

Commentary

When “Sinusitis” Is Actually Cancer: Diagnostic Red Flags for Unilateral or Refractory Sinonasal Disease

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Abstract

Sinonasal malignancies are rare, accounting for fewer than 3% of head and neck cancers, but their early presentation often overlaps with benign rhinosinusitis. Unilateral nasal obstruction, rhinorrhoea, facial pressure, and intermittent epistaxis may initially appear inflammatory, which contributes to diagnostic delay and late-stage presentation. Recent clinical guidance emphasizes that persistent unilateral symptoms, especially when accompanied by bleeding, focal endoscopic abnormalities, or orbital, dental, or neurologic features, should prompt specialist assessment rather than repeated empiric treatment. This commentary argues that the central clinical problem is not failure to recognize advanced disease, but failure to reconsider a benign working diagnosis when “sinusitis” stops behaving like sinusitis. This commentary proposes a pragmatic triage framework for unilateral or refractory sinonasal disease that prioritizes pattern recognition, focused nasal endoscopy, appropriate imaging, and timely biopsy where indicated. Its contribution is to connect three clinically relevant observations: sinonasal malignancy is rare and therefore easily deprioritized; unilateral, progressive, refractory, bleeding, orbital, dental, or neurologic features should prompt earlier cancer exclusion; and emerging AI-assisted endoscopy should currently be viewed only as a triage adjunct, not a substitute for imaging, histopathology, or multidisciplinary assessment.

Keywords: sinonasal malignancy; rhinosinusitis; early diagnosis; unilateral sinonasal disease; nasal endoscopy; artificial intelligence

1. Introduction

Sinonasal malignancies, although rare, carry a disproportionate clinical burden because they are difficult to recognize early and often present close to the orbit, skull base, and cranial nerves. Population-based data estimate the incidence of sinonasal malignancy at approximately 0.556 cases per 100,000 population, and these tumors account for fewer than 3% of head and neck cancers, and <1% of all malignancies affecting humans [1,2]. Their rarity is part of the diagnostic problem. Most clinicians will see far more inflammatory sinonasal disease than cancer, so the initial assumption is usually benign disease unless a clear warning sign supporting a diagnosis of malignancy is present.

What makes these tumors especially deceptive is that their early symptoms overlap with usual clinical rhinosinusitis. Nasal obstruction, rhinorrhea, facial pressure or pain, reduced smell, and intermittent epistaxis are all common in benign disease and can also mark the first phase of a sinonasal neoplasm. Early symptoms are nonspecific enough that many patients are diagnosed only when disease is already locally advanced or metastatic.



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Evidence suggests that more than 80% of sinonasal squamous cell carcinomas are diagnosed at T3 or T4 stage [3]. Primary-care data support this ambiguity. In a matched case-control study of 155 cases and 697 controls from UK electronic records, symptoms associated with sinonasal cancer included nasal mass, head and neck lump, epistaxis, rhinorrhoea, visual disturbance, sinusitis, sore throat, otalgia, headache, and raised white cell count. Epistaxis had an odds ratio of 17, rhinorrhoea 14, and sinusitis 7.3. However, the positive predictive values remained below the 3% NICE urgent-referral threshold; combined PPVs for epistaxis with rhinorrhoea, epistaxis with sinusitis, and rhinorrhoea with sinusitis were each 0.62% [4]. This explains why indiscriminate investigation is inappropriate, but also why safety-netting and escalation are important when symptoms cluster, persist, recur on one side, or are associated with focal findings.

The clinical challenge, then, is not to treat every patient with sinus symptoms as having cancer. It is to identify the subgroup whose presentation is atypical enough that the working diagnosis should shift from “sinusitis” to “sinusitis with red flags until proven otherwise.” Laterality is especially important in that distinction. In a surgical cohort from Emory, unilateral sinonasal disease was significantly associated with both benign neoplasms and malignancy. Among patients with unilateral disease, malignancy accounted for 19% of final diagnoses [5]. Earlier algorithmic work on unilateral sinus disease similarly found a non-trivial malignant yield, particularly when a unilateral polyp or mass was seen on endoscopy [6].

This commentary argues that delayed diagnosis is often less a failure of access than a failure of pattern recognition. The most useful response is not indiscriminate imaging, but a practical escalation strategy for unilateral, refractory, progressive, or otherwise atypical sinonasal disease. Against that background, the sections that follow examine why sinonasal cancer is missed, when “sinusitis” stops behaving like sinusitis, which red flags should trigger further work-up, and whether newer tools such as AI-assisted endoscopy could improve triage in everyday practice.

