

Computed tomography findings in sinonasal Wegener's granulomatosis

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ABSTRACT

Background: Wegener's granulomatosis (WG), an autoimmune disease, is intimately associated with the sinonasal tract, with involvement reported in 85% of patients during the course of the disease process. The objective of this study was (1) to describe Lund-Mackay (L-M) scores, (2) to delineate patterns of neo-osteogenesis and bony erosion, and (3) to analyze the impact of surgery on the computed tomography (CT) findings of WG patients.

Methods: A retrospective review was performed on 74 patients with WG presenting to a tertiary care referral center. CT analysis was performed and graded by two independent reviewers.

Results: The mean age was 53 years with a male/female ratio of 0.6:1. The average L-M score was 10.0. Neo-osteogenesis was evident in 78% of the patients with overall average neo-osteogenesis score of 4.2 (range, 0–16). Bony erosion was noted on imaging in 62% of patients with overall average score for bony erosion of 2.0 (range, 0–8). Patients having undergone previous sinus surgery compared with no previous surgery had statistically significant elevation of overall L-M, bony erosion, and neo-osteogenesis scores ($p = 0.024, 0.0009, \text{ and } 0.0015$, respectively).

Conclusion: CT imaging in WG patients shows elevated L-M scores and evidence of bony erosion and neo-osteogenesis. Furthermore, surgical manipulation in WG patients is associated with increased bony abnormalities and greater elevations of L-M scores, possibly because of worsening vasculitis and/or inflammation. The presence of concurrent neo-osteogenesis and bony destruction of the paranasal sinuses should raise clinical suspicion of WG in patients presenting with symptoms of chronic rhinosinusitis.

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Key words: Autoimmune disease, bony erosion, chronic rhinosinusitis, computed tomography, neo-osteogenesis, sinus surgery, Wegener's granulomatosis

Wegener's granulomatosis (WG) is a systemic disease process characterized by the presence of necrotizing granulomatous inflammation of the upper and lower airways in addition to small to medium vessel vasculitis.¹ The hallmark of WG is the presence of antineutrophil cytoplasmic antibodies that target proteinase-3, a serine protease enzyme primarily expressed in neutrophils, and initiate an inflammatory reaction that leads to endothelial damage.^{2,3} This leads to a necrotizing granulomatous vasculitis that involves the lungs, kidneys, and/or the upper respiratory tract, including the paranasal sinuses.⁴

Head and neck involvement in WG has been reported to be between 72 and 100%.^{5–7} Rhinologic manifestations are the most commonly reported clinical findings, occurring in >80% of WG patients.⁸ Nasal manifestations include nasal crusting, friable erythematous mucosa, and septal perforation, while paranasal sinus involvement typically manifests as sinusitis or granuloma formation resulting in mucosal thickening, neo-osteogenesis, and/or bone erosion.^{9,10}

Radiographic findings, including computed tomography (CT) and magnetic resonance imaging, may serve as an important adjunct in facilitating accurate diagnosis in sinonasal WG.^{11–13} In particular, the presence of mucosal thickening in conjunction with bony destruction and/or bony thickening of the paranasal sinus wall should raise the clinical suspicion of WG.¹⁴ However, the currently available studies are limited by small sample size.^{12,14–16}

This relative paucity of imaging data on WG underscores the importance for larger studies to better elucidate the CT profile in these patients. This may facilitate better understanding of paranasal sinus changes and

enhance accurate diagnosis in WG. With this in mind, the goal of this study was to establish the Lund-Mackay (L-M) score and to further characterize bony changes in the paranasal sinuses associated with WG.

