

Hairy Leukoplakia

EBV-associated oral epithelial lesion

Clinical recognition • Morphology • Differential diagnosis

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Learning objectives

- Recognize the characteristic site and surface appearance of oral hairy leukoplakia.
- Connect EBV infection and impaired immune surveillance with epithelial changes.
- Interpret hyperparakeratosis, acanthosis, balloon cells and lesional EBV detection.
- Distinguish this entity from candidiasis and potentially malignant oral leukoplakia.

An oral white patch is a clinical finding

Describe before naming

- Document anatomical site, distribution, surface contour and removability.
- Use the immune history to refine the differential.
- Consider infection, reactive keratosis and dysplastic processes.

Then establish the cause

- A white appearance alone does not identify the pathogen.
- Scrapability may separate a surface pseudomembrane from keratosis.
- A suspicious lesion may still require tissue assessment.

Defining oral hairy leukoplakia

- A distinctive EBV-associated epithelial lesion of the oral mucosa.
- Most characteristically involves the lateral border of the tongue.
- Produces a persistent white, keratotic and often corrugated plaque.
- Typically occurs with immunosuppression, but is not specific to HIV.

EBV is the causal agent; Immune dysfunction is a common host context.

Why the oral cavity matters

Systemic immune disorder

Altered host–microbe control

Recognizable oral lesion



- Oral examination can expose evidence of otherwise unrecognized systemic disease.
- Hairy leukoplakia is a named example in the systemic-disease section of Robbins.

Anatomic predilection

Characteristic

- Lateral lingual mucosa is the classic site.
- An edge-of-tongue view is essential during the examination.
- The lesion may be unilateral or bilateral.

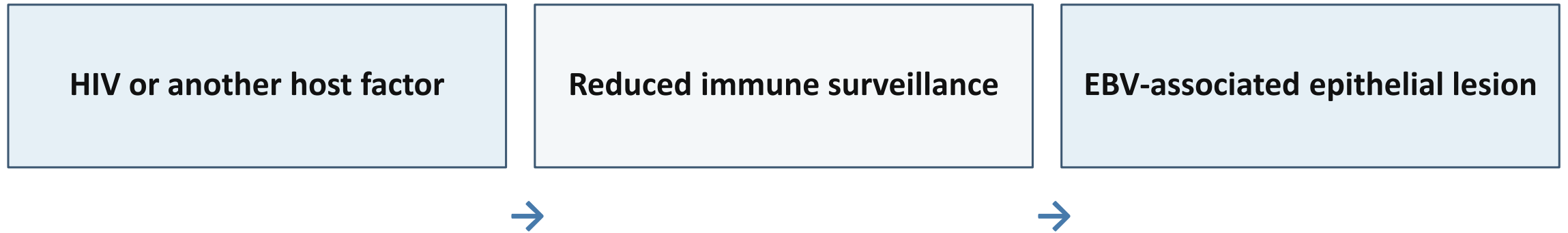
Less characteristic

- Other oral sites are possible but less typical.
- A lesion confined to a different site needs a broader differential.
- Do not diagnose solely from white color.

Epstein–Barr virus is central

- EBV is implicated by viral nucleic acids and proteins in lesional squamous cells.
- The characteristic abnormality involves oral epithelial cells rather than a tumor mass.
- Lesional viral detection connects the clinical plaque to a specific infection.

Separate the roles of HIV and EBV



- HIV infection can establish the permissive immunosuppressed setting.
- EBV—not HIV—is the directly implicated virus in hairy leukoplakia.

Immunosuppressive clinical contexts

Clinical setting	Relevant observation	Interpretive implication
HIV infection	Classic association; May accompany immune decline	Evaluate broader HIV care context
Cancer therapy	Reported setting	Review therapy-associated suppression
Organ transplantation	Immunosuppressive treatment association	Review transplant medications
Advanced age	Also encountered in older adults	Do not assume HIV infection

HIV: A marker, not a diagnosis of AIDS

- In a patient with HIV, hairy leukoplakia may indicate weakening immune control.
- It may portend progression to AIDS.
- The lesion alone does not establish an AIDS diagnosis or quantify immune function.
- Its interpretation belongs with current systemic assessment.

Avoid equating “hairy leukoplakia” with “AIDS” in isolation.

Cancer therapy and oral hairy leukoplakia

- Therapy-related immunosuppression is a recognized setting.
- A characteristic lateral-tongue lesion should not be dismissed because HIV is absent.
- Review exposure and timing; Do not infer a particular drug mechanism without evidence.

Transplant-associated immunosuppression

- Robbins specifically includes transplant-related immunosuppression.
- Clinical appearance and tissue findings remain the same diagnostic targets.
- An EBV-associated lesion can emerge despite an unrelated transplant indication.

Older adults and atypical host profiles

- Advanced age is listed among additional immunocompromising contexts.
- Rare reports describe hairy leukoplakia without overt immunodeficiency.
- A normal or incomplete history should prompt assessment, not automatic exclusion.

What is established—and what is not

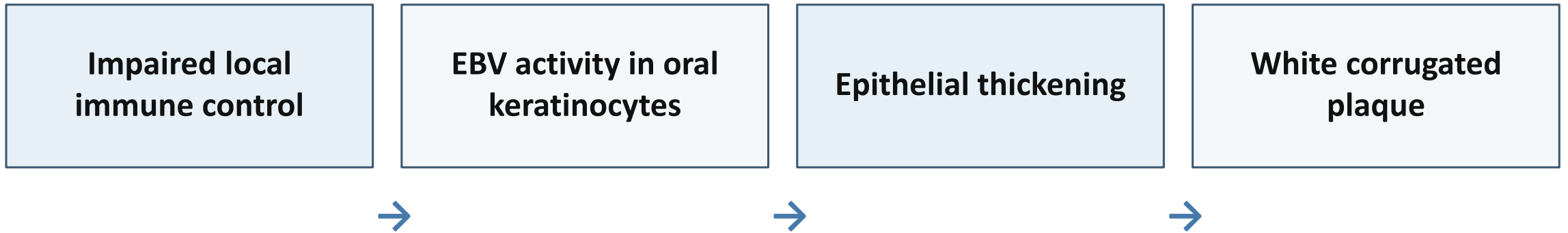
Well supported

- Lesional squamous epithelium contains EBV material.
- Immunosuppression is a major clinical association.
- Viral activity is prominent in superficial differentiated cells.