2. When Sinusitis Stops Behaving Like Sinusitis

Concern should increase when symptoms persist despite appropriate medical therapy. In presumed inflammatory rhinosinusitis, appropriate initial medical therapy generally includes saline irrigation and intranasal corticosteroids over several weeks. Antibiotics are reserved for clinical features suggesting acute bacterial rhinosinusitis or acute bacterial exacerbation, rather than used repeatedly for nonspecific chronic symptoms [7].

Failure of treatment is an important warning sign, especially when the problem recurs on the same side. A patient who has repeated courses of antibiotics or steroids with only brief relief should not automatically be labelled as having “refractory chronic rhinosinusitis.” Existing unilateral sinus disease, including polyps or mass algorithms support structured work-up based on endoscopy, imaging, and selective biopsy, although standardized and externally validated pathways for primary-care and general ENT triage remain limited [6,8].

Certain symptoms should shift the clinical frame more quickly. Recurrent unilateral epistaxis, blood-stained discharge, a friable or irregular lesion on endoscopy, facial numbness, cheek swelling, dental symptoms, orbital complaints, or cranial nerve findings are not typical of uncomplicated sinusitis. In patients with unilateral nasal polyposis, epistaxis has been linked with a higher likelihood of neoplastic pathology [9].

The difficulty is that sinonasal cancer often begins with ordinary complaints such as rhinorrhoea, obstruction, or a prior diagnosis of sinusitis. Primary care data show that these symptoms are individually low risk [4], which is why delay is common. The practical lesson is not to over-investigate every patient, but to escalate when symptoms are unilateral,

refractory, progressive, or anatomically focal. At that point, further endoscopy, imaging, and sometimes biopsy become part of good sinus care rather than excessive investigation.

3. Red Flags in Unilateral or Refractory Disease

Laterality is a major warning pattern but not diagnostic in isolation. Bilateral mucosal disease is common in inflammatory rhinosinusitis, but a unilateral presentation deserves closer scrutiny, especially when symptoms persist or recur on the same side. Reviews of unilateral sinonasal disease have emphasized that neoplasms can mimic inflammation and that unilateral pathology should be approached with a lower threshold for endoscopy, imaging, and, when indicated, biopsy [10,11].

Among symptoms, recurrent unilateral epistaxis is particularly important. Nasal obstruction and discharge are common in both benign and malignant disease, but bleeding, blood-stained discharge, or a friable lesion should raise suspicion. In multiple sinonasal tumor series, the typical presenting pattern includes unilateral nasal obstruction with epistaxis, underscoring how often malignancy enters practice through what first looks like routine sinonasal disease [12,13].

Concern should also increase when symptoms extend beyond the usual inflammatory pattern. Facial numbness, cheek swelling, dental symptoms, proptosis, diplopia, visual change, severe unilateral headache, or cranial nerve findings suggest disease that is no longer confined to the mucosa. Patients may present with involvement of nearby structures such as the orbit, brain, or cranial nerves, and that early diagnosis depends heavily on maintaining suspicion when these features appear [11,12].

Endoscopic and imaging findings matter as much as symptoms. A visible unilateral mass, especially if irregular, pigmented, necrotic, highly vascular, or easily bleeding, should not be assumed to be an inflammatory polyp. Likewise, bone destruction, extrasinus extension, or focal soft-tissue mass on imaging should prompt escalation. Office-based biopsy can be useful, but Han et al. [14] found that biopsy alone had limited sensitivity for malignancy and performed best when interpreted alongside preoperative imaging.

The practical message is simple: red flags are rarely dramatic in isolation. What matters is the combination of unilateral disease, treatment failure, bleeding, abnormal endoscopy, or symptoms pointing to local extension. When those features cluster, the question is no longer whether to continue treating sinusitis more aggressively, but whether the diagnosis itself needs to be revised. Table 1 describes these clinical patterns and next line of action.

Table 1. Clinical features that should prompt escalation beyond routine sinusitis management.

Clinical Patterns or Finding	Why It Matters	Recommended Next Step	Urgency Levels	Key Evidence
Persistent unilateral nasal obstruction	Laterality is one of the clearest signals that disease may not be routine inflammatory rhinosinusitis. Unilateral disease has a higher neoplastic yield than bilateral disease.	Do not continue repeated empiric treatment without reassessment; perform careful nasal endoscopy and consider imaging if symptoms persist.	Expedited specialist assessment	Unilateral disease was significantly associated with neoplasia in surgical cohorts [5,6].