MATERIALS AND METHODS

A retrospective review of medical records and paranasal sinus CTs was performed on all patients with WG referred for sinonasal complaints to the Section of Nasal and Sinus Disorders at the Cleveland Clinic Head and Neck Institute from March 2001 to July 2008. Patient selection criteria included the diagnosis of WG as established by the Cleveland Clinic Foundation Department of Rheumatology and the presence of a 3-mm coronal or 1-mm axial CT with triplanar reconstruction of the paranasal sinuses performed at the Cleveland Clinic Foundation. CT imaging of the paranasal sinuses was performed as part of the comprehensive rhinologic evaluation. Institutional Review Board approval was obtained before the study.

Seventy-four patients were included in the analysis. The medical records were reviewed for demographic data, comorbidities, WG manifestations, and previous sinonasal surgeries. CT imaging was independently reviewed and graded by two authors; consensus was developed for all diverging data points by joint review.

Each CT scan was graded for mucosal disease according to the L-M staging system.¹⁷ Right and left frontal, maxillary, anterior ethmoid, posterior ethmoid, and sphenoid sinus subsites were evaluated for neo-osteogenesis and bony erosion and assigned scores of 0, 1, or 2, with a maximum overall score of 20 for each parameter. For neo-osteogenesis, a score of 0 signified absence of neo-osteogenesis, 1 indicated presence of neo-osteogenesis, and 2 denoted complete bony obliteration of the sinus (Fig. 1, A–C). For bony erosion, a score of 0 indicated absence of bony erosion, 1 signified presence of bony erosion, and 2 denoted complete bony erosion.

Statistical Analysis

Statistical analysis was performed using JMP v6.0 software from SAS (Cary, NC). Comparison between surgery and nonsurgery groups was performed using Student's paired *t*-test (see Table 3). Comparison between groups was performed using chi-squared analysis (see Table 4). Both tests assumed use of a 0.05 significance level.

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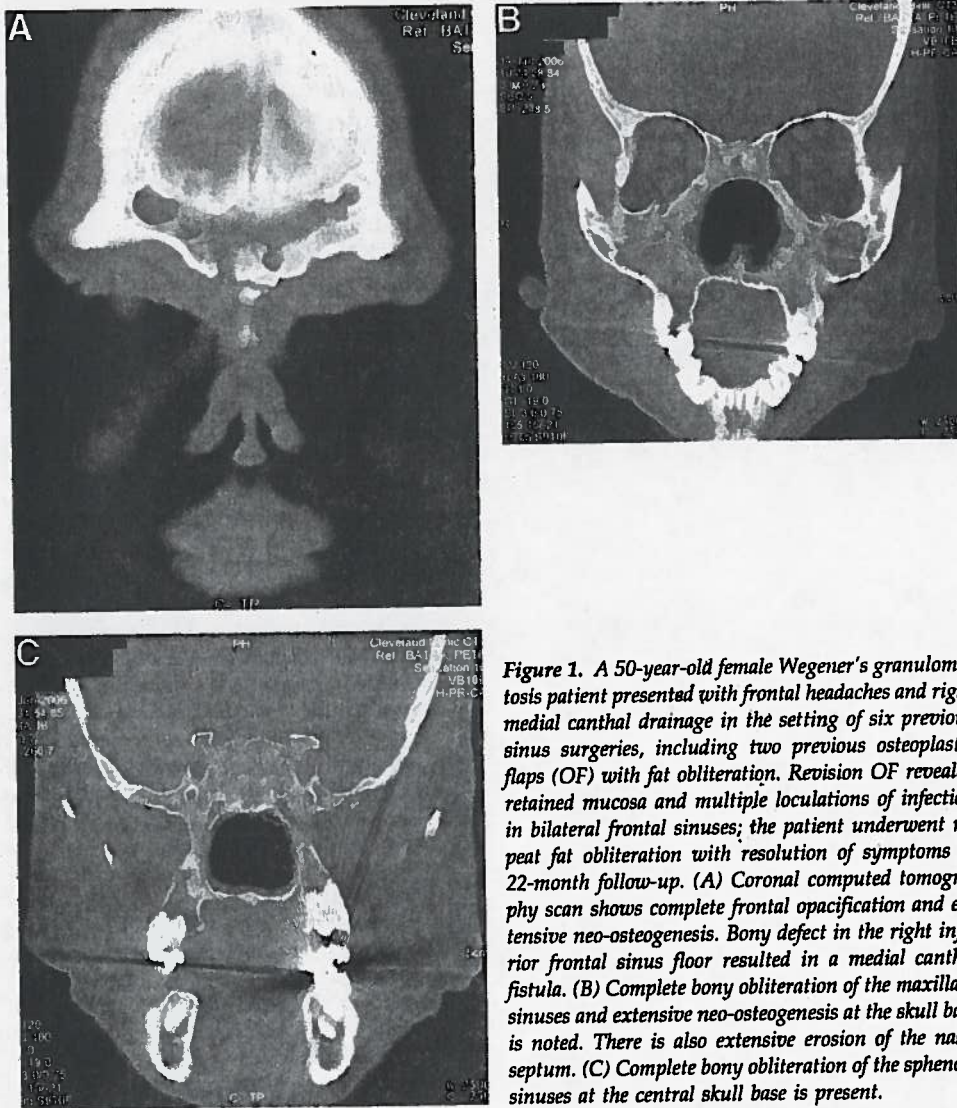