Do not overclaim

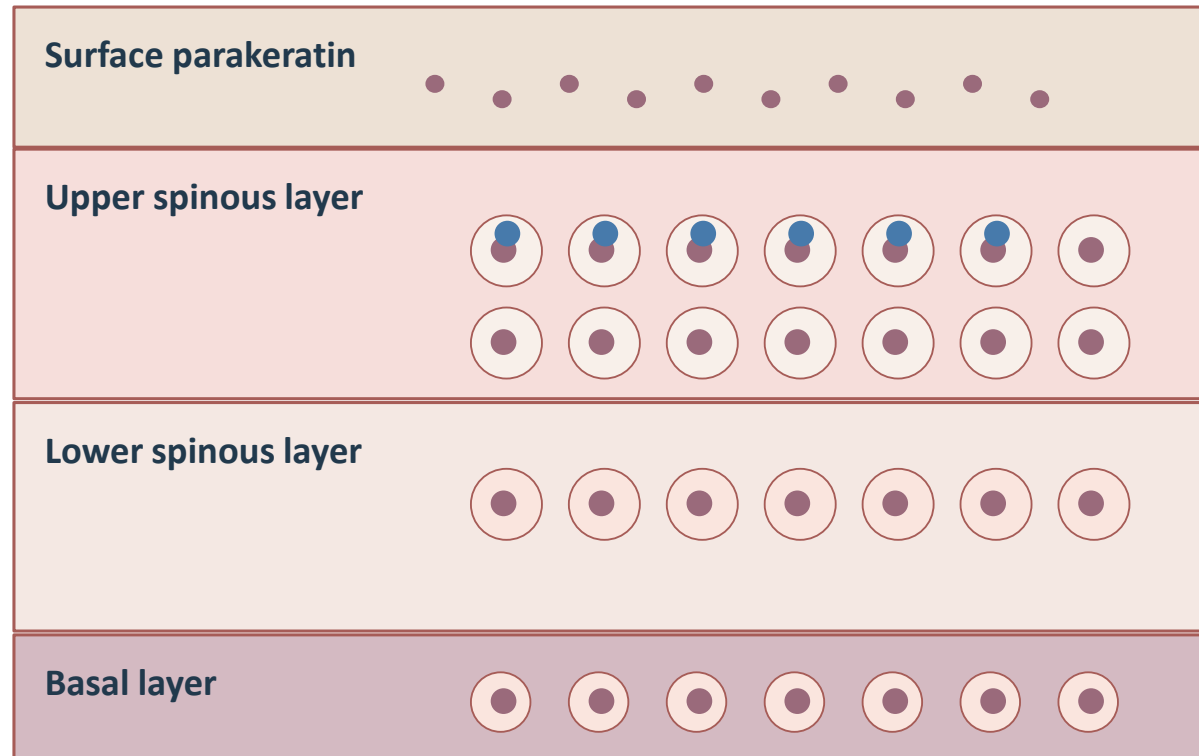
- The specific trigger in each patient is not usually known.
- The reason for the lateral-tongue predilection is not fully established.
- EBV seropositivity alone is not lesion confirmation.

Mechanistic sequence: Immune context to plaque



- This is a teaching synthesis; It does not imply that every intermediate molecular mechanism is settled.

EBV-related epithelial involvement



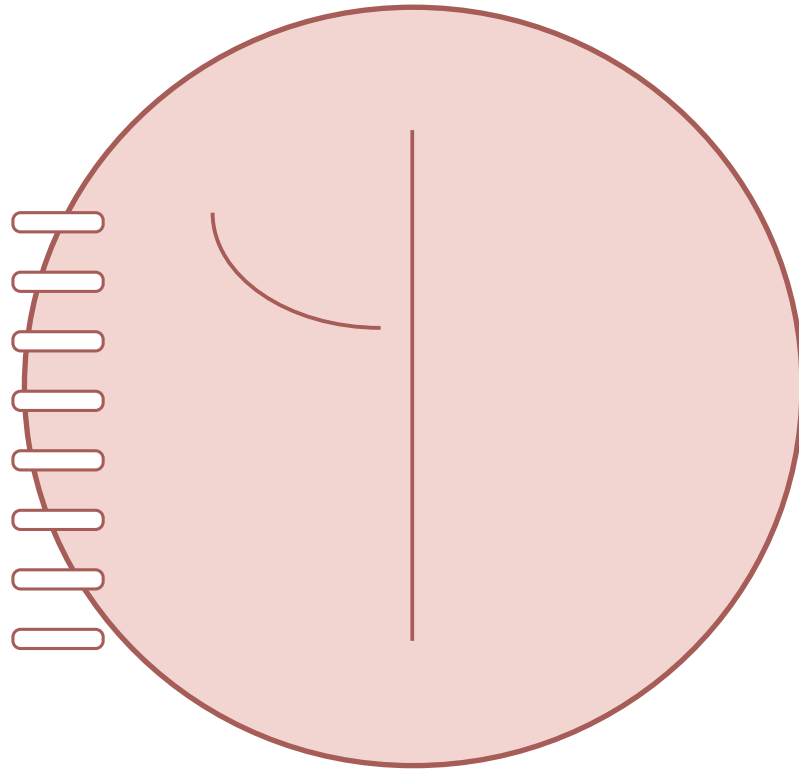
- Viral activity is concentrated in the more differentiated superficial epithelial compartment.
- The upper spinous layer is where characteristic swollen cells are described.
- Basal invasion is not required to explain the surface lesion.

Gross appearance: Why it is distinctive

- White confluent patches form a non-wipeable mucosal plaque.
- The surface is fluffy, corrugated or “hairy” rather than smooth.
- Keratotic epithelial thickening produces the distinctive raised contour.