Table 1. *Cont.*

Clinical Patterns or Finding	Why It Matters	Recommended Next Step	Urgency Levels	Key Evidence
Recurrent unilateral epistaxis or blood-stained discharge	Bleeding may occur in inflammation, but repeated unilateral bleeding is a classic warning feature in sinonasal tumors and should raise suspicion, especially when paired with obstruction or a focal lesion.	Escalate to specialist assessment, endoscopy, and imaging rather than treating as uncomplicated sinusitis alone.	Expedited to urgent, depending on severity and associated findings	Matched primary-care case-control study: epistaxis OR 17; combined PPV with rhinorrhoea/sinusitis 0.62% [4,15].
Visible unilateral mass or polyp, especially if friable, irregular, pigmented, or necrotic	Not all unilateral polyps are inflammatory; benign and malignant neoplasms can mimic inflammatory polyps on presentation.	Image first if lesion is suspicious, then obtain biopsy when appropriate.	Urgent specialist assessment	Algorithmic and unilateral-disease studies emphasize this distinction [5,6].
Persistent or recurrent symptoms despite appropriate medical therapy	Failure of standard treatment should trigger reconsideration of the diagnosis, particularly when relapse is rapid or always affects the same side.	Reframe the problem as diagnostic rather than therapeutic; proceed to endoscopy and selective imaging.	Expedited	Diagnostic algorithms for unilateral disease recommend structured work-up rather than repeated empiric treatment [6,15].
Facial numbness, cheek swelling, dental pain, or palatal symptoms	These features suggest extension beyond the mucosa and are atypical for uncomplicated sinusitis.	Arrange prompt imaging and specialist referral.	Urgent	Observational study suggests these as concerning symptoms of locally invasive disease [16].
Orbital symptoms: diplopia, proptosis, visual change, epiphora	Orbital symptoms may indicate spread to adjacent structures and should not be attributed to simple sinusitis without further work-up.	Urgent imaging, usually CT with MRI when soft-tissue extent is a concern, and urgent ENT/skull-base review.	Urgent/emergency if visual loss	Guidelines for sinonasal malignancy emphasize orbital involvement as a key red flag [7].
Cranial neuropathy, severe focal headache, or neurologic features	Neurologic symptoms may reflect skull-base, perineural, or intracranial extension and fall outside the expected spectrum of routine rhinosinusitis.	Urgent imaging and specialist referral; MRI is usually helpful when skull-base or intracranial extension is suspected.	Urgent	Guideline and review literature support escalation when neurologic features are present [15,17].
Bone destruction, extrasinus extension, or focal soft-tissue mass on imaging	These are imaging features more consistent with neoplasia or aggressive pathology than with uncomplicated inflammatory disease.	Proceed to targeted biopsy and oncology-capable referral pathway.	Urgent	CT/MRI imaging and unilateral-disease algorithms support this approach [6,18].

PPV: Positive predictive values.

4. A Practical Diagnostic Algorithm

A useful algorithm should help clinicians decide who can safely remain on a routine inflammatory rhinosinusitis pathway and who requires earlier cancer exclusion. The proposed pathway is an expert synthesis of available observational studies and guideline recommendations. It is not presented as a validated evidence-based guideline. The first step is pattern recognition. Bilateral, fluctuating, treatment-responsive symptoms without focal findings can usually remain on a standard rhinosinusitis pathway. In contrast, unilateral, persistent, recurrent, progressive, bleeding, or anatomically focal symptoms should trigger

diagnostic reassessment. This distinction is supported by studies of unilateral sinonasal disease, where neoplasia represents a clinically meaningful minority of cases, including 19% malignancy among unilateral cases in one surgical cohort and 14% malignancy among patients with unilateral mass or polyp on endoscopy in another cohort [5,6].

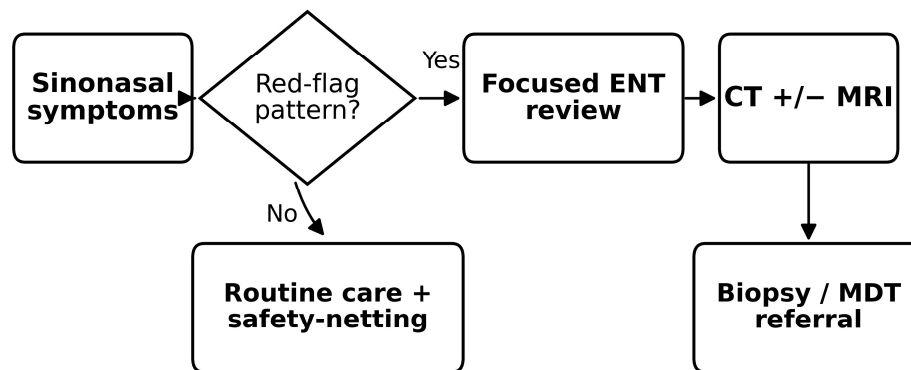
The second step is focused reassessment rather than reflex escalation of medical therapy. History should document laterality, duration, progression, prior short-lived treatment responses, epistaxis, facial numbness, dental symptoms, orbital complaints, smoking history, occupational exposures, and prior malignancy. Nasal endoscopy should then look specifically for unilateral mass, friability, irregular surface, pigmentation, necrosis, or unexpected vascularity. At this stage, the practical question is not whether cancer is likely in statistical terms, but whether the presentation still behaves plausibly as uncomplicated sinusitis. Recurrent unilateral obstruction, unilateral bleeding, or an abnormal focal lesion should move the case into a higher-risk pathway.

