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Beyond Burkitt: an emerging maxillofacial tumor pattern in equatorial Africa and a shared ecological context

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Abstract

Burkitt lymphoma represents a classical model of clinical-epidemiological discovery, in which recognition of a reproducible anatomical and geographical pattern preceded identification of its etiological determinants. Across equatorial Africa, clinicians are increasingly reporting recurrent maxillofacial lesions, including odontogenic tumors such as ameloblastoma and fibro-osseous entities such as fibrous dysplasia and ossifying fibroma. Although biologically heterogeneous, these lesions share key clinical features, including preferential maxillofacial localization, bone-expanding growth, and often indolent presentation. Observations from Central, West, and East Africa suggest clustering within specific populations and geographic regions, frequently overlapping with areas historically associated with endemic Burkitt lymphoma. Current evidence remains limited by the absence of systematic case definitions, population-level denominators, and structured datasets. However, the convergence of clinical and geographic features suggests the emergence of a consistent but under-recognized pattern. While distinct from Burkitt lymphoma, these lesions may arise within a shared ecological context characterized by high infectious burden and sustained human-environment interaction. As with Burkitt lymphoma, early recognition of such patterns may precede mechanistic understanding and should prompt integrated clinical, environmental, and molecular investigation.

Key words: infectious disease ecology; Burkitt lymphoma; maxillofacial tumors.

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Introduction

Medical progress has often begun with recognition of recurring clinical patterns rather than immediate identification of underlying mechanisms. A paradigmatic example is Burkitt lymphoma, first described in equatorial Africa through the consistent association of pediatric jaw tumors with specific geographic and demographic patterns.[1,2] This pattern-based recognition preceded elucidation of its etiology, later linked to early Epstein-Barr virus (EBV) infection in the presence of cofactors such as chronic malaria exposure.[3-5] Clinicians in these regions increasingly report recurrent cases of bone-expanding jaw lesions, including ameloblastoma, fibrous dysplasia, and ossifying fibroma.[6,7] Although biologically distinct from Burkitt lymphoma, these lesions share converging features such as preferential maxillofacial localization and often indolent progression. They are frequently diagnosed at advanced stages, reflecting both slow evolution and limited access to early care. Notably, these tumors are often observed in regions overlapping with endemic Burkitt lymphoma, including Central and East Africa.[3,8] This spatial convergence, together with shared environmental conditions – high infectious burden, ecological biodiversity, and frequent human-animal interaction – suggests a broader contextual framework influencing disease occurrence.[9,10] Parallels with historical observations are striking. Clinical reports from regions such as northern Uganda and the Congo basin suggest that a similar process of pattern recognition may be emerging. As with early Burkitt lymphoma descriptions, these lesions appear clinically evident yet underreported, raising questions about their limited capture within formal health systems. However, current knowledge is constrained by the absence of systematic data collection, standardized case definitions, and population-level epidemiological information. In this context, there is a need to move beyond isolated observations toward structured characterization. This work aims to describe these findings within a clinical and epidemiological framework and examine their relationship to the Burkitt paradigm. By integrating clinical, geographic, and ecological perspectives, it seeks to generate hypothesis-driven insights to guide future molecular, virological, and epidemiological investigations.

From observation to pattern

The recognition of Burkitt lymphoma as a distinct entity illustrates how reproducible clinical patterns can precede biological understanding. The association between pediatric jaw tumors and a restricted equatorial distribution led to syndrome conceptualization before its etiology was defined.[1,2] This sequence – observation, pattern recognition, and hypothesis generation – remains central to the study of emerging diseases.[11] A similar trajectory may be unfolding for maxillofacial lesions in Sub-Saharan Africa. Across multiple settings, recurrent observations describe jaw-localized lesions with progressive bone expansion and often an indolent onset. These include odontogenic tumors and fibro-osseous lesions such as ameloblastoma, fibrous dysplasia, and ossifying fibroma,[5-7,12,13] which, despite histopathological differences, share osteo-expansive behavior and delayed presentation.[14] Several features support a coherent emerging pattern: consistent maxillofacial localization, locally expansive growth, and a clinical course that is often slow but can occasionally accelerate. Repeated observations also suggest clustering within specific populations and regions, although this remains insufficiently captured in formal epidemiological systems.[15] A notable aspect is the geographic overlap with regions historically associated with endemic Burkitt lymphoma, including Uganda, the Democratic Republic of Congo, and parts of West Africa.[2,8] While this does not imply shared pathogenesis, it suggests that common ecological or environmental determinants may contribute to distinct disease entities. Another key feature is the gap between clinical visibility and epidemiological recognition. Despite their often-striking presentation, these lesions appear underrepresented in registries and national reporting systems,[15] echoing early Burkitt lymphoma observations. However, the absence of standardized case definitions, structured datasets, and population-level denominators limits current understanding. These findings should therefore be interpreted as an emerging but underdefined clinical signal requiring further investigation.

