

Sinonasal manifestations of sarcoidosis: a single institution experience with 38 cases

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Background: Sarcoidosis is a chronic disease process characterized by non-caseating granulomatous inflammation, usually involving the lower respiratory tract. Given the rarity of rhinologic involvement, the objectives of the present study were (1) to describe clinical features, and (2) to review outcomes of rhinologic surgery for sinonasal sarcoidosis.

Methods: Retrospective analysis was performed of patients evaluated at a tertiary care referral center between January 2006 and July 2011.

Results: The mean age of the 38 patients with sinonasal sarcoidosis was 52 years, with a female:male ratio of 2.8:1. The most common presenting symptoms included nasal obstruction (65.8%), crusting (29.9%), and epistaxis (18.4%). Most frequent endoscopic findings included crusting (55.3%), mucosal thickening (44.7%), and subcutaneous nodules (21%). Computed tomography (CT) imaging demonstrated turbinate or septal nodularity (21%), osteoneogenesis (15.8%), and bone erosion (10.5%). Medical management was typically comprised of saline irrigations (73.3%), topical nasal steroids (68.4%), and oral steroids

(63.2%). Refractory sinus symptoms required sinonasal surgery in 4 cases. Overall subjective symptom improvement was noted in 39.5% at mean follow-up of 16.2 months.

Conclusion: Sinonasal involvement was noted in approximately 30% of patients with known sarcoidosis evaluated in the otolaryngology clinic. Patients typically present with nasal obstruction and endoscopic evidence of crusting and mucosal thickening. Medical therapy with irrigations and topical/oral steroids suffices in majority of patients, with surgery for refractory symptoms being required in a small subset of cases. © 2013 ARS-AAOA, LLC.

Key Words:

sarcoidosis; granulomatous disease; sinonasal; chronic sinusitis; endoscopy; sinus surgery

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Sarcoidosis is a systemic noncaseating granulomatous disorder of unknown etiology that typically afflicts

young to middle-aged adults.¹ It has a clear predilection for women and certain ethnic and racial groups, with annual age-adjusted incidence rate of 35.5 per 100,000 in U.S. blacks and 50 per 100,000 in Scandinavian countries.^{1,2} Sarcoidosis primarily affects the lungs and lymphatic system; however, the presentation can be variable and can involve multiple organ systems, including the skin, eyes, liver, spleen, muscles, bones, heart, kidneys, and central nervous system.² Otolaryngologic manifestations of sarcoidosis as a component of the multisystem disease process are observed in 10% to 15% of cases, though rarely it may present with isolated primary head and neck complaints.^{2,3} Commonly affected sites include the salivary glands, larynx, nose, sinuses, ear, and cervical lymph nodes.³

Involvement of the sinonasal region has been recognized since Boeck⁴ first described granulomatous infiltration of the nasal mucosa in 1905. Early data suggested low prevalence of sinonasal involvement, with McCaffrey and McDonald⁵ noting histologic involvement of the nasal

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mucosa in 0.73% of 2319 sarcoid cases. A more recent cross-sectional survey suggested higher prevalence of rhinologic involvement, with 61% of 159 consecutive patients reporting intermittent or persistent nasal symptoms.⁶ The studies on sinonasal sarcoidosis accrued to date have been limited to small case series, thus precluding a clear diagnostic or management strategy for this patient group.^{3,7-15} With this in mind, the present study reports an additional 38 patients managed in a tertiary care rhinology clinic and reviews the previous literature to better elucidate the clinical presentation, diagnostic aspects, and treatment schema.

Patients and methods

Retrospective chart analysis was performed at the University of Texas Southwestern Medical Center between January 2004 and October 2011. A total of 113 patients were evaluated in the otolaryngology practice. Seventy patients were excluded given no clinical evidence for head and neck sarcoidosis; an additional 9 patients demonstrated findings of head and neck sarcoidosis without sinonasal involvement. Thirty-four patients for this group had evidence of sinonasal involvement. An additional 4 patients that initially presented to the otolaryngology clinic with primary sinonasal complaints were subsequently diagnosed with sarcoidosis. Thus, 38 patients were included in this analysis based on the following criteria: (1) clinical features compatible with diagnosis of sinonasal sarcoidosis; (2) histological confirmation of noncaseating granuloma in the nasal or sinus tissue; and (3) exclusion of other causes of granulomatous disease, including Wegener granulomatosis. Institutional review board approval was obtained prior to commencing the study.