Figure 1. A 50-year-old female Wegener's granulomatosis patient presented with frontal headaches and right medial canthal drainage in the setting of six previous sinus surgeries, including two previous osteoplastic flaps (OF) with fat obliteration. Revision OF revealed retained mucosa and multiple loculations of infection in bilateral frontal sinuses; the patient underwent repeat fat obliteration with resolution of symptoms at 22-month follow-up. (A) Coronal computed tomography scan shows complete frontal opacification and extensive neo-osteogenesis. Bony defect in the right inferior frontal sinus floor resulted in a medial canthal fistula. (B) Complete bony obliteration of the maxillary sinuses and extensive neo-osteogenesis at the skull base is noted. There is also extensive erosion of the nasal septum. (C) Complete bony obliteration of the sphenoid sinuses at the central skull base is present.

RESULTS

Patient Demographics and WG Manifestations

Seventy-four patients were included consisting of 45 women (60.8%) and 29 men (39.2%). The mean age of patients was 53 years (range, 28–95 years). Forty-four patients (59%) had undergone prior sinus surgery and 30 patients (41%) had no prior surgical intervention. Procedures performed included endoscopic sinus surgery in 43 cases and Caldwell-Luc surgery in 1 case.

In this study, 91% of patients met criteria for chronic rhinosinusitis (CRS) as set forth by the Rhinosinusitis Task Force.¹⁸ The next most common head and neck manifestations were orbital disease (36.5%), septal perforation (35.1%), saddle nose deformity (33.8%), subglottic stenosis (31.1%), and paranasal sinus mucocele (16.2%; Table 1).

CT Analysis (Fig. 2)

L-M Scores. The average L-M score for WG patients was 10.0 (range, 1–24). The maxillary sinuses (98%) were most frequently noted to have elevated scores, followed by the anterior ethmoid (85%), posterior ethmoid (74%), sphenoid (70%), and frontal sinuses (66%; Table 2).

Neo-osteogenesis. Neo-osteogenesis was noted on 78% of the CT scans. The overall mean neo-osteogenesis score was 4.2 (range, 0–16).

Table 1 Presenting rhinological and systemic findings in Wegener's granulomatosis patients

Wegener's Manifestations	No. Patients	Percent
Chronic rhinosinusitis	67	90.5
Lung disease	38	51.4
Orbital disease	27	36.5
Septal perforation	26	35.1
Saddle nose deformity	25	33.8
Subglottic stenosis	23	31.1
Chronic otitis media	23	31.1
Kidney disease	20	27.0
Paranasal sinus mucocele	12	16.2

Sixteen patients exhibited no signs of neo-osteogenesis. The maxillary sinus was the most common site of neo-osteogenesis (60%), followed the anterior ethmoid (58%), posterior ethmoid (49%), sphenoid (45%), and frontal (23%; Table 2). Bony obliteration was most frequently observed in the sphenoid sinus (8%), followed by the posterior ethmoid (7%), maxillary sinus (7%), and frontal sinus (4%). No bony obliteration was noted in the anterior ethmoid sinuses.

