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Vocal Folds: An Unusual Hideout for Systemic Sarcoidosis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors participated in the writing of the manuscript and the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Sarcoidosis is a chronic inflammatory granulomatous disease of unknown etiology. It can expand to all organs and tissues. Lungs and lymph nodes are the most commonly involved tissues. Laryngeal sarcoidosis is rare, accounting for no more than 1% of patients with systemic sarcoidosis. We herein report the case of a 51-year-old female presenting a two-year history of persistent voice hoarseness with direct laryngoscopy findings of epiglottis swelling and irregular swelled and bruised left vocal fold. Histological examination highlighted the presence of non-caseating granulomas. Further investigations revealed similar histological findings in the nasal cavity as well as lymphocytic alveolitis. It also showed the presence of phalangeal bone lesions of both hands. All these pointed to the diagnosis of sarcoidosis with upper respiratory tract (nasal and laryngeal), lung and bone involvement. The patient was started on 0.5 mg/kg daily of prednisone for 1 month followed by progressive tapering with lasting favorable outcome.

Keywords: Sarcoidosis; chronic inflammatory granulomatous disease; etiology; lymph nodes.

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1. BACKGROUND

Sarcoidosis is a multisystem disease with great diversity of clinical manifestations. It involves the formation of granulomas in multiple organs with lungs being its primary target followed by lymph nodes [1]. While sarcoidosis can expand to any organ, laryngeal sarcoidosis remains a rare and potentially life-threatening site. Laryngeal involvement in sarcoidosis has been reported in about 1% of patients [2]. It can manifest as dyspnea, dysphagia and dysphonia and can even lead to airway obstruction [3]. Diagnosis may be challenging, more so if laryngeal symptoms are the presenting feature of the disease.

We hereby present the case of a 51-year-old female patient whose initial complaint was voice hoarseness with findings of non-caseating granulomas on vocal fold biopsy. Further investigations identified similar findings in the nasal cavity biopsy as well as pulmonary and skeletal involvement. Treatment with corticosteroid allowed for complete regression of clinical symptoms.

2. CASE PRESENTATION

A 51-year-old female patient was referred by otolaryngologists to our internal medicine department for dysphonia. The patient had a 2-year history of hoarseness. In addition, she reported shortness of breath and oropharyngeal dysphagia for solid food spanning for the last 6 months. She also had inflammatory joints pain involving the metacarpophalangeal joints. She denied smoking or alcohol intake. She had no allergy and did not take any medications. She had no recent medical history of upper respiratory tract infections or vocal overuse. She had no fever, weight loss or night sweat.

On clinical examination, a hoarse, breathy voice was noted. She had a saddle nose deformity along with nasal crusting (Fig. 1). Joint examination noted dactylitis of the second and third finger of the right hand as well as similar swelling of the third finger of the left hand. Oral cavity examination was normal. The patient vitals were stable and generalized examination was otherwise unremarkable especially with no identified lymphadenopathy or parotid glands swelling. Larynx examination through direct laryngoscopy revealed an irregular, swelled and bruised left vocal fold as well as swelled epiglottis with conserved movement of both vocal folds. Histological examination of the left vocal fold biopsy highlighted the presence of non-caseating epithelioid cell granulomas. Thus, further investigations were required to ascertain the cause of our patient condition.

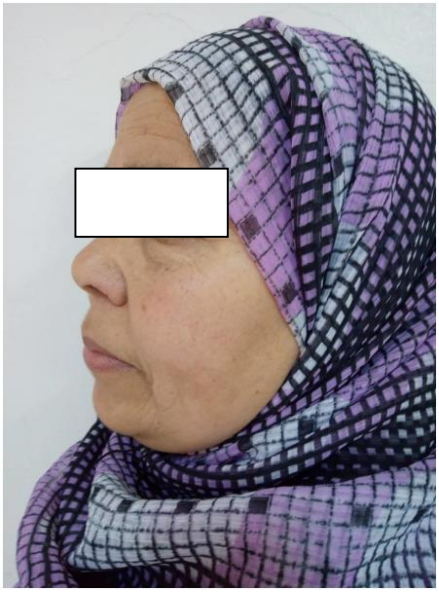

Fig. 1. Side view of the patient face showing saddle-nose deformity

Laboratory routine tests showed no evidence of inflammation with C-reactive protein: 1 mg/L, erythrocyte sedimentation rate: 18 mm-h1 and fibrinogen: 3.6 g/L. Serum proteins electrophoresis was without abnormalities. Complete blood count revealed low white blood cell count at 2.6x10^9/L with low neutrophil and lymphocyte count respectively at 1.2x10^9/L and 1.1x10^9/L. Eosinophil count was normal. Hemoglobin was at 130 g/L and platelet count was at 196x10^9/L. Kidneys and liver function tests were both normal. Blood and urine phosphate and calcium balance was within normal range. Thyroid function tests were normal.