Site + texture + non-removability is the core clinical pattern.

Lateral border localization



Lateral border

- Inspect both lateral surfaces of the tongue directly.
- A lesion on the lateral border is more characteristic than a random oral white patch.
- Distribution remains supportive—not diagnostic—evidence.

White confluent mucosal patches

- “White” describes the visible surface phenotype, not a microscopic diagnosis.
- “Confluent” indicates that neighboring areas form a larger continuous plaque.
- The surface must still be characterized by its texture and response to wiping.

What does “hairy” mean?

- The word refers to a fluffy, shaggy or corrugated surface texture.
- It does not indicate hair follicles or true hair on oral mucosa.
- Exaggerated superficial keratin contributes to the clinical contour.

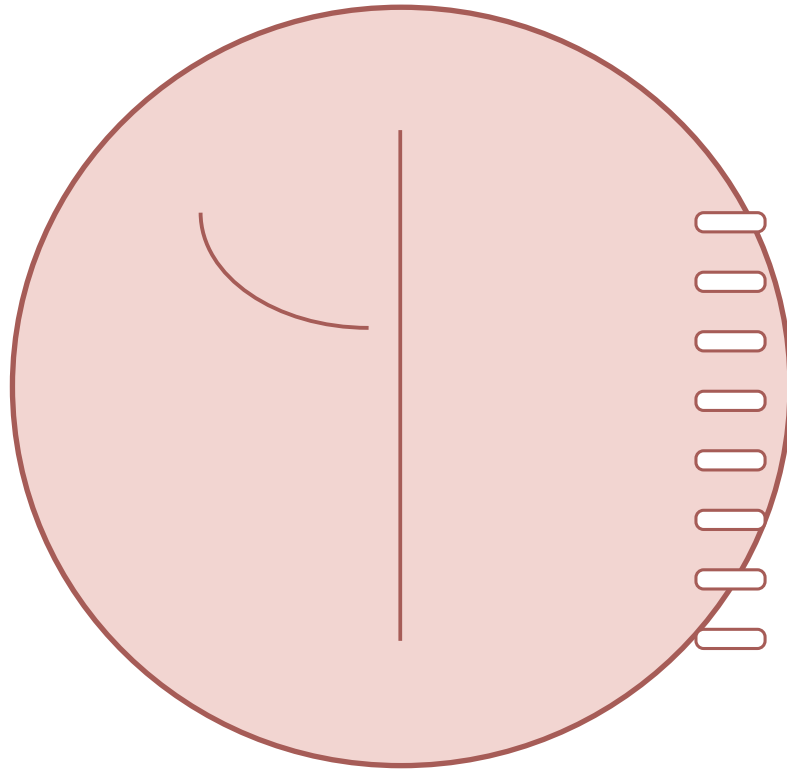
White appearance and keratin

- The superficial epithelial compartment exhibits conspicuous keratin accumulation.
- An optically pale surface is consistent with the hyperkeratotic pathology.
- The visible phenotype must be interpreted together with EBV-related cytopathic changes.

The non-scrapability test

- A characteristic hairy-leukoplakia plaque cannot be removed by gentle scraping.
- Pseudomembranous thrush usually separates, exposing an erythematous surface.
- Wiping is one bedside discriminator; It is not a substitute for the entire workup.

Distribution: Unilateral or bilateral



Lateral border

- Lesions may affect one or both lateral borders.
- Symmetry is variable and should not be treated as a required criterion.
- Note any additional oral lesions separately.

Symptoms may be minimal

- Oral hairy leukoplakia is often asymptomatic.
- An obvious lesion can be discovered incidentally during oral examination.
- Symptom burden alone should not determine whether a white lesion merits assessment.

Candida superinfection changes the surface

**EBV-associated keratotic
plaque**

Secondary Candida colonization

More conspicuous “hairiness”



- Candida may coexist with hairy leukoplakia; Its presence does not change EBV causation.
- Interpret fungal staining together with the rest of the lesional findings.

