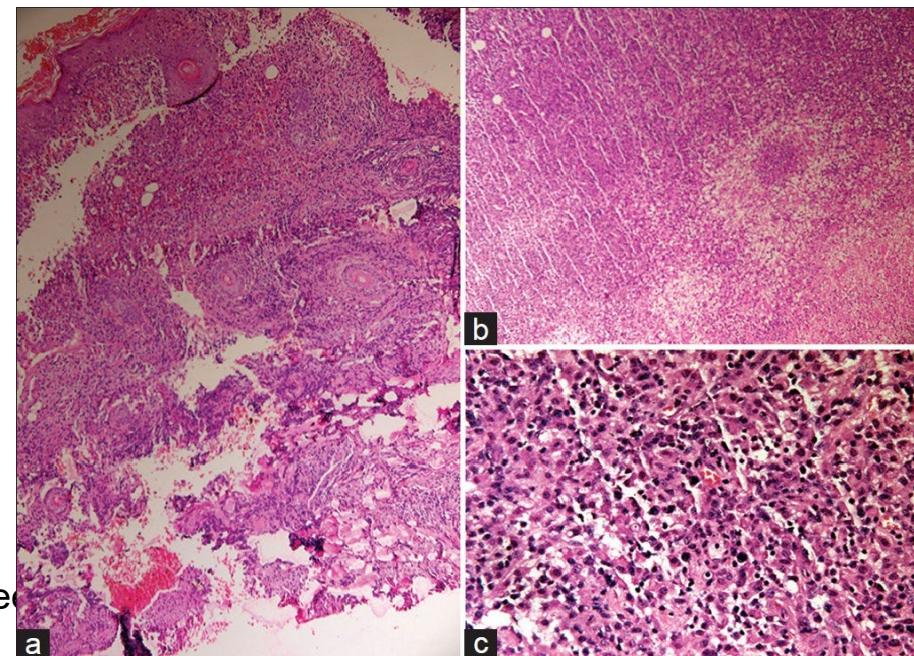


Histology:

- Varying amount of granulation tissue & necrosis
- Medium and large atypical lymphocytes with clear cytoplasm & irregular nuclear outline.
- Angiocentricity & epitheliotropism are also common histopathological features.

Treatment:

Chemo & radiotherapy



Dr. Natha

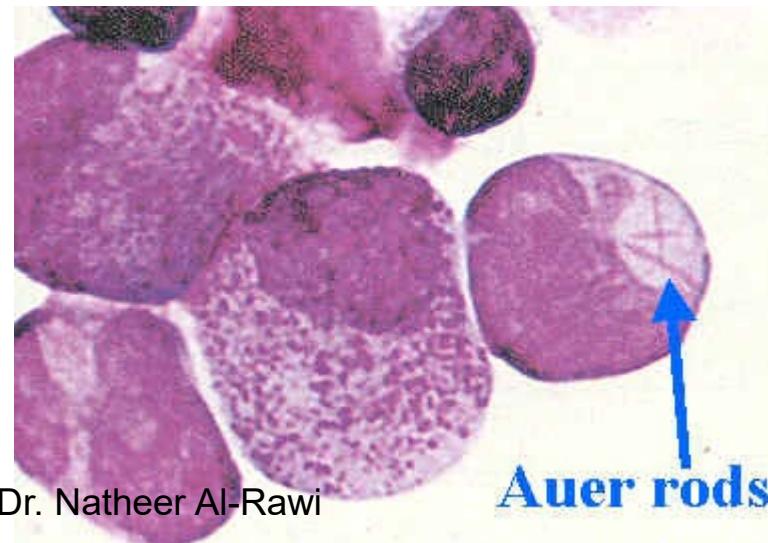
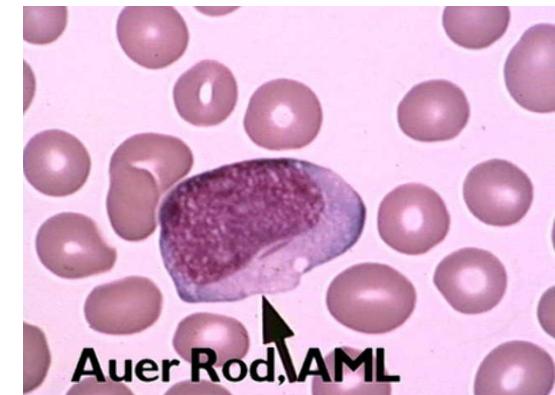
Granulocytic Sarcoma(Extra medullary Myeloid tumor)

- **Orally:** Localized soft tissue mass.
- Occurs in three setting:
 - In patients previously known to have **AML** as a sign of blast transformation.
 - In patients with **CML** or other myeloproliferative diseases.
 - In patients who was **previously ill**.