Chest X-ray was normal without mediastinal widening or signs of interstitial lung disease. CT of the chest and cervical region showed a discreet asymmetry of the vocal folds without focal lesion or contrast enhancement. It also revealed sub-centimeter sized cervical lymph nodes. There were no mediastinal lymphadenopathies. However, we noted the presence of bilateral perifissural nodules the largest measuring 6 mm in the right lung upper lobe with no signs of malignancy (Fig. 2).

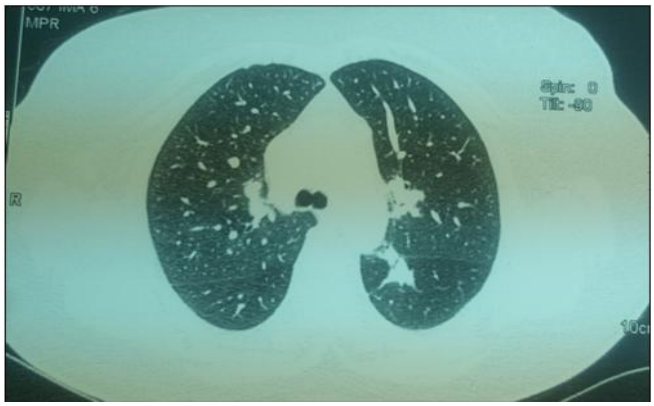

Fig. 2. CT of the chest showing bilateral perifissural nodules

Sputum smear and culture showed no evidence of acid-fast bacilli. Tuberculin skin test was negative. Broncho alveolar lavage fluid examination showed lymphocytic alveolitis with an increased CD4/CD8 T-lymphocyte ratio at 4.2. No Koch bacilli were identified. Spirometry test showed normal lungs capacity. Angiotensin-converting enzyme (ACE) was normal at 30 UACE (normal range: 12-68 UACE). Minor salivary glands biopsy yielded no pathological findings.

Given the association of laryngeal granulomas and saddle nose deformity, although histological examination showed no signs of vasculitis, we still requested anti-neutrophil cytoplasmic antibodies which were negative. We also performed nasal cavity biopsy which histological examination revealed non-caseating granulomas without vasculitis.

As the patient presented dactylitis, we performed X-rays of the hands which showed diffuse demineralization with grid-like appearance associated with cysts of the 2nd and 4th digit of the right hand (Fig. 3) and the 3rd digit of the left hand (Fig. 4) consistent with tuberculosa multiplex cystica. We also noted dislocation of the proximal interphalangeal joint of the 2nd digit of the right hand.

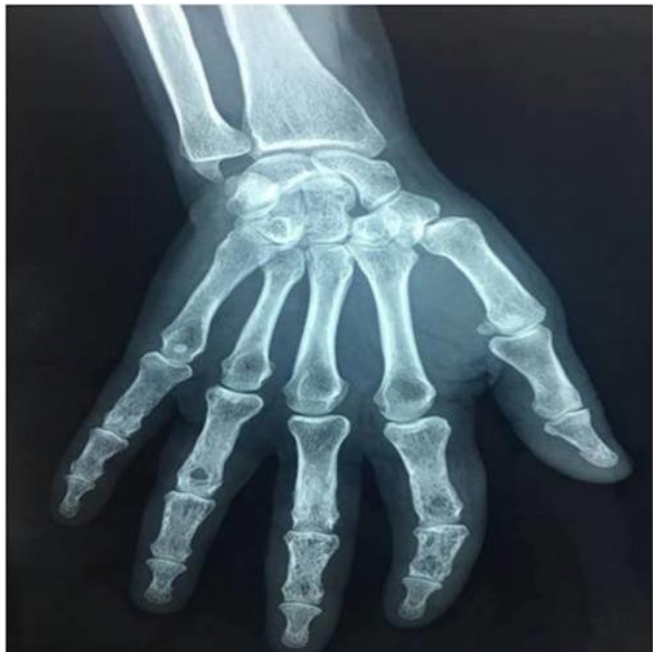

Fig. 3. Bone sarcoidosis with large cysts involving the 2nd and 4th digit of the right hand