Data collated included age, gender, presenting sinonasal symptoms, endoscopic and radiographic findings, and medical therapy. Indications and types of sinonasal surgery were recorded. Outcomes from medical and surgical therapy were categorized as improved, same, and worse as retrospectively noted in patient medical records.

Results

The overall prevalence of sinonasal sarcoidosis in patients evaluated in the otolaryngology clinic was 30.1% (34/113). The mean age of the 38-patient group was 52.5 years, with a female:male ratio of 2.8:1. The mean follow-up was 16 months. The time interval between the first sinonasal symptoms and the diagnosis of sarcoidosis varied widely, ranging from 2 months to 31 years. Table 1 demonstrates the initial presenting otolaryngologic symptoms, endoscopic findings, and presenting signs/diagnoses for this patient subset. Computed tomography (CT) imaging illustrated inferior turbinate and/or septal nodularity in 8 (21%), osteoneogenesis in 6 (16%), and bone erosion in 4 (11%) patients.

TABLE 1. Presenting otolaryngologic symptoms, endoscopic findings, and presenting signs/diagnoses for 38 patients with sinonasal sarcoidosis

Clinical presentation	n (%)
Symptoms	
Nasal obstruction	25 (65.8)
Crusting	11 (29.9)
Dysphagia	10 (26.3)
Hoarseness	9 (23.7)
Epistaxis	7 (18.4)
Hearing loss	5 (13.6)
Smell and/or taste disorder	3 (7.9)
Epiphora	1 (2.3)
Nasal endoscopic findings	
Nasal crusting	21 (55.3)
Mucosal thickening	17 (44.7)
Sinonasal scarring	8 (21)
Subcutaneous nodules	8 (21)
Septal perforation	2 (5.3)
Presenting signs/diagnoses	
Chronic rhinosinusitis	10 (26.3)
Lupus pernio	4 (10.3)
Supraglottic nodules	3 (7.9)
Salivary gland enlargement	3 (7.9)
Saddle nose deformity	2 (5.3)
Cervical lymphadenopathy	2 (5.3)

Medical therapy was employed in all patients presenting with rhinologic symptoms. Nasal saline irrigations and topical steroids were employed in 28 (74%) and 26 (68%) patients, respectively. Oral steroids were used in 24 (63%) cases. Endoscopic sinus surgery (ESS) was required in 4 (10.5%) patients. Indications for surgery included expansile frontal mucocele (1), chronic rhinosinusitis (CRS) with peri-orbital cellulitis (1), CRS with polyposis (1), and CRS without polyposis (1). Nonrhinologic surgery was required in 2 cases, including mastoidectomy for repair of cerebrospinal fluid (CSF) otorrhea and laser excision of supraglottic laryngeal scar. Patient global symptom improvement was noted in 15 (39.5%) patients with comprehensive medical therapy, coupled with targeted surgery in select cases. Eleven (28.9%) patients reported no symptom improvement, whereas 3 (8%) patients noted worsening despite medical measures. No follow-up was available in 9 (23.6%). Table 2 presents the composite data from the salient studies on sinonasal sarcoidosis to date.

TABLE 2. Composite data on sinonasal sarcoidosis accrued in the literature to date