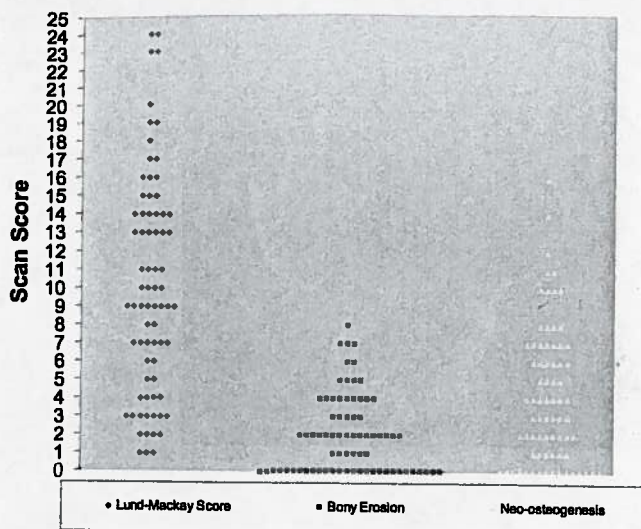


Figure 2. Scatterplot of Lund-Mackay, bony erosion, and neo-osteogenesis scores of sinus computed tomography scans in patients with Wegener's granulomatosis.

Bony Erosion. Bony erosion was noted in 62% of patients. The overall average score for bony erosion was 2.0 (range, 0–8). Twenty-eight WG patient scans exhibited no signs of bony erosion. The anterior ethmoid was the most common site of bony erosion (62%), followed by the posterior ethmoid (39%), sphenoid (27%), frontal (11%), and maxillary (8%; Table 2).

Effect of Surgery. The mean L-M score of WG patients who had undergone prior surgery and no surgery were 11.3 and 8.1, respectively. The mean neo-osteogenesis score of WG patients with prior sinus surgery was 5.3, compared with 2.6 in WG patients with no prior sinus surgery. The mean bony erosion score of WG patients with prior surgery was 2.7, compared with a mean score of 1.1 for patients with no prior surgery (Table 3). Statistical analysis revealed statistically significant increase in L-M, bony erosion, and neo-osteogenesis in the surgery group ($p = 0.024$, 0.0009 , and 0.0015 , respectively).

Analysis of WG patients without previous surgery indicated that 18 of 30 (60%) had evidence of neo-osteogenesis and 14 of 30 (46.7%) exhibited evidence of bony erosion. Nineteen of 30 (63.3%) displayed evidence of either bony erosion or neo-osteogenesis, while 13 of 30 (43.3%) had evidence of both neo-osteogenesis and bony erosion (Table 4).

Review of WG patients with previous surgery revealed that 40 of 44 (90.9%) displayed evidence of neo-osteogenesis and 32 of 44 (72.7%) exhibited evidence of bony erosion. Forty of 44 (90.9%) sinus CT scans were noted to have both bony erosion and neo-osteogenesis (Table 4). Chi-squared analysis showed that the surgery group had a statistical increase in the number of patients with bony erosion and neo-osteogenesis compared with the no surgery group ($p = 0.01$).

DISCUSSION

WG has intimate association with the sinonasal tract with involvement noted in >85% of patients.⁸ Paranasal sinus CT changes in sinonasal WG are common and may manifest as varied findings, including mucosal thickening, sinus opacification, bone erosion, neo-osteogenesis, sclerosing osteitis, or frank bony destruction of the paranasal sinuses.^{12,14-16} However, previous studies have been limited by small sample size (9–28 patients), thus precluding meaningful analysis of CT manifestations of this rare disease entity.