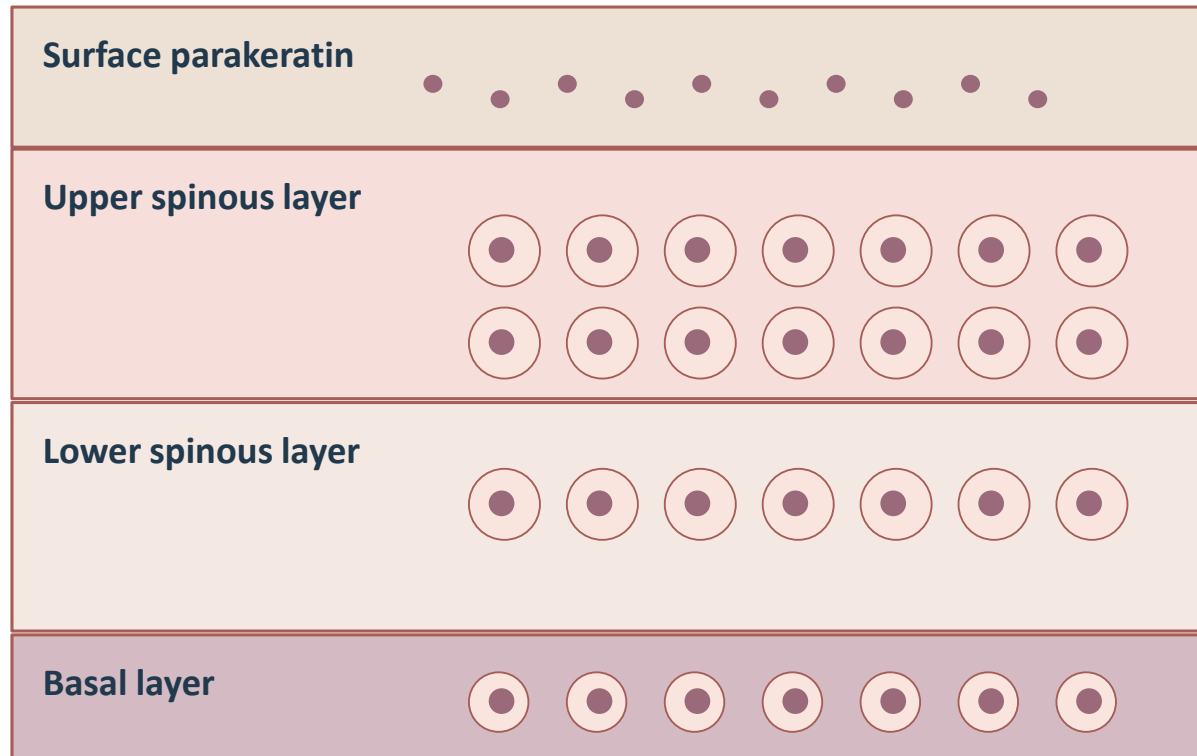
Observed clinical clues

Observation	Typical hairy leukoplakia	Diagnostic weight
Color	White	Sensitive visually, not specific
Surface	Fluffy or corrugated	Supports pattern recognition
Site	Lateral tongue	Strong distribution clue
Gentle wiping	Plaque remains	Helpful vs pseudomembranous thrush
Immune setting	Frequently immunosuppressed	Raises pretest suspicion

Histology: A recognizable combination

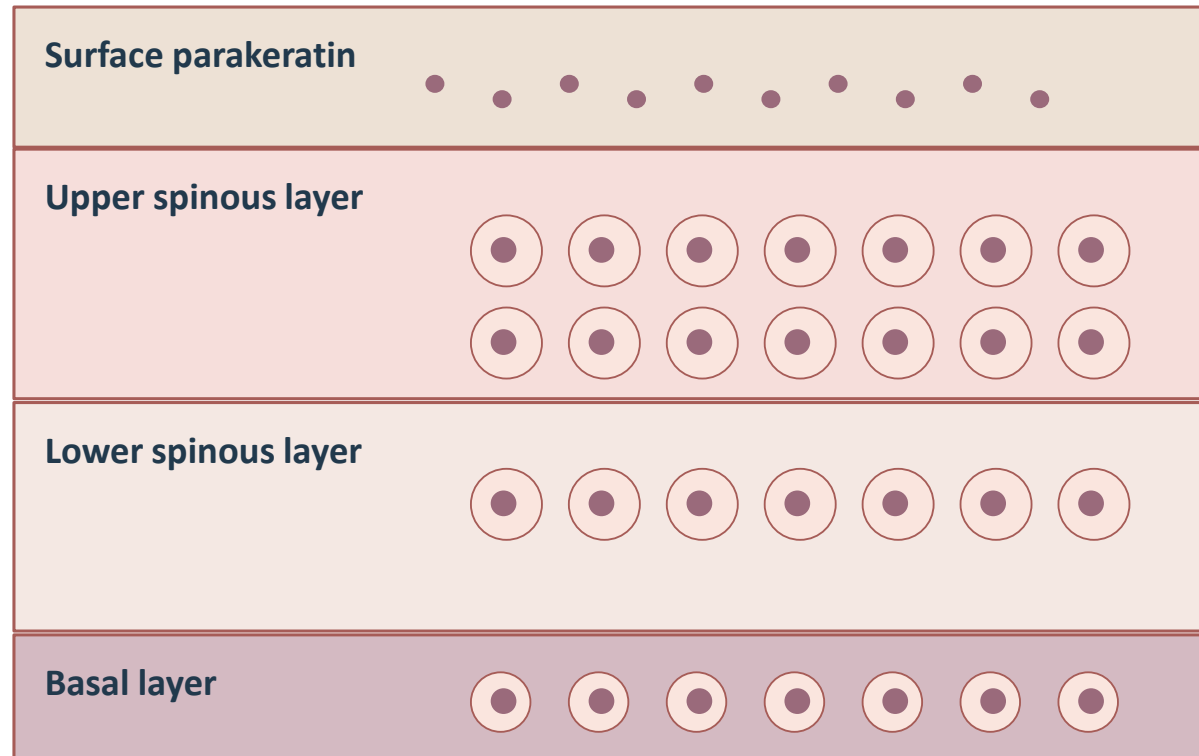
- Prominent hyperparakeratosis at the surface.
- Epithelial acanthosis (expansion of squamous epithelial thickness).
- Ballooned pale cells in the upper spinous layer.
- EBV is demonstrable within the lesional epithelium.