Author	Year	With SNS ^a (%)	N	Mean age (years)	Female (n)	Primary symptom(s)	Physical exam/endoscopy	Medical therapy	Surgery	Outcome
James et al. ⁷	1982	6	53	35	35	NAO, crusting, discharge	Mucosal hypertrophy, erythema	SS (24); TNS (4)	NR	NR
McCaffrey and McDonald ⁸	1983	1	17	43	13	NAO (11)	Nasal crusting (11); submucosal nodules (5)	NR	NR	NR
Wilson et al. ⁸	1988	3.6	27	41	14	NAO (24); crusting (17)	Nodules; mucosal hypertrophy	SS (22); TNS (9)	Biopsy (21)	All with SS improved
Shikowitz and Alvi ⁹	1993	NR	3	34	2	NAO (3)	Nodules; nasal stenosis, crusting	SS (1); TNS (2)	Biopsy (3)	All 3 improved
Marks and Goodman ¹⁰	1998	NR	6	32	6	NAO (3); HA (3)	Turbinate hypertrophy; crusting	SS (5); TNS (4)	FESS (2); ITR (2); external sinus surgery (2)	All 6 improved, required a total of 12 surgeries
deShazo et al. ¹¹	1999	NR	6	31	3	NAO (6); chronic sinusitis (3)	Erythematous; edematous, friable; hypertrophic mucosa	SS (5); TNS (1)	FESS (5)	Improved (3); unchanged (2)
Fergie et al. ¹²	1999	NR	6	44	6	NAO (7); epiphora (3)	Granular mucosa (4); crusting (4)	SS (3); TNS (5)	Biopsy (6)	Resolved (2); improved (3); unchanged (1); lost to follow-up (2)
Zeitlin et al. ⁶	2000	4	18	39	12	NR	NR	SS or IS (18)	FESS (8); biopsy (8)	Improved (4); unchanged (4)
Kay and Har-El ¹³	2001	NR	4 ^b	40	4	NAO (3); sinusitis (1)	Polypoid mucosa (3)	SS (?); TNS (4)	FESS (4)	Improved (4)
Long et al. ¹⁴	2001	NR	6	51	6	Chronic sinusitis (6)	Erythematous, granular, and atrophic mucosa (6)	SS (6); TNS (6)	FESS (6)	Improved (2); unchanged (4)
Braun et al. ³	2004	NR	15	44	8	NAO (12); rhinorrhea (9)	Nodules (14); inflammatory mucosa (9); crusting (8)	SS (14)	Biopsy (15)	Relapse after steroids (8); stable (3); asymptomatic (1)
Aubart et al. ¹⁵	2006	1.6	20	32	13	Stiffness (18); rhinorrhea (14); Anosmia (14)	Mucosal hypertrophy (15); purplish mucosa with granulations (10)	SS (20)	FESS (7)	Unchanged (6); worse (1)
Aloulah et al. (this work)	2013	4.5	38	53	28	NAO (15); crusting (11)	Crusting (21); mucosal thickening (17)	SS (24); TNS (26); saline rinses (28)	FESS (4)	Improved (15); unchanged (11); worse (3)

^aPercent of cases with documented sinonasal sarcoidosis from a larger general sarcoid patient population.

^bThe study reported 6 cases but individual patient data was only provided for 4 cases.

FESS = functional endoscopic sinus surgery; HA = headaches; IS = immunosuppressive agents (not specified); ITR = inferior turbinate reduction; NAO = nasal airway obstruction; NR = not reported; SNS = sinonasal sarcoidosis; SS = systemic steroids; TNS = topical nasal steroid.

Discussion

Sarcoidosis represents a multisystem granulomatous disease process that may involve the head and neck region in 10% to 15% of cases. Otolaryngologic presentation can be quite variable, with involvement of salivary glands, larynx, nose, sinuses, ear, cervical lymph nodes, lacrimal system, and/or skin.^{2,3} The data accrued to date on sinonasal sarcoidosis is sparse, largely limited to small case series.⁹⁻¹⁴ The largest series in the past 20 years have reported 18 and 20 patients with sinonasal sarcoidosis, respectively.^{6,15} This underscores the need for larger clinical series and more robust analysis of the existing literature to elucidate the optimal diagnostic and management strategy for sinonasal sarcoidosis.