Benoudiba *et al.* examined sinus CT scans of nine WG patients in 2003. Their findings suggested that nodular mucosal thickening, punctate bony destruction, periantral soft tissue infiltration with associated bone demineralization, and midline bone destruction should alert the clinician

to the possibility of WG.¹⁵ Similarly, the present study noted that midline bone destruction was common; 50 of 74 (67.6%) WG patients showed evidence of septal bony erosion. Our analysis also showed that ethmoid sinuses are not spared in the WG disease process. In contrast, the anterior ethmoid region was the most frequent site of bony erosion (62%) and was highly likely (85%) to have an elevated L-M score.

Yang *et al.* reviewed sinus CT scans of nine WG patients, excluding from analysis sinuses that had undergone prior surgery. They described sinus neo-osteogenesis (56%), bony erosion of the septum (22%), and bony erosion of the turbinates (22%) as specific bony changes in WG patients (Fig. 3).¹⁶ Similarly, the present study noted neo-osteogenesis and septal erosion to be common CT findings albeit at a higher rate of 78 and 68%, respectively. Given the inclusion of larger numbers of patients in the current analysis, the prevalence rates noted may more accurately reflect the presence of these bony changes in WG. Our study did not report bony changes of the inferior, middle, and superior turbinates. Although this was initially attempted, the wide variation in the bony thickness and multiple previous surgical interventions of the turbinates subjected this parameter to interrater variability, thus precluding meaningful analysis.

The most recent analysis by Lohrman *et al.* evaluated CT findings of the paranasal sinuses in 28 WG patients without previous surgery.¹⁴ This study showed that 75% of patients had mucosal thickening, 25% had subtotal opacification, 54% had bony erosion, 21% had sclerosing osteitis, and 18% had bony thickening. Although the bony erosion/destruction prevalence is similar (62% versus 54%) between the two studies, the current study indicates that neo-osteogenesis may be more prevalent than previously reported, 78% versus 18–21%. Similar to the current study, Lohrman *et al.* also noted that the maxillary sinus was most frequently affected by mucosal disease and neo-osteogenesis, although one-way ANOVA analysis of L-M scores of each sinus revealed no significant difference between the specific sinuses.

The exact pathophysiological mechanisms leading to the observed changes in the paranasal sinuses in WG have not been conclusively elucidated. Previous reports have identified multiple potential causative factors, including fibrinoid necrosis of small blood vessels, epithelial granulomas, chronic inflammation, and/or prior surgical intervention.^{16,19} Acute and chronic inflammation, coupled with epithelioid granuloma formation, leads to obliteration of the adjacent small to medium-sized vessels. The resultant avascular necrosis may account for the bone destruction, typically starting in the midline with the septum and turbinates and eventually spreading to the paranasal sinuses.¹⁹ Punctate demineralization is also noted, further suggestive of demineralization located along the pathway of the perforating arteries in the vasculitic process.¹⁵

Chronic inflammation, in the form of CRS, was present in >90% of WG patients in this study. Prior studies have shown that CRS can affect underlying bone, with resulting microscopic osteitis and neo-osteogenesis.^{20,21} The incidence of neo-osteogenesis observed in the present study (78%) is greater than reported with CRS alone (42% and 41%).²² The presence of chronic inflammation, along with the underlying vasculitis, may result in the higher prevalence of observed changes on the CT scans of WG patients.