The third step is imaging before biopsy when a suspicious mass is present. Computed tomography (CT) remains the best initial test for defining bony change, sinus opacification pattern, and local anatomy. Magnetic resonance imaging (MRI) becomes particularly useful when there is concern for soft-tissue characterization, orbital or skull-base extension, intracranial spread, or perineural disease. Comparative work in unilateral maxillary sinus opacification suggests that MRI is more specific than CT for characterization and may reduce diagnostic delay in selected cases [19]. Imaging before biopsy is also a safety issue. Radiologic assessment can reduce morbidity from invasive testing of lesions such as angiofibroma or encephalocele, which may mimic inflammatory disease [20]. This recommendation should not be interpreted as a reason to delay diagnosis where imaging access is limited. In centres without timely CT or MRI, the appropriate action is urgent referral to a service that can arrange imaging and safe biopsy in parallel, rather than repeated empirical treatment. If a lesion is anterior, clearly mucosal, non-pulsatile, and judged safe by an experienced ENT surgeon, biopsy may proceed according to local practice. However, biopsy should be deferred until imaging is obtained when the lesion is superior, posterior, highly vascular, pulsatile, associated with skull-base defect or CSF leak, or when vascular tumor, encephalocele, orbital extension, or intracranial extension is possible.

The fourth step is tissue diagnosis when imaging and endoscopy remain concerning. Office-based endoscopic biopsy can be useful and is generally safe in experienced hands, but its limitations should be acknowledged. Biopsy findings should be interpreted alongside imaging and clinical suspicion, and persistently discordant cases should proceed to formal surgical evaluation or repeat sampling.

In practice, the algorithm can therefore be summarized as follows: (1) identify unilateral, refractory, progressive, or red-flag symptoms; (2) perform focused endoscopy; (3) obtain CT, with MRI when soft-tissue extent or tumor characterization is a concern; (4) biopsy suspicious lesions after appropriate imaging; and (5) refer early to an ENT/skull-base or head-and-neck oncology pathway when imaging, biopsy, or symptoms suggest neoplasia. The goal is not to image every patient with sinus symptoms. It is to reduce delays in the subgroup whose disease has already stopped behaving like routine inflammation. Figure 1 schematically illustrates an algorithm of actions clinicians can follow to achieve early diagnosis and minimise delays in the diagnosis of sinonasal tumors.

Red flags: unilateral, persistent/recurrent, progressive, epistaxis/bleeding, focal lesion, orbital/dental/neurologic features



Avoid blind biopsy if vascular, pulsatile, skull-base-adjacent, or possible encephalocele.

Figure 1. An algorithm intended as a pragmatic triage aid for unilateral, refractory, progressive, or anatomically focal sinonasal disease. CT, computed tomography; MRI, magnetic resonance imaging; ENT, ear, nose, and throat; MDT, multidisciplinary team.

5. Can AI-Assisted Endoscopy Improve Triage?

Possibly, but the current evidence supports a triage role, not a diagnostic replacement role. The practical appeal is obvious because sinonasal tumors are often first seen through routine endoscopy, yet the visual distinction between inflammatory polyps, inverted papilloma, fungal disease, and malignancy can be difficult, especially outside subspecialist practice. Recent studies suggest that machine-learning models trained on endoscopic images can identify and classify sinonasal masses with performance that is good enough to justify further study as a support tool. Levi et al. [21] used 1242 endoscopic images from 311 patients with normal, benign or malignant sinonasal masses via a machine-learning model to identify the presence of a sinonasal mass with 90.5% accuracy and achieved 80.4% test accuracy overall. These results are encouraging, but they do not establish readiness for routine diagnosis. The evidence remains limited by dataset size, single-centre or selected-image design, variable image quality, and the lack of prospective outcome validation.