Traditional teaching holds that sinonasal involvement is rare, with McCaffrey and McDonald⁵ noting histologic evidence in 1% of 2319 patients with sarcoidosis. Conversely, Zeitlin et al.⁶ reported high prevalence of nasal symptoms in prospective evaluation of 159 consecutive sarcoid patients. Specifically, 38% and 23% reported persistent and intermittent nasal symptoms, respectively. The present data suggests that rhinologic involvement in the group of sarcoid patients evaluated in the otolaryngology clinic is also higher, being noted in 30% of cases. Though true incidence may only be discerned from large rigorous prospective studies, the current series suggests that sinonasal involvement is more common than previously reported. This is in direct contrast to patients with Wegener's granulomatosis where sinonasal involvement has been observed in up to 89% of cases.¹⁶ Given the lower overall prevalence of sinonasal involvement in sarcoidosis, high index of suspicion must be maintained by clinicians managing sarcoidosis.

The challenge in accurate diagnosis rests in part with presenting symptoms, which are often nonspecific and indistinguishable from general CRS patients. The current study noted that nasal obstruction was the most common symptom, being noted in 66% of cases. Similarly, most previous studies reported nasal obstruction to be the most common presenting symptom.^{3,5,8,11,12} Given sarcoid predilection for the nasal septum and inferior turbinates, nasal blockage likely ensues early with progressive edema and hypertrophy of the nasal mucosa. Crusting and epistaxis were reported in 30% and 18% of cases, respectively. Given that these are not typical symptoms of CRS patients, clinical presentation of nasal obstruction predominantly with crusting and bleeding should prompt consideration of underlying granulomatous disease as the potential etiology of the sinonasal symptoms.

Rigid or flexible nasal endoscopy serves as the key diagnostic test for rhinologic evaluation. In the current series, endoscopic findings, including crusting and mucosal thickening, were noted in 55% and 45% of the cases, respectively, while submucosal nodules were only noted in 21% of cases (Fig. 1). Previous studies have also noted that nasal crusting represents the most common endoscopic finding (Fig. 2).^{3,5,9,10,12} The underlying mucosa can be erythematous, friable, and/or hypertrophic in the acute phase of the

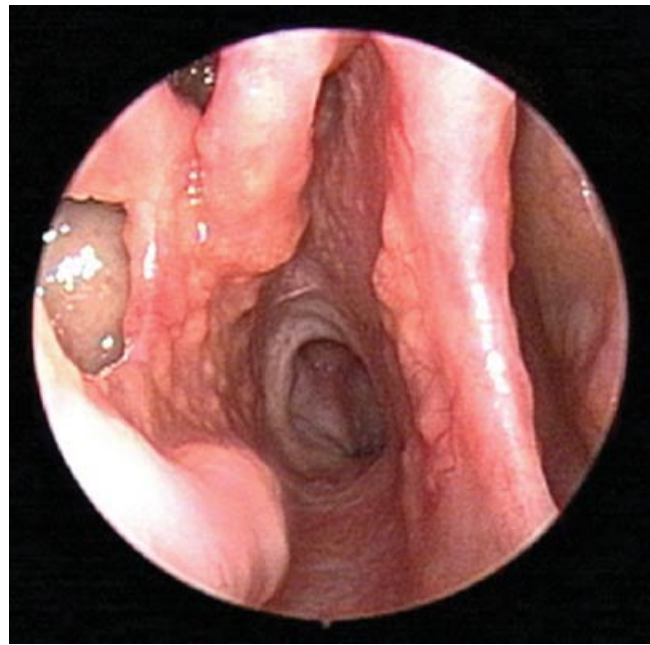


FIGURE 1. Endoscopic view of right nasal cavity demonstrates granulomatous nodules on the septum and lateral nasal wall. Patient has a large central septal perforation resulting from previous surgery.



FIGURE 2. Endoscopic view of left nasal cavity demonstrates extensive crusting along the septum and middle meatus. The mucosa is nodular and hyperemic.

disease. Submucosal granuloma formation may also occur along the septum and inferior turbinates, though it is seen in a smaller subset of cases.^{3,5,8} Ongoing granulomatous inflammation, previous surgical manipulation, and bacterial superinfection may further contribute to nasal scarring, and eventually stenosis during the chronic phase of the disease. Septal perforation and saddle nose deformity may also be

observed, being noted in 2 cases each (5.3%) in the present study.