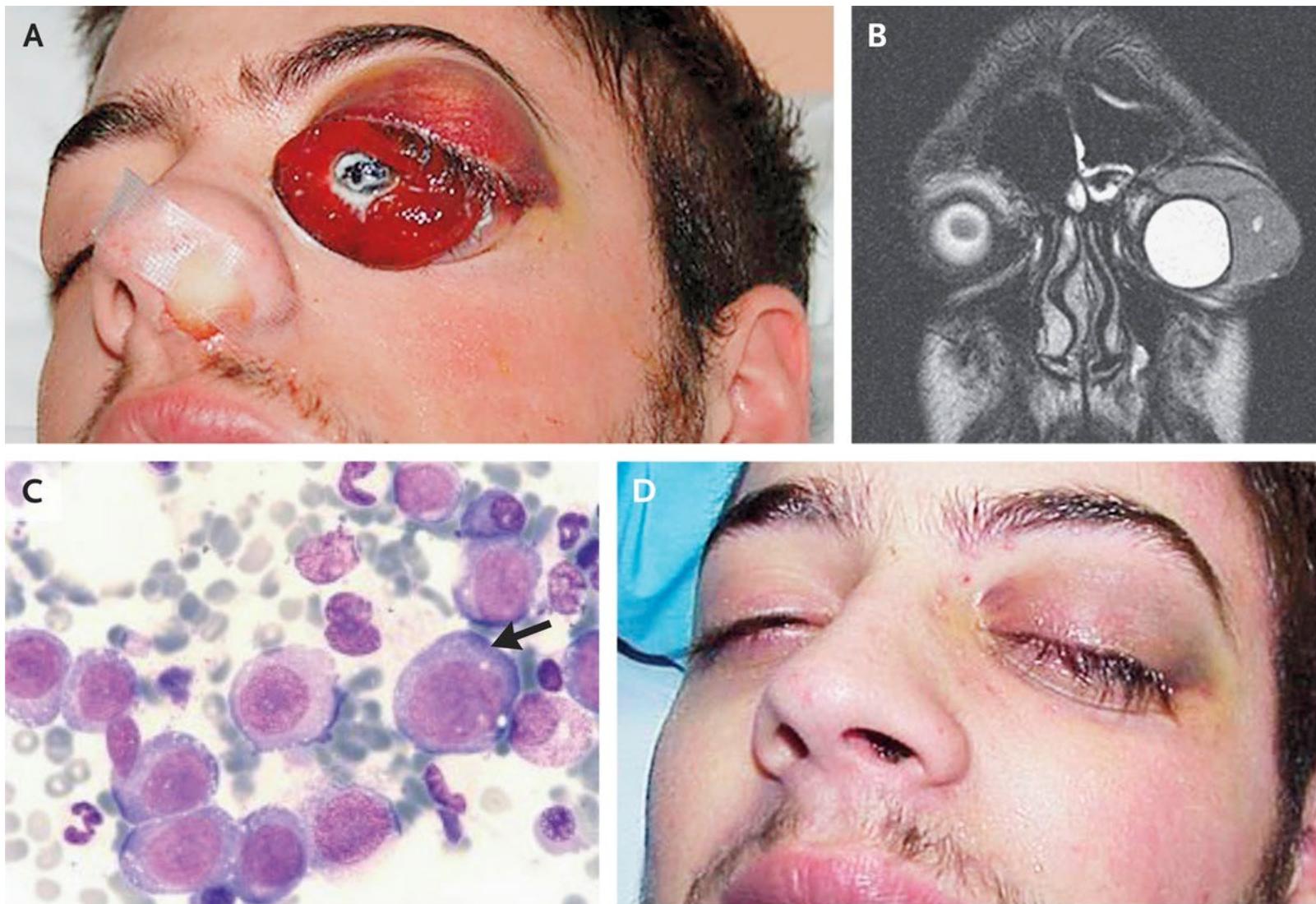


Difficult to diagnose histologically from :

- Large cell lymphoma
- Poorly differentiated carcinoma.
- Plasmacytoma
- **Auer rods**: crystalline, rod-like , intracytoplasmic acidophilic bodies can establish diagnosis of both granulocytic sarcoma & AML.
- Poor prognosis



Dr. Natheer Al-Rawi



That's all Thank You