The appropriate clinical framing is therefore narrow. AI may eventually help flag lesions that deserve earlier imaging, biopsy, or referral, particularly when the visual impression is equivocal or when subspecialist expertise is not immediately available. It should not be presented as a tool that can diagnose sinonasal cancer. Definitive diagnosis still depends on clinical assessment, endoscopy, CT/MRI, histopathology, and multidisciplinary review. Future AI studies should move beyond technical accuracy and test whether AI-assisted triage reduces diagnostic interval, improves appropriateness of imaging and biopsy, or shifts stage at diagnosis.

6. Implications for Clinicians and Future Research

For clinicians, the main implication is straightforward, which is unilateral or persistent sinonasal symptoms should not remain indefinitely on a routine sinusitis pathway. The recent ESMO–EURACAN clinical practice guideline for sinonasal malignancy notes that the common presenting symptoms are unilateral nasal obstruction or discharge, facial or dental pain, and epistaxis. They are often vague and easily mistaken for benign disease, and it advises specialist assessment when such symptoms persist after a short course of medical therapy [15]. This is a useful threshold for practice because it shifts attention from symptom severity alone to pattern, laterality, and persistence.

The UK primary-care data clarify why both over-investigation and under-recognition are risks. In that study, no individual or combined positive predictive value reached the 3% NICE urgent cancer referral threshold. However, the combined PPV for epistaxis with rhinorrhoea, epistaxis with sinusitis, and rhinorrhoea with sinusitis was 0.62% for each combination [4]. This value is low in absolute terms, but clinically meaningful when symptoms are unilateral, recurrent, progressive, treatment-resistant, or accompanied by an abnormal endoscopic finding. The implication is not automatic urgent cancer referral for every patient with rhinorrhoea or epistaxis; it is disciplined safety-netting and earlier escalation when low-PPV symptoms occur in a high-risk pattern.

For rhinologists and ENT surgeons, the important clinical shift is to treat refractory unilateral disease as a diagnostic problem before treating it as a therapeutic problem. Existing unilateral sinus disease algorithms support a structured pathway based on endoscopy, imaging, and selective biopsy because neoplasms can mimic inflammatory disease. In practical terms, that means a visible unilateral mass, recurrent unilateral epistaxis, or symptoms extending beyond the usual inflammatory pattern should prompt CT, consideration of MRI, and timely tissue diagnosis rather than repeated empiric treatment.

The research agenda is equally clear. First, the field needs prospective validation of red-flag criteria for unilateral or refractory disease, ideally with endpoints such as diagnostic interval, stage at diagnosis, and false-positive referral burden. Second, AI tools for sinonasal triage need external, multicentre validation. Current reviews suggest that AI in rhinology is promising but still early, and the recent endoscopy-based mass-classification study, while encouraging, was based on a limited dataset and requires testing across broader populations, devices, and practice settings.

Third, future studies should move beyond technical accuracy alone. What matters clinically is whether earlier recognition changes management with resultant fewer delayed diagnoses, more appropriate imaging, earlier biopsy, or detection at a less advanced stage. That is the standard AI systems will ultimately have to meet if they are to influence care meaningfully. For now, the most defensible position is that careful clinical assessment, disciplined safety-netting, and earlier escalation in unilateral or refractory cases remain the most immediate ways to reduce missed or delayed diagnosis.

7. Conclusions

Sinonasal malignancy is rare, but its rarity should not obscure a consistent clinical problem: early disease may present with symptoms that overlap with benign rhinosinusitis, contributing to diagnostic delay. The risk is greatest when symptoms are unilateral, persistent, progressive, recurrent, or refractory to appropriate treatment, particularly when accompanied by epistaxis, a focal endoscopic abnormality, or orbital, dental, facial, or neurologic features. Current guidance and observational data support a lower threshold for specialist assessment, imaging, and biopsy in these settings.

The practical message is not that every patient with sinus symptoms requires aggressive investigation. It is that patients should not remain indefinitely on a routine sinusitis pathway once the clinical pattern no longer fits uncomplicated inflammatory disease. A structured approach based on laterality, treatment response, endoscopic findings, and timely imaging before biopsy may reduce the risk of missed or delayed diagnosis, although prospective validation is still needed.

AI-assisted endoscopy may eventually strengthen this pathway by helping clinicians identify lesions that deserve earlier escalation, but the evidence remains preliminary. At present, its most realistic value is as a triage adjunct, not a substitute for imaging, histopathology, or multidisciplinary review.

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Abbreviations

The following abbreviations are used in this manuscript:

CT	Computed tomography
MRI	Magnetic resonance imaging
AI	Artificial intelligence
ESMO	European society for medical oncology
EURACAN	European reference network for rare adult solid cancers
MDT	Multidisciplinary team

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