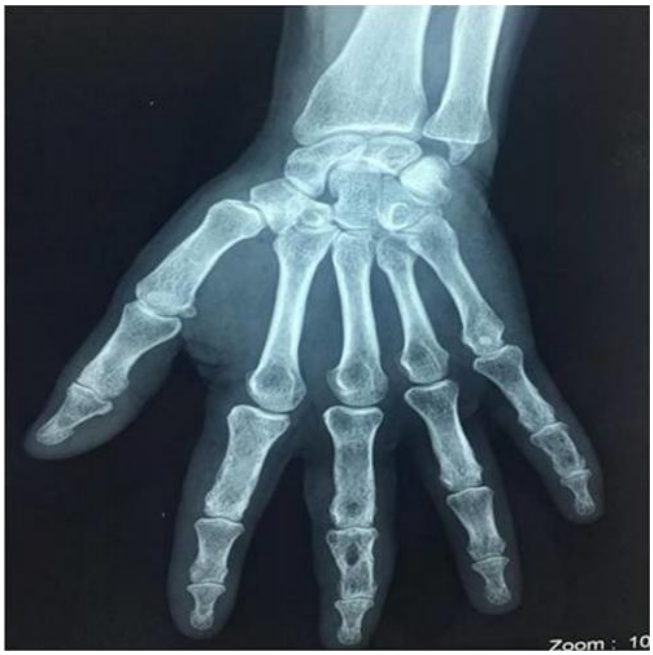

Fig. 4. Bone sarcoidosis showing large cysts of the 3rd digit of the left hand

These findings all pointed to the diagnosis of sarcoidosis with upper respiratory tract (nasal and laryngeal), skeletal and pulmonary involvement.

The patient was started on corticosteroid at 0.5 mg/kg/day of prednisone for four weeks followed by progressive tapering. As she didn't present signs of airways obstruction, no endoscopic procedure was required.

Clinical outcome was favorable as the patient almost recovered the voice she had prior to the disease onset within three weeks of treatment. Follow-up direct laryngoscopy was suggested but it was refused by the patient. Treatment was discontinued after one year and the patient has yet to present any signs of relapse after three years of follow-up.

3. DISCUSSION

We herein report the case of persistent hoarseness in a 51-year-old female leading to the diagnosis of systemic sarcoidosis with upper respiratory tract, lung and skeletal involvement. Vocal fold biopsy and nasal biopsy both confirmed the presence of non-caseating granulomas. The patient was successfully treated with corticosteroid and sustained clinical remission was obtained after treatment was discontinued.

Sarcoidosis is a multisystem granulomatous disease that primarily targets the lungs followed by the lymph nodes. However, this disease may expand to all organs and tissues resulting in diverse clinical presentations [1]. As a specific diagnostic test has yet to be identified, diagnosis requires the association of three criteria: concordant clinical and radiological presentation, histological evidence of non-caseating epithelioid cell granulomas and exclusion of other granulomatous disorders [4].

Otorhinolaryngologic involvement in sarcoidosis occurs in 3% of patients and may be easily overlooked [5]. Laryngeal sarcoidosis is very rare as it has been reported in no more than 1% of patients [2]. Clinical symptoms mostly consist of progressive hoarseness, dyspnea, chronic cough and dysphagia. Obstructive sleep apnea has also been reported [3,6]. Such non-specific upper respiratory tract symptoms commonly result in an important delay in diagnosis. However, acute presentation may be observed with severe airway obstruction requiring urgent intervention such as tracheostomy in 10 to 20% of cases [7].

Macroscopic appearance usually presents as diffuse thickening and edema of the supraglottic region. Epiglottis, aryepiglottic folds, arytenoid cartilages and false vocal folds are commonly involved in laryngeal sarcoidosis. Subglottic involvement is rare [8]. Involvement of the true

vocal folds, which was observed in our patient, is extremely rare given the relative lack of lymphatic tissues [9]. Larynx examination can also reveal vocal folds immobility; such occurrence could be linked to compression of the recurrent laryngeal nerve by lymphadenopathy, neurosarcoidosis or infiltration of the larynx by non-caseating granulomas [10].

Laryngeal involvement is often diagnosed prior or concomitantly to sarcoidosis [11]. Given that sarcoidosis is a diagnosis of exclusion, patients must be screened for other organs involvement as to assess the likelihood of sarcoidosis and to rule out other granulomatous disorder such as tuberculosis and granulomatosis with polyangiitis. This may also unveil organs damage requiring more aggressive therapy.

Head and cervical region involvement, especially nasosinusal, was reported at a higher frequency in patients with laryngeal sarcoidosis. Our patient had nasal crusting without nasal obstruction, epistaxis or anosmia. Nasal cavity biopsy confirmed the presence of non-caseating granulomas. Ophthalmological involvement and lupus pernio were also more observed in patients with laryngeal sarcoidosis [11].

Skeletal involvement in sarcoidosis includes joint and bone manifestations. Bone sarcoidosis is rare with a reported prevalence of 0.5 to 34% [12]. Lesions of the small bone of the hand, as portrayed in our case, are reported in 5 to 7% of sarcoidosis. They usually occur in patients with active sarcoidosis and commonly involve the distal and intermediary phalanges of the second and third digits. They manifest as diffuse demineralization, cortical thinning and formation of cyst resulting in a grid appearance and at a later stage pathological fractures may be observed [13].