Surgical manipulation may further exacerbate the neo-osteogenesis noted in the patient population. Our data indicate that prior surgery is associated with an increased severity of pathological bony changes and increased L-M scores in patients with WG. Similarly, Lee *et al.* observed an increased incidence of neo-osteogenesis on sinus CT scans in patients with CRS and prior sinus surgery (41%) compared with patients with CRS and no prior surgical manipulation (5%).²³ Kennedy *et al.* also showed increased incidence of histological bony remodeling in CRS patients who underwent sinus surgery when compared with patients who had sinus surgery with no prior evidence of CRS (71% versus 31%).²⁴ Furthermore, Cho *et al.* showed that CRS patients undergoing revision sinus surgery had elevated L-M and new bone formation scores compared with CRS patients undergoing primary sinus surgery and controls.²⁵

Table 2 Lund-Mackay (L-M), bony erosion, and neo-osteogenesis scores and percentages for specific sinuses in Wegener's granulomatosis patients

Sinus	L-M Mean*	Bony Erosion# (No.)	Bony Erosion (%)	Neo-osteogenesis§ (No.)	Neo-osteogenesis (%)	Bony Obliteration¶ (No.)	Bony Obliteration (%)
Frontal	0.76	6	8.10	17	23.00	3	4.10
Maxillary	1.12	31	41.90	44	59.50	5	6.80
Anterior ethmoid	1.05	29	39.20	43	58.10	0	0
Posterior ethmoid	0.83	20	27.00	36	48.70	5	6.80
Sphenoid	0.85	8	10.80	33	44.60	6	8.10
Overall	10	46	62.20	58	78.40	13	17.60

*L-M Mean represents the average Lund-Mackay score for a specific sinus.

#Bony erosion number represents the number of patients with a score >0 for bony erosion.

§Neo-osteogenesis number represents the number of patients with score >0 for neo-osteogenesis.

¶Bony obliteration number represents the number of patients with complete bony obliteration of any sinus due to neo-osteogenesis.

Table 3 Comparison of Lund-Mackay, bony erosion, and neo-osteogenesis scores in Wegener's granulomatosis (WG) patients with previous paranasal sinus surgery to WG patients with no prior surgery

	No.	Mean Age (yr)	Mean Lund-Mackay	Mean Bony Erosion	Mean Neo-osteogenesis
Surgery	44	52.9	11.3	2.7	5.3
No surgery	30	53.5	8.1	1.1	2.6

Table 4 Breakdown of the number of computed tomography scans with evidence of bony erosion and/or neo-osteogenesis in patients with and without prior surgical manipulation

No.	Bony erosion	Neo-osteogenesis	Percent
Prior surgery			
32	Present	Present	72.7
0	Present	Absent	0
8	Absent	Present	18.2
4	Absent	Absent	9.1
No prior surgery			
13	Present	Present	43.3
1	Present	Absent	3.3
5	Absent	Present	16.7
11	Absent	Absent	36.7

In the present study, 40 of 44 (90.1%) patients with prior sinus surgery had radiological evidence of bony changes, while 19 of 30 (63.3%) patients with no prior sinus surgery had evidence of bony changes. Although the increased incidence of bony changes after surgery is consistent with the CRS data from prior studies, WG patients tend to have an increased incidence of bony changes in the absence of prior surgery (63.3%) when compared with CRS patients with no prior surgery (42%²⁰ and 41%²²). This suggests that surgical intervention is not a prerequisite to bony changes noted in WG patients, although the bony abnormalities are more commonly associated with surgical manipulation (Fig. 4). Moreover, it is also plausible that patients with higher L-M scores and more extensive bony changes may have been more likely to undergo surgery. However, without longitudinal data, this important distinction can not be discerned from the present data.

The high prevalence of sinonasal involvement, coupled with mucosal and bony abnormalities on CT imaging, should not be viewed as a sufficient indication for surgical intervention in the WG patient. In the senior author's experience, endoscopic sinus surgery in the setting of WG represents a significant surgical challenge. Cannady *et al.* reviewed