Given the myriad of otolaryngologic manifestations observed in sarcoidosis, comprehensive head and neck evaluation is also a requisite to identify all potential sites of involvement. Lupus pernio, a chronic, persistent, violaceous skin lesion with a predilection for the nose, cheeks, and ears, was noted in 11% of cases in our series. This dermatologic lesion has been closely associated with upper respiratory tract sarcoidosis, with Neville et al.¹⁷ noting that patients with sinonasal sarcoidosis have a 50% risk of developing lupus pernio. Similar to the present series, Braun et al.³ also reported cervical lymphadenopathy and salivary gland enlargement in 4 and 2 cases, respectively. Flexible laryngoscopy revealed supraglottic nodules in 3 cases (7.9%) in the current study.

CT imaging serves as an important diagnostic adjunct in patients with persistent rhinologic symptoms. Mucosal thickening is common, being noted in 93% and 60% of maxillary and ethmoid sinuses.¹⁵ A distinct feature that may be observed is nodularity of the septum and inferior turbinates. Braun et al.³ noted the presence of nodular lesions on the septum and inferior turbinates in 86.7% and 67.7% of the cases, respectively. In contrast, Aubart et al.¹⁵ noted classic nodular lesions in only 20% of cases. The present series, similar to the latter study, observed inferior turbinate and/or septal nodularity in 8 (21%) patients. Bony changes secondary to granulomatous inflammation may also be seen; osteoneogenesis and bone erosion was present in 6 (16%) and 4 (11%) of the cases in this series, respectively (Fig. 3). Aubart et al.¹⁵ reported “perforation

or lysis” of the bony septum in 40% and inferior turbinates in 27%. These unique CT findings should provide the clinician with potential cues as to the presence of an underlying granulomatous disease process.

The management of sinonasal sarcoidosis remains a significant therapeutic challenge. Saline irrigations and topical nasal steroids are frequently employed for rhinologic symptoms, being utilized in 74% and 68% of the cases, respectively, in the present series. Though it may be useful in the scenario of mild mucosal inflammation and crusting, the effectiveness is limited in severe cases.^{3,12,15} Intralesional steroid injections have also been purported to provide local symptom relief.¹⁸ This strategy has been successfully employed for lacrimal, cutaneous, and laryngeal sarcoidosis; this may also hold potential utility in obstructive nasal lesions, thus decreasing the need for systemic steroids. The treatment dilemma may at least in part rest on the more recalcitrant nature of the sinonasal sarcoidosis. Aubart et al.¹⁵ compared disease activity in sarcoidosis patients with and without sinonasal involvement. The group comparison demonstrated that patients with sinonasal sarcoidosis had more frequent and severe involvement of vital organs and had a longer history of sarcoidosis. Further, they required systemic treatment more frequently and for a longer period of time.¹⁵

Systemic steroids remain the mainstay for treatment of severe sinonasal sarcoidosis, being reported as a component of the management algorithm in 11 of the 12 previous series.^{3,7-15} Though effective in control of sinonasal symptoms, the required maintenance dose may be as high at 10.5 mg daily to achieve symptom control, with median treatment duration of 82 months (range, 22–121 months).¹⁵ Moreover, Braun et al.³ reported a high rate of relapse after tapering of systemic corticosteroids after initial control of sinonasal symptoms. The present data mirrors these previous observations, with global symptom improvement being noted in 39.5% of cases and no change or worsening in 36.9% of cases.

ESS as a treatment alternative has been reported in several series for refractory sinonasal sarcoidosis.^{6,10,11,13,14} Marks and Goodman¹⁰ reported sinonasal surgery in 6 patients with sinonasal sarcoidosis. A total of 12 procedures, including 8 endoscopic and 4 open surgeries, were required to achieve symptom relief. Similarly, DeShazo et al.¹¹ and Zeitlin et al.⁶ performed ESS in patients with refractory sinonasal sarcoidosis, noting relief in only 60% and 50% of the patients, respectively. Indeed, surgical failures are not uncommon. Long et al.¹⁴ presented a series of 6 cases with persistent sinonasal symptoms; all 4 patients with pathology demonstrating sarcoid involvement of the nasal mucosa had ongoing sinus symptoms, despite aggressive postoperative medical therapy.