Defining a working clinical entity

In the absence of systematic datasets and standardized reporting, a necessary step toward interpreting these observations is the formulation of a working clinical definition. The lesions described across multiple field settings can be broadly framed as a heterogeneous group of predominantly benign maxillofacial lesions, including odontogenic tumors and fibro-osseous entities, identified on the basis of clinical presentation and radiological features,[12,13] and often characterized by an osteo-expansive growth pattern. While these lesions are grouped here within a common descriptive framework, it is important to recognize their biological heterogeneity, including odontogenic tumors such as ameloblastoma and non-odontogenic fibro-osseous lesions, which may differ in origin and pathogenesis. To facilitate comparability across observations, cases can be described using a minimal descriptive framework including age, sex, anatomical site, clinical course, and geographic origin, as is commonly applied in descriptive oncological and epidemiological reporting.[15] This approach does not aim to establish formal diagnostic criteria, but rather to provide a consistent structure through which recurrent features can be identified and communicated. It is important to emphasize that this work does not represent a formal epidemiological or analytical study. Rather, it constitutes a structured clinical and conceptual description of a recurring observational signal. In this context, the definition of a working clinical entity serves primarily as a heuristic tool, enabling the transition from individual case observations to the recognition of a potentially meaningful pattern. To contextualize these observations, we propose a conceptual comparison with the clinical and epidemiological features of Burkitt lymphoma, providing a framework to highlight both convergences and key differences between the two entities (Table 1).

Beyond Burkitt: pattern, context, and exposure

The historical trajectory of Burkitt lymphoma provides a useful framework for interpreting these observations, where recognition of a reproducible clinical-geographic pattern preceded identification of its biological determinants.[2-4] In this context, the observed maxillofacial lesions show both similarities and differences with the Burkitt paradigm (Table 1). Both conditions exhibit jaw involvement and geographic clustering within Sub-Saharan Africa, particularly across the "Burkitt lymphoma belt", character-

Table 1. Comparative clinical and epidemiological features of Burkitt lymphoma and fibro-osseous tumors.

Feature	Burkitt lymphoma	Maxillofacial lesions (observed pattern)
Nature of disease	Malignant B-cell lymphoma	Heterogeneous group of predominantly benign odontogenic and fibro-osseous lesions
Age distribution	Predominantly pediatric (2-14 years)	Variable; often young adults, occasionally pediatric
Anatomical localization	Frequent jaw involvement, also abdomen and orbit	Predominantly maxillofacial (mandible/maxilla)
Growth pattern	Rapid, aggressive proliferation	Frequently osteo-expansive; often indolent but occasionally rapidly progressive
Clinical presentation	Symptomatic; rapidly evolving	Often asymptomatic or pauci-symptomatic initially
Systemic involvement	Frequent (multicentric disease)	Rare or absent
Histopathology	Monomorphic malignant lymphoid cells	Heterogeneous lesions including odontogenic tumors (*e.g.,* ameloblastoma) and fibro-osseous entities (*e.g.,* fibrous dysplasia, ossifying fibroma)
Geographic distribution	Equatorial Africa ("Burkitt belt"), extending from West to East Africa	West, Central, and East Africa; apparent overlap with endemic Burkitt lymphoma regions
Epidemiological characterization	Well-defined through decades of study	Primarily based on field observations; lacks systematic epidemiological characterization
Infectious associations	Early EBV infection in the presence of cofactors such as chronic malaria exposure	No established association; potential environmental or infectious context under investigation
Ecological context	High infectious burden; malaria-endemic regions	Similar ecological settings across equatorial Africa; shared environmental exposures and human-animal interactions (hypothesized)
Stage of understanding	Established clinical entity with known etiological contributors	Emerging clinical pattern; currently at a hypothesis-generating stage