Orient to squamous epithelial layers



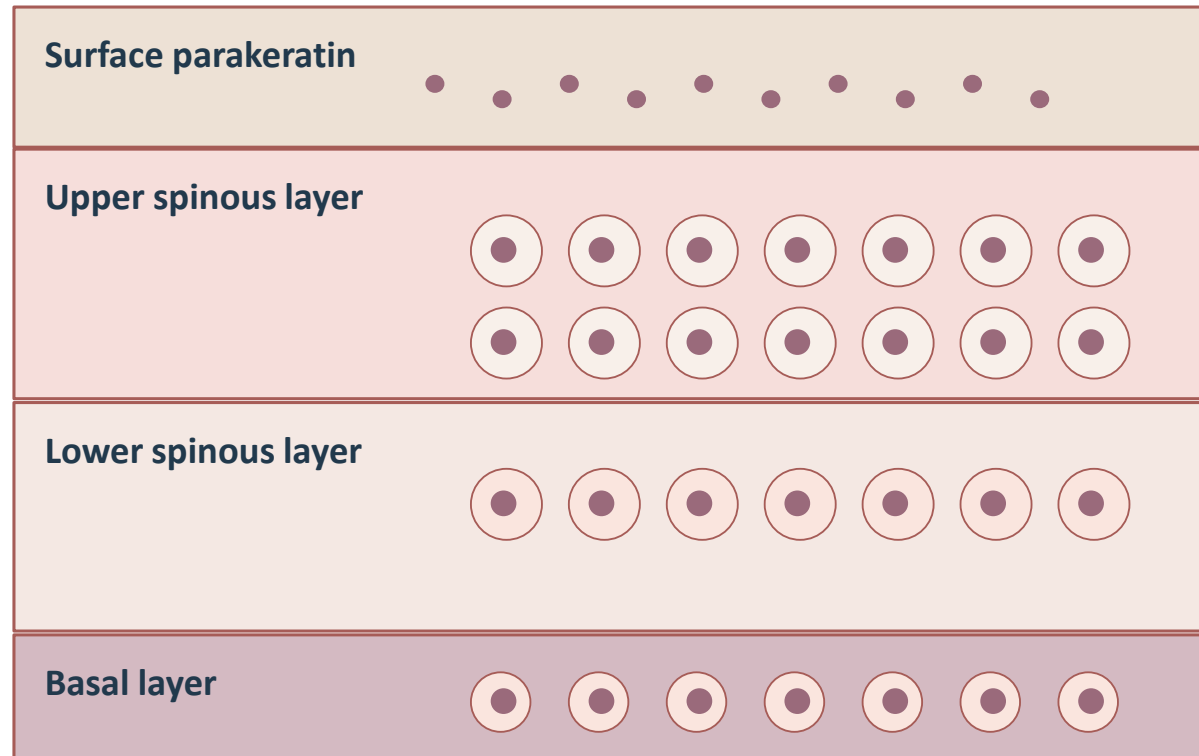
- Parakeratin forms the most superficial covering.
- The spinous compartment lies beneath and contains differentiating keratinocytes.
- The basal cell layer remains the deep epithelial boundary.
- Distribution of the abnormal cells matters as much as their morphology.

Hyperparakeratosis



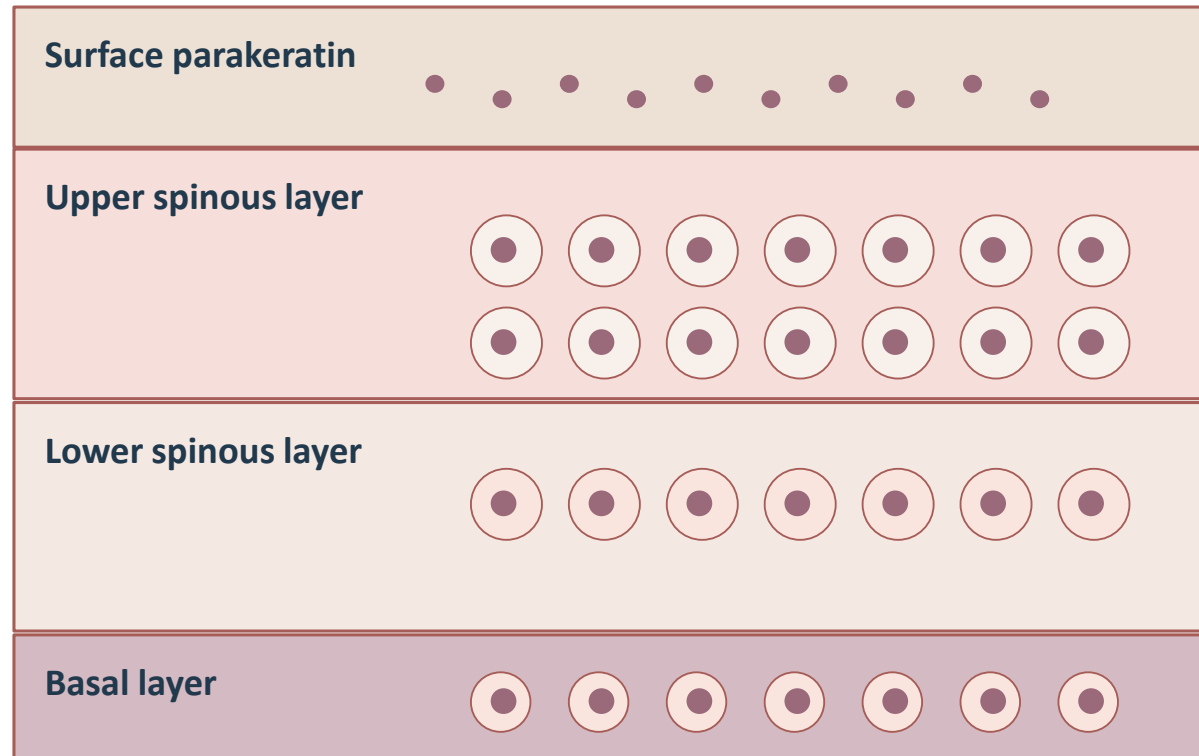
- The surface keratin is conspicuously thickened.
- Parakeratosis denotes retention of nuclei within the keratinized surface layer.
- This is a key histologic component but not specific to EBV by itself.