Thus, overwhelming data suggests that the success rate of ESS for sinonasal sarcoidosis is mixed at best. The rate of relapse is high, persistent sinus symptoms are a common postoperative sequelae, and surgery may not be a solitary event. This in turn emphasizes the need for considering



FIGURE 3. Coronal bone window CT scan of the sinuses illustrates extensive osteoneogenesis of the ethmoid and maxillary sinuses. Bone erosion of the septum is noted.

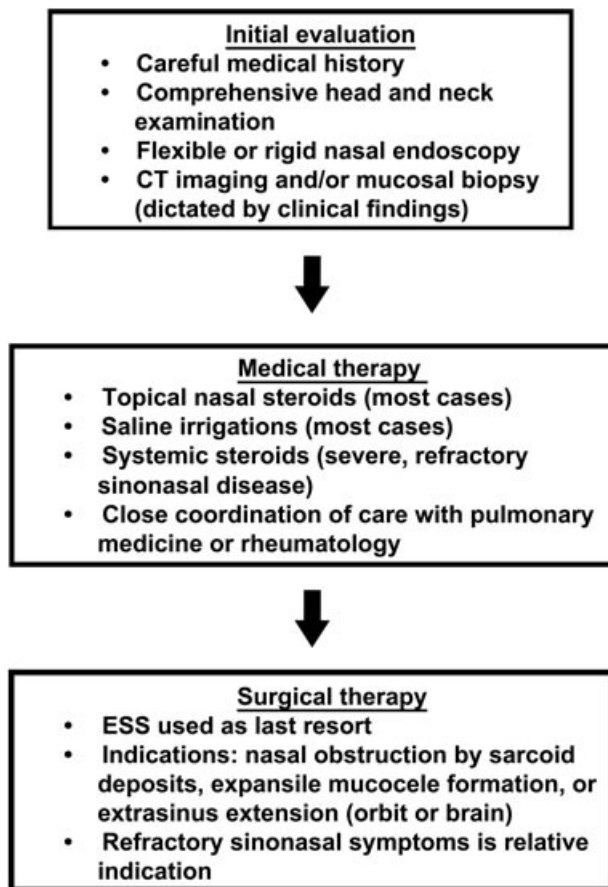


FIGURE 4. Summary of diagnostic and management scheme utilized at our institution for patients presenting with sinonasal sarcoidosis.

surgery as a last resort after exhausting all medical measures. Potential indications include nasal obstruction by sarcoid deposits, expansile mucocele formation, or extension into contiguous structures such as the orbit or brain. However, the mere presence of CRS should only be considered

a relative indication given the high risk of symptom recurrence. The present study corroborates this dictum as only 4 of 38 (10.5%) underwent ESS for specific indications. Figure 4 highlights the management schema for sinonasal sarcoid patients at our institution.

The present study further contributes to the growing body of literature on sinonasal sarcoidosis. It serves to provide the clinical construct of the patient subset, with presenting symptoms, endoscopic/CT findings, and management strategy. Inherent limitations exist which must be carefully considered if the data is to be applied to sarcoid patients. The patient group is a select population evaluated in a tertiary care rhinologic clinic and may not be representative of all patients presenting to otolaryngologists or other medical specialties. All data was accrued over 7 years and, despite diligent efforts to achieve uniformity of the data collection process, is subject to recall bias. This could only be circumvented by large prospective studies, which may not be realistic for a rare clinical entity. Nonetheless, it serves to provide a clinical context for clinicians managing this difficult disease process and may facilitate more informed patient counseling and treatment decisions.

Conclusion

Sinonasal sarcoidosis was observed in 30% of sarcoid patients evaluated in a tertiary care rhinology practice. Sinonasal morbidity is high, with nasal obstruction and crusting being common presenting complaints. Medical therapy with topical nasal steroids and saline irrigations is used in most cases, though 63% still require systemic steroids for symptom control. Sinus surgery is used sparingly, being performed in 4 cases for specific indications. Sinonasal involvement should be recognized as a potentially recalcitrant manifestation of sarcoidosis that requires close multispecialty coordination and aggressive medical therapy. 🌐

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