ized by high transmission of *Plasmodium falciparum* malaria and a substantial infectious disease burden.[3,4,16] This ecological context contributes to Burkitt lymphoma through early EBV infection combined with cofactors such as chronic malaria exposure.[3-5,17] EBV, although ubiquitous, is not sufficient alone; repeated malaria exposure may sustain B-cell activation, impair immune control, and promote expansion of infected cells, facilitating additional alterations such as *MYC* translocation and malignant transformation.[17,18] Endemic Burkitt lymphoma exemplifies infection-associated oncogenesis shaped by viral infection, immune modulation, and environmental cofactors. This aligns with the concept of syndemics, where co-occurring conditions cluster within shared social, environmental, and biological contexts, as illustrated by the EBV-malaria interaction. In contrast, the lesions described here are generally benign and localized, with heterogeneous presentation, slower progression, and distinct histopathology compared to malignant lymphoproliferative disorders.[5-7] These differences indicate that the parallel reflects not a shared disease entity but a common ecological and exposure context. Sub-Saharan Africa is characterized by high biodiversity, frequent human-animal interaction, and widespread exposure to infectious agents.[9,10,19] Dietary practices, including bushmeat handling, and environmental conditions such as limited sanitation create sustained exposure interfaces, often linked to specific cultural behaviors and wildlife contact. Some patients report non-specific prodromal symptoms (fever, sore throat, headache), which, although non-diagnostic, are consistent with infectious exposures and warrant further investigation. Rodent populations, particularly *Mastomys* species, are especially relevant as reservoirs of zoonotic pathogens, including Lassa virus, and represent a significant source of human exposure.[10,20-22] Although no causal relationship can be established, the prevalence of such exposures suggests that infectious or pathogen-mediated mechanisms may contribute. As in Burkitt lymphoma – where EBV was identified after the clinical syndrome – these observations highlight the importance of considering infectious agents within a broader ecological framework. The key implication is that the parallel lies in shared ecological and exposure conditions from which distinct clinical entities may emerge. This framework is summarized in Figure 1, integrating pattern recognition, ecological exposures, biological mediation, and host factors to illustrate a spectrum of disease outcomes.

Interpretation and hypothesis

The recurrent clinical and geographic features observed across independent settings suggest that these maxillofacial lesions are unlikely to be sporadic. Their distribution points to a shared eco-