Acanthosis expands the epithelium



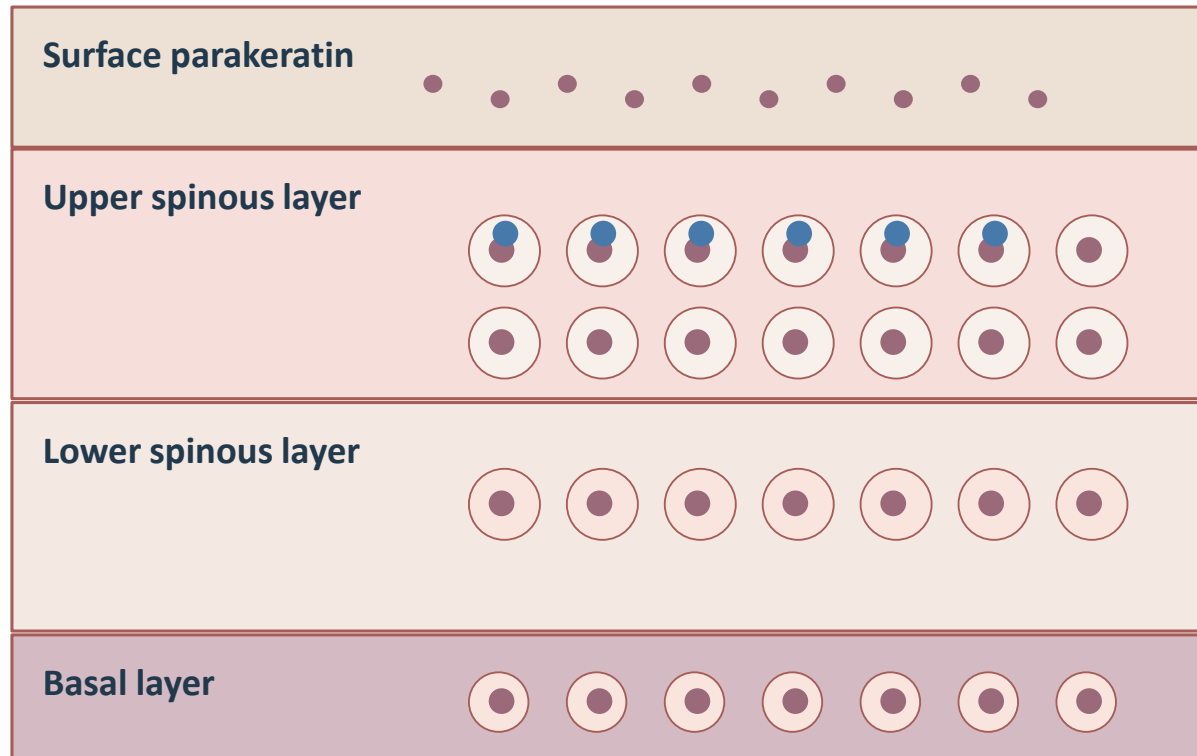
- Acanthosis denotes thickening of the prickle-cell (spinous) compartment.
- It accounts for increased epithelial thickness rather than stromal tumor invasion.
- Combine acanthosis with superficial cytopathic changes for pattern recognition.

Ballooned keratinocytes



- Pale, swollen epithelial cells appear in the upper spinous layer.
- The ballooned-cell band is an important clue to EBV-associated cytopathic change.
- A ballooned cell is not in itself a virus-specific laboratory test.

Why the upper spinous position matters



- The distribution places affected cells toward epithelial maturation.
- It corresponds to descriptions of productive superficial EBV infection.
- This relationship is more informative than identifying an isolated pale cell.

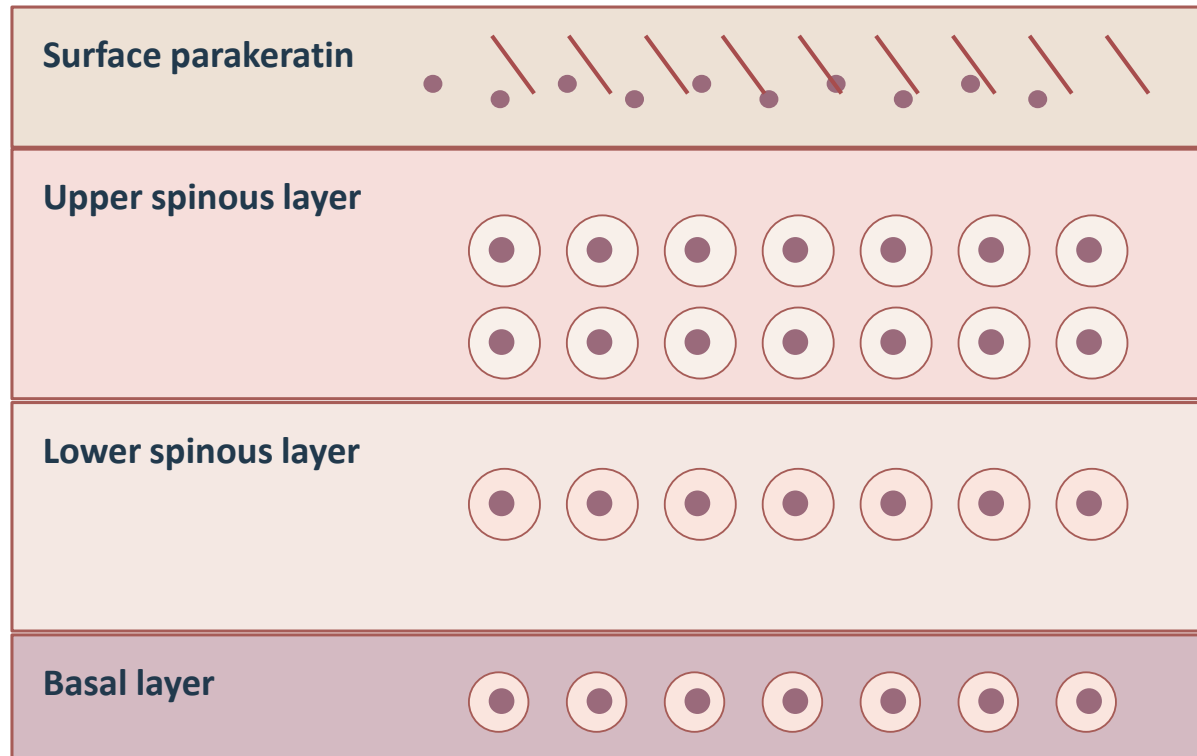
Nuclear changes and HPV resemblance

- Koilocyte-like superficial squamous cells may show perinuclear clearing.
- Nuclear “beading” has been reported in EBV-associated lesions.
- Resemblance to HPV-related koilocytosis can mislead interpretation.
- Demonstration of lesional EBV resolves the viral-attribution question.

Inflammation may be inconspicuous

- Published histologic descriptions emphasize sparse underlying inflammation.
- A dramatic inflammatory response is not required for a pronounced epithelial plaque.
- Low inflammatory activity does not negate a viral etiology.

Superimposed superficial Candida



- Fungal hyphae may be present in superficial keratin.
- Colonization may coexist with the EBV-driven epithelial abnormality.
- PAS fungal staining can demonstrate fungi but cannot establish EBV causation.