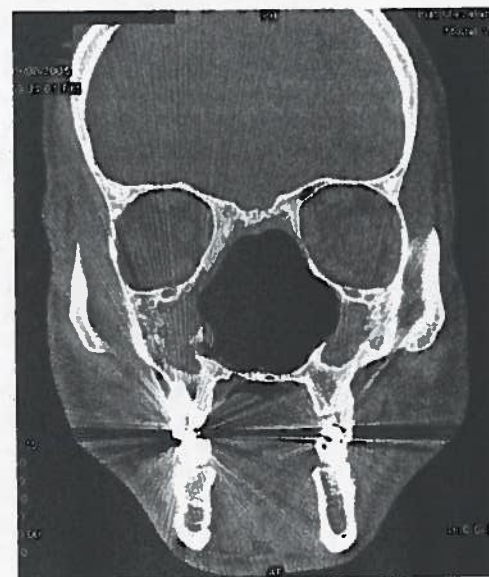


Figure 3. Coronal computed tomography scan from a 37-year-old man with long-standing Wegener's granulomatosis and four prior sinus surgeries. Note the "common cavity" configuration with complete erosion of nasal turbinates and septum.

management of sinonasal WG in 120 patients; functional endoscopic sinonasal procedures were performed in 19 (16%) patients. Improvement of the primary surgical indication was noted in 83, 76, and 76% at 1, 6, and 12 months, respectively. However, a total of 12 revision surgeries were performed over a mean follow-up period of 50 months (range, 19–107 months).²⁶ Thus, a complete surgical cure is uncommon; symptom relapses and need for revision surgery and ongoing medical therapy are common expected outcomes. Surgical intervention in this patient subgroup should be considered as a last resort measure, especially in light of the potential to further exacerbate preexisting bony abnormalities as noted in this analysis.



Figure 4. Coronal computed tomography scan from an 83-year-old woman Wegener's granulomatosis (WG) patient with no prior sinus surgery who presented with several months history of worsening nasal crusting and bleeding. The maxillary and ethmoid sinuses show bilateral extensive neo-osteogenesis. Multiple ethmoid mucocoeles are also present with erosion of the lamina papyracea on the right side with subtle mass effect (arrowhead). Bony changes in the calvarium are also noted. This was not typically observed in most patients with sinonasal WG and the significance is unknown.

Despite the unique CT findings noted in WG patients, these observations must be carefully considered in the context of diagnosis of WG. The mere presence of concurrent bone erosion and neo-osteogenesis, coupled with mucosal inflammation, is not pathognomonic for the WG process. Although it should alert the physician for underlying possibility of WG, similar CT findings may be noted in sarcoidosis and T-cell lymphoma. The diagnosis of WG rests on the criteria set forth by the American College of Rheumatology and careful rheumatologic input is instrumental in arriving at the proper diagnosis.⁹ Furthermore, these findings should not be generalized to all WG patients; the CT findings noted in this review represent a subset of patients referred specifically for rhinologic complaints.

To the best of our knowledge, this represents the largest series in the world literature reviewing CT findings in WG to date. Nevertheless, important limitations should be highlighted. The study did not take into account the underlying systemic activity of WG at time of CT scanning. Furthermore, the impact of systemic WG treatment was not assessed. The exact impact of these factors on CT findings is not clear. Every effort was made to review the initial presenting sinus CT to the Section of Nasal and Sinus Disorders. Given the retrospective design of the current study, it is possible that the WG patients with a history of prior sinus surgery represented a group with more severe WG disease. Future studies will focus on longitudinal CT analysis of WG patients to assess impact of disease activity and surgery to control for these confounding factors.

CONCLUSION

CT analysis of the paranasal sinuses of patients with WG reveals high prevalence of bony abnormalities and mucosal changes. Any of the paranasal sinuses can be affected and frequently patients showed involvement of multiple sinuses. Furthermore, this study shows that surgical manipulation in the WG patient is associated with increased severity of bony abnormalities, although previous surgery is not a prerequisite for development of these changes. These data suggest that the presence of these striking bony changes with simultaneous bony erosion, neo-osteogenesis, and bony obliteration should alert the clinician of possibility of underlying WG.

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