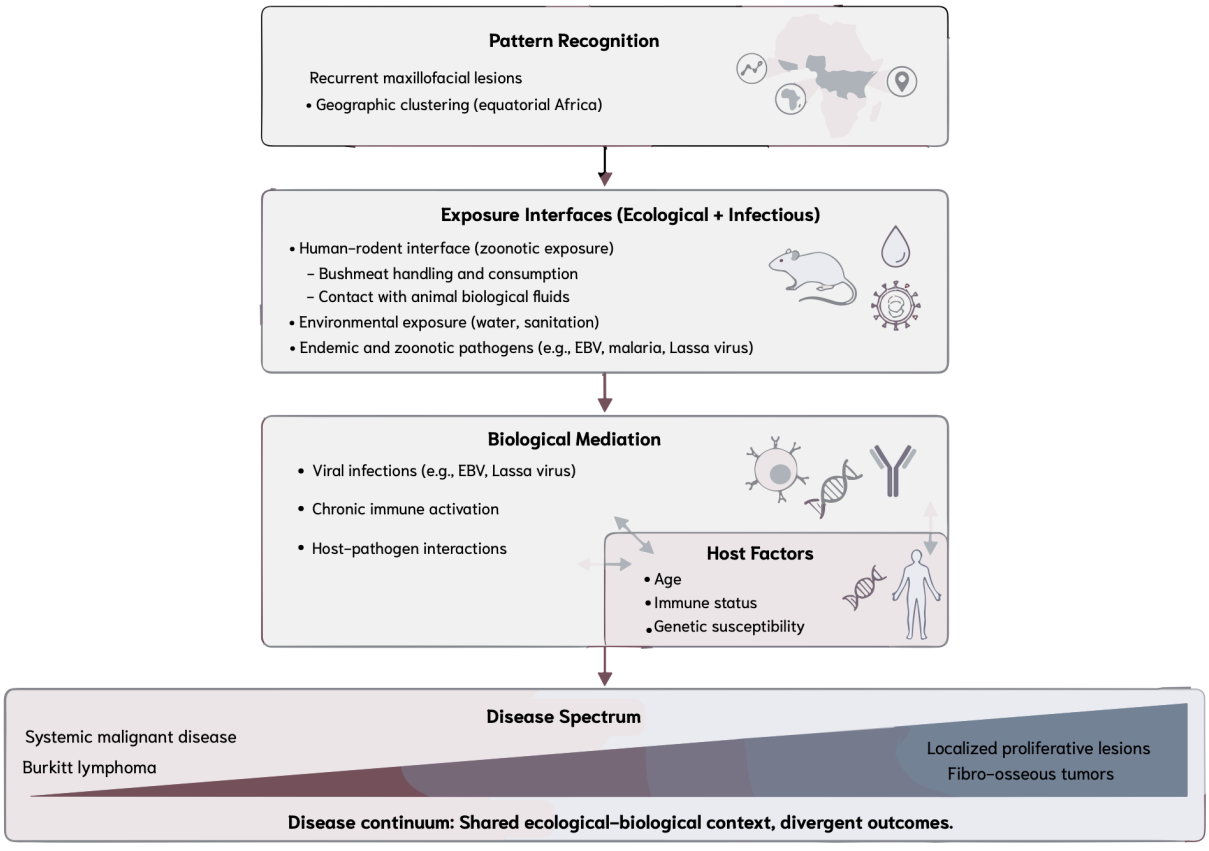

Figure 1. Ecological-biological framework of disease emergence in equatorial Africa. Schematic representation of how shared ecological and infectious exposures may contribute to a spectrum of disease phenotypes. Pattern recognition of recurrent maxillofacial lesions leads to the identification of exposure interfaces, including zoonotic and environmental pathways. These exposures interact with host and biological factors to produce divergent outcomes, ranging from systemic malignancies such as Burkitt lymphoma to localized odontogenic and fibro-osseous lesions. The model is hypothesis-generating and does not imply direct causality.

logical background shaped by environmental exposures and human-animal interactions in equatorial Africa. At the same time, available evidence indicates that they represent a distinct clinical entity, with benign, localized growth and specific histopathological features that differentiate them from systemic malignancies such as Burkitt lymphoma. No causal mechanism has been established, and interpretations must remain cautious and hypothesis-generating. A proof-of-concept hypothesis is that a common environmental and zoonotic exposure context, interacting with host-specific factors, contributes to a spectrum of disease phenotypes. At one end, systemic malignancies such as Burkitt lymphoma may arise; at the other, localized odontogenic and fibro-osseous lesions may develop. This suggests that similar environmental conditions can lead to distinct biological outcomes, reflecting different pathological responses within a shared ecological landscape. Preliminary clinical observations suggest possible exposure to zoonotic viral agents in affected populations, although these findings remain exploratory and require validation. This framework may also accommodate zoonotic viral exposures, including pathogens associated with rodent reservoirs, pending formal investigation.

Limitations and implications

These observations are limited by their exploratory nature. The data derive from non-systematic clinical observations and lack population-level denominators or structured registries, preventing estimation of frequency or comparison with unaffected populations. In addition, direct virological or molecular evidence linking environmental exposures to tumor development is lacking. Despite these limitations, the consistency of clinical and geographic features across independent observations suggests that the findings are unlikely to be incidental. Rather, they represent an early-stage clinical signal. As illustrated by Burkitt lymphoma, recognition of reproducible patterns may precede understanding of underlying mechanisms. These observations, therefore, highlight the need for systematic investigation integrating clinical characterization, environmental assessment, and molecular analysis.

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