Histopathology: Integrate rather than isolate

Epithelial architecture

- Thick superficial parakeratin.
- Expansion of the spinous compartment.
- Band of swollen cells in the upper squamous layers.

Etiologic demonstration

- Demonstrate EBV within epithelial lesional cells.
- Investigate Candida if superficial organisms are suspected.
- Interpret with site, appearance and immune status.

Evidence linking EBV to the lesion

Characteristic morphology

EBV nucleic acid or protein in
cells

Clinicopathologic correlation

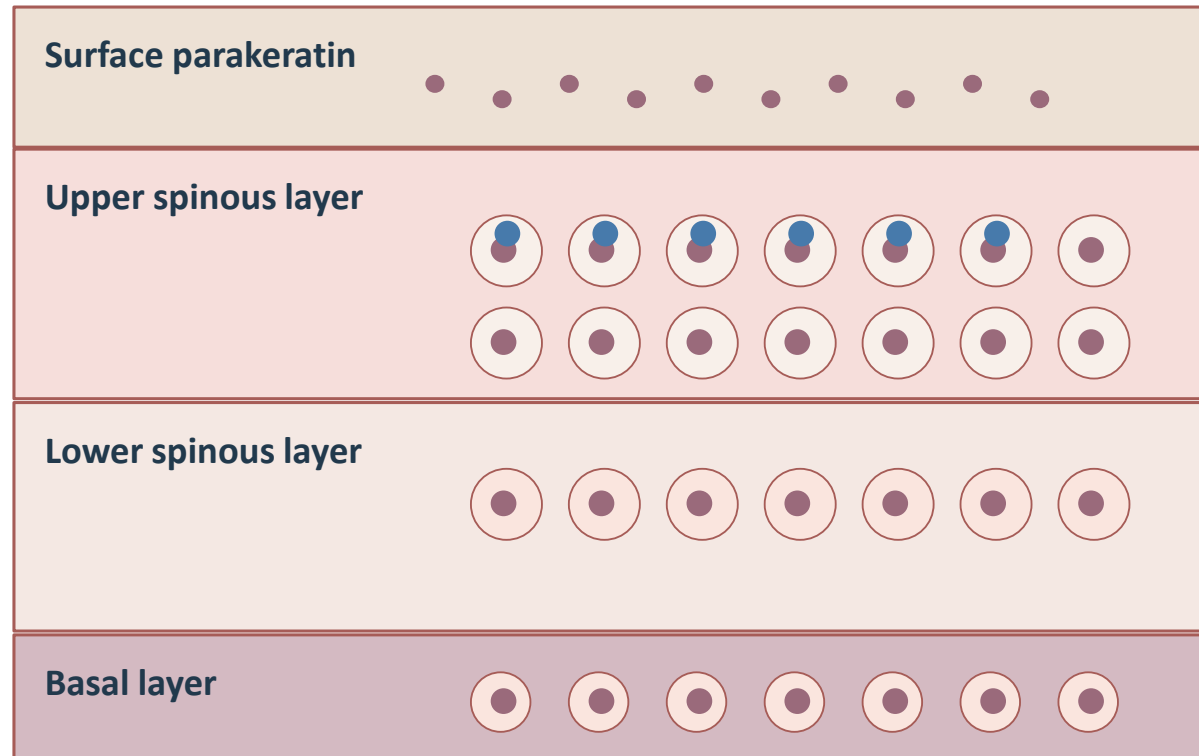


- Viral demonstration supplies stronger etiologic support than morphology alone.
- Lesional epithelial localization is important to the interpretation.

EBV in situ hybridization

- In situ hybridization detects EBV nucleic acids in tissue sections.
- EBV-encoded RNA (EBER) testing is used for confirmatory assessment.
- Positive signal in lesional epithelial cells supports an EBV-associated process.
- Assess staining localization together with morphology and appropriate controls.

A schematic reading of EBV-positive epithelium



- Identify the signal within squamous epithelial cells—not merely on the surface.
- Review the compartment distribution and staining specificity.

What individual investigations answer

Investigation	What it shows	What it does not prove alone
H&E	Acanthosis, parakeratin, ballooning	EBV etiology with certainty
EBV ISH	Lesional viral nucleic acid	Clinical context without morphology
PAS fungal stain	Superficial fungal organisms	Cause of EBV lesion
Clinical examination	Site, texture, wipe response	Histologic exclusion of dysplasia

Clinical recognition and confirmation

- A classic presentation suggests hairy leukoplakia clinically.
- Biopsy and lesional EBV assessment provide stronger diagnostic confirmation.
- The threshold for tissue sampling changes if the appearance is atypical or suspicious.
- Avoid labeling an unexplained high-risk white lesion on appearance alone.

When a white lesion needs tissue assessment

- Persistent or unusual non-removable white lesions merit differential diagnosis.
- Erythema, ulceration, induration or a focal atypical area should not be ignored.
- The need to exclude dysplasia or carcinoma is distinct from confirming EBV.

What a defensible pathology report addresses

Descriptive findings

- Specimen site and epithelial architecture.
- Parakeratosis, acanthosis and upper-level ballooning.
- Any suspicious dysplasia or atypia.

Etiology and modifiers

- Status and epithelial distribution of EBV studies.
- Presence of superficial fungi when assessed.
- Clinicopathologic concordance or unresolved uncertainty.

Hairy leukoplakia versus thrush

Feature	Hairy leukoplakia	Pseudomembranous thrush
Dominant cause	Epstein–Barr virus	Candida
Surface	Keratotic, corrugated plaque	Fibrinofungal pseudomembrane
Wiping	Classically not removable	Typically removable
After removal	Plaque generally persists	Erythematous mucosa exposed
Coexistence	Candida may colonize OHL	Fungal disease can occur alone

Scrapability is helpful but not infallible

- A non-removable plaque favors a keratotic process over classic thrush.
- Some candidal disease is not pseudomembranous.
- Candida may be superimposed on hairy leukoplakia.
- Histology and microbiology resolve ambiguous mixed lesions.