Spontaneous remission in laryngeal sarcoidosis is rare, occurring in less than 10% of patients [14]. As such, treatment mainly consists of systemic corticosteroid. Inhaled corticosteroid has been used successfully in nasosinusal sarcoidosis but their effectiveness in laryngeal sarcoidosis is still to be confirmed. Local injections of corticosteroid have also been proposed with favourable results and reduced side effects [3,5]. Our patient received corticosteroid at 0.5 mg/kg daily with prompt clinical improvement. This favourable outcome was maintained even after treatment discontinuation. In case of corticosteroid resistance or severe adverse effects, other therapeutic options include hydroxychloroquine, methotrexate and azathioprine [15].

4. CONCLUSION

Laryngeal sarcoidosis, although rare, is ought to be considered in patients presenting persistent laryngeal symptoms if no clear cause is identified. It can be isolated or presents as the initial manifestation of the disease thus making the diagnosis more challenging. Clinical presentation may range from non-specific chronic symptoms such as voice hoarseness to life-threatening airway obstruction requiring immediate intervention. Therapeutic options are diverse with corticosteroid whether local or systemic being the most common treatment.

CONSENT AND ETHICAL APPROVAL

As per international standard guideline participant consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Martusewicz-Boros MM, Boros PW, Wiatr E, Roszkowski-Śliż K. What comorbidities accompany sarcoidosis? A large cohort (n=1779) patients analysis. Sarcoidosis Vasc Diffuse Lung Dis 2015;32:115–20.
2. Judson MA. Extrapulmonary sarcoidosis. Semin Respir Crit Care Med. 2007;28:83–101.
3. Edriss H, Kelley JS, Demke J, Nugent K. Sinonasal and laryngeal sarcoidosis - An uncommon presentation and management challenge. Am J Med Sci. 2019;357(2):93-102.
4. Ben Abdelghani K, Mahfoudhi M, Hriz A, El Kossai I, Khefifi A, Turki S, et al. AA amyloidosis complicating sarcoidosis: Two cases and literature review. Rev Med Interne. 2010;31(5):369-71.
5. Butler CR, Nouraei SA, Mace AD, Khalil S, Sandhu SK, Sandhu GS. Endoscopic airway management of laryngeal sarcoidosis. Arch Otolaryngol Head Neck Surg. 2010;136(3):251-5.

6. Ahmed M, Sulaiman I, Rutherford R, Gilmartin JJ. First presentation of sarcoidosis with severe obstructive sleep apnoea and epiglottic involvement. Sarcoidosis Vasc Diffuse Lung Dis. 2013; 30(2):146-8.
7. Ryu C, Herzog EL, Pan H, Homer R, Gulati M. Upper airway obstruction requiring emergent tracheostomy secondary to laryngeal sarcoidosis: A case report. Am J Case Rep. 2017;18:157-9.
8. Mayerhoff RM, Pitman MJ. Atypical and disparate presentations of laryngeal sarcoidosis. Ann Otol Rhinol Laryngol. 2010;119(10):667-71.
9. Van den Broek EM, Heijnen BJ, Verbist BM, Sjögren EV. Laryngeal sarcoidosis: A case report presenting transglottic involvement. J Voice. 2013;27(5):647-9.
10. Hintze JM, Gnagi SH, Lott DG. Sarcoidosis presenting as bilateral vocal fold immobility. J Voice. 2018;32(3):359-62.
11. Duchemann B, Lavolé A, Naccache JM, Nunes H, Benzakin S, Lefevre M, et al. Laryngeal sarcoidosis: A case-control study. Sarcoidosis Vasc Diffuse Lung Dis. 2014;31(3):227-34.
12. Sparks J, McSparron J, Shah N, Aliabadi P, Paulson V, Fanta C. Osseous sarcoidosis: Clinical characteristics, treatment, and outcomes - experience from a large, academic hospital. Semin Arthritis Rheum. 2014;44:371–9.
13. Aptel S, Lecocq-Teixeira S, Olivier P, Regent D, Teixeira PG, Blum A. Multimodality evaluation of musculoskeletal sarcoidosis: Imaging findings and literature review. Diagn Interv Imaging. 2016;97(1):5-18.
14. Tsubouchi K, Hamada N, Ijichi K, Umezaki T, Takayama K, Naka nishi Y. Spontaneous improvement of laryngeal sarcoidosis resistant to systemic corticosteroid administration. Respirol Case Rep. 2015;3(3):112-4.
15. Agrawal Y, Godin DA, Belafsky PC. Cytotoxic agents in the treatment of laryngeal sarcoidosis: A case report and review of the literature. J Voice. 2006;20 (3):481–8.

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