Hairy leukoplakia versus conventional leukoplakia

Feature	Oral hairy leukoplakia	Conventional leukoplakia
Basis	Named EBV-associated lesion	Unexplained white plaque after exclusion
Common site	Lateral tongue	Variable oral mucosal sites
Immune link	Often immunosuppression	Not required by definition
Cancer framing	Not ordinarily classified as OPMD	Potentially malignant clinical category
Confirmatory focus	EBV with compatible morphology	Histology to assess dysplasia

The word “leukoplakia” can mislead

- Conventional leukoplakia is a diagnosis of exclusion for an unexplained white plaque.
- Hairy leukoplakia has an identified viral etiology and characteristic morphology.
- Do not transfer premalignant risk estimates from conventional leukoplakia to OHL.
- Unexpected atypia requires assessment on its own merits.

Other plausible non-removable white lesions

Frictional or lichenoid patterns

- Trauma-related keratosis depends on a credible local irritant.
- Oral lichen planus may form reticulated, lace-like white lines.
- Anatomy and morphology determine the next diagnostic step.

Cytopathic viral patterns

- HPV can show koilocytosis; OHL may look koilocyte-like.
- Do not assign viral etiology by cell shape alone.
- EBV studies should localize to the epithelial lesion.

Differential diagnosis: Reasoning matrix

Finding	Most supportive possibility	Next distinction
Scrapable white membrane	Thrush	Surface fungus and erythema
Corrugated lateral-tongue plaque	Hairy leukoplakia	EBV and epithelial morphology
Reticular white striae	Lichen planus	Clinical pattern and histology
Unexplained persistent white plaque	Conventional leukoplakia	Exclude other causes; Biopsy
Atypical ulcerated or indurated area	Potential dysplasia/carcinoma	Targeted tissue examination

Practical approach to a lateral-tongue white plaque

Describe site, contour, distribution and removability.



Review immunosuppressive disease and treatment exposure.



Compare EBV-associated plaque with Candida and other keratoses.



Sample atypical or suspicious lesions; Demonstrate EBV when confirmation is needed.



Integrate pathologic findings with the clinical history.

How clinical management is framed

- Oral hairy leukoplakia itself is often a low-morbidity, asymptomatic lesion.
- Recognition may trigger assessment of underlying immune status.
- In patients with HIV, effective antiretroviral therapy is part of systemic immune care.
- Clinical follow-up addresses persistence, new symptoms or altered morphology.

Lesion-directed treatment is usually secondary

- Mild asymptomatic lesions often need no specific local intervention.
- More troublesome lesions may receive clinician-directed treatment.
- An antiviral response does not replace evaluation of a suspicious white plaque.
- Do not treat presumed OHL empirically when malignancy remains a concern.

Case 1 — immune context

A person living with HIV has a persistent, corrugated white plaque on the lateral border of the tongue. The plaque does not wipe away.

QUESTION

Which diagnosis best links the site, texture and immune history?

Oral hairy leukoplakia is strongly suggested.

EBV is the implicated agent; Review clinical history and consider confirmation if the appearance is atypical.

Case 2 — transplant recipient

A patient receiving transplant-associated immunosuppression develops a non-removable white lateral-tongue plaque. HIV infection is not reported.

QUESTION

Does absence of known HIV exclude hairy leukoplakia?

No. HIV infection is not a prerequisite.

Transplant-related immunosuppression is a recognized setting; Evaluate the lesion and clinical context.

Case 3 — removable white plaque

A white creamy plaque is readily removed, exposing an erythematous mucosal surface.

QUESTION

Which diagnosis is more consistent with this wiping response?

Pseudomembranous oral candidiasis (thrush).

This contrasts with the intrinsically keratotic and non-removable plaque of hairy leukoplakia.

Case 4 — atypical plaque

An older adult has a persistent irregular white lesion with a focal ulcerated or indurated region on the lateral tongue.

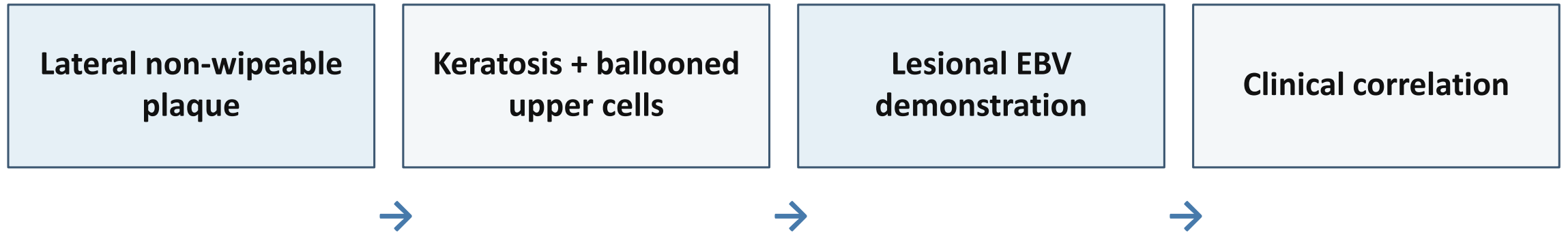
QUESTION

Is pattern recognition alone sufficient to declare hairy leukoplakia?

No: Exclude dysplasia or carcinoma by appropriate assessment.

A possible EBV-associated lesion must not distract from evaluation of an atypical area.

Integrated interpretation



- The complete diagnosis uses phenotype, histologic pattern and viral evidence.
- Candida may be a superimposed modifier rather than the primary explanation.

Core conclusions

- Oral hairy leukoplakia is an EBV-associated, often immunosuppression-linked oral lesion.
- The classic lesion is a non-removable, corrugated white plaque of lateral tongue.
- Hyperparakeratosis, acanthosis and ballooned upper spinous cells are key findings.
- EBV localization supports confirmation; Candidiasis and conventional leukoplakia require distinction.

Selected sources and image provenance

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Source images were located but could not be embedded; no synthetic clinical specimens were used.