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Orofacial Sarcoidosis and Granulomatosis

Mohammad Hosein Kalantar Motamedi¹,
Mohammad Ghasem Shams² and Taghi Azizi³

¹Trauma Research Center, Oral and Maxillofacial Surgery Clinic,

²Oral and Maxillofacial Surgery Clinic,

³Pathology Department,

^{1,2,3}Baqiyatallah Medical Center, Baqiyatallah University of Medical Sciences, Tehran,
IR Iran

1. Introduction

Sarcoidosis is a multi-systemic inflammatory disorder of unknown etiology. It is classified as an acquired systemic granulomatous disease. Because of the fact that sarcoidosis affects multiple tissues and organs it is characterized by many potential signs and symptoms, as well as by the presence of noncaseating granulomas in the organs involved. Although orofacial sarcoidosis is relatively rare, it may however, present in the oral and maxillofacial region. The respiratory system is the most commonly affected system, with approximately 90% of patients presenting pulmonary findings during the course of their disease. Cutaneous manifestations occur in around 25% of cases and are more common in chronic cases. Head and neck lesions of sarcoidosis are manifested in 10 to 15% of patients (Samtsov, 1992; Newman et al., 1997; Suresh & Radfar, 2005).

In the maxillofacial region the salivary glands may be involved, while sometimes, xerostomia and bilateral parotid swelling may be seen (Piattelli et al., 1998; Batal et al., 1999). Lesions occurring in the soft tissues of the oral cavity and/or in the jaws are rare. Orofacial granulomatosis (OFG) is a granulomatous disease. This clinicopathological entity describes patients with oral lesions characterized by persistent and/or recurrent labial enlargement, ulcers, and a variety of other orofacial features, which on biopsy have lymphedema and noncaseating granulomas. The cause is idiopathic but appears to represent an abnormal immune reaction. This may be a manifestation of Crohn's disease (CD) since some patients with oral lesions develop typical bowel symptoms of CD in ensuing months to years; tooth associated infections, viruses, food or contact allergies have been implicated in causing OFG. Sarcoidosis has also been implicated in causing OFG. Clinical features of OFG are highly variable and sometimes so insidious that signs and symptoms are frequently not severe enough to cause alarm. The lips are most commonly involved and demonstrate a nontender, persistent swelling. Because of the relatively nonspecific clinical findings associated with granulomatous diseases, a microscopic diagnosis of granulomatous inflammation per se often presents a diagnostic dilemma (Shams et al., 2007).

2. Etiology

The cause of sarcoidosis is idiopathic but appears to represent an abnormal immune reaction. OFG may be a manifestation of Crohn's disease (CD) since some patients with oral lesions

develop typical bowel symptoms of CD in ensuing months to years; tooth associated infections, viruses, food or contact allergies have been implicated in causing OFG. Sarcoidosis has also been implicated in causing OFG. Although the etiology of sarcoidosis is unknown, many factors may be accused in the pathogenesis of this disease. Implicated causative factors are: infections (fungal, viral, bacterial), genetic predisposition, environmental factors and miscellaneous factors (DiAlberti et al., 1992; Mendelsohn et al., 1992; Rybicki et al., 1997; Armstrong et al., 2004). The specific tests for fungal (mycology tests for *Candida* spp-cultivation in SDA and CHROMAgar *Candida*), viral (Abs to HIV, EBV, CMV) and bacterial (for mycobacterium-skin test and AFB) infections may also be investigated.

3. Presentation

3.1 General findings

The respiratory system is the most commonly affected system in sarcoidosis, with approximately 90% of patients presenting pulmonary findings during the course of their disease. Cutaneous manifestations occur in around 25% of cases and are more common in chronic cases. Head and neck lesions of sarcoidosis are manifested in 10 to 15% of patients (Armstrong et al., 2004).

3.2 Oral and maxillofacial involvement

In the maxillofacial region the clinical features of OFG are highly variable and sometimes so insidious that signs and symptoms are frequently not severe enough to cause alarm. The lips are most commonly involved and demonstrate a nontender, persistent swelling (Fig. 1). Salivary glands may be involved and xerostomia and bilateral parotid swelling may be seen. Lesions occurring in the soft tissues of the oral cavity and/or in the jaws are rare. Orofacial granulomatosis (OFG) is a granulomatous disease. This clinicopathological entity describes patients with oral lesions characterized by persistent and/or recurrent labial enlargement, ulcers, and a variety of other orofacial features, which on biopsy have lymphedema and noncaseating granulomas (DiAlberti et al., 1992; Mendelsohn et al., 1992; Rybicki et al., 1997; Armstrong et al., 2004; Shams et al., 2007).

Oral involvement generally appears in patients with chronic multisystem sarcoidosis and seldom occurs in the acute stage. The oral lesions may be solitary, multiple or part of a generalized disease. In some cases, oral involvement is the first or only, manifestation of the disease and appears as a nontender well-circumscribed brownish red or violaceous swelling, as papules, or as submucosal nodules that can occasionally either show superficial ulceration or be symptomatic. Gingival involvement presents as red gingival enlargement (DiAlberti et al., 1992; Mendelsohn et al., 1992; Rybicki et al., 1997; Armstrong et al., 2004; Shams et al., 2007). In some cases the lesions are multifocal, including the lips, the gingiva and the hard palate. The clinical signs (red-violet nodular mass in the middle of the palate, and the erythematous and hyperplastic gingival in the upper incisor area) may be seen. Alternatively, oral sarcoidosis may be asymptomatic or mildly symptomatic with minimal discomfort during eating or drinking, especially if the lesions involve the tongue (Mendelsohn et al., 1992).

4. Diagnosis

In most cases of oral involvement, sarcoidosis is diagnosed before the oral manifestations become apparent. Occasionally, oral involvement is the first or only manifestation of the

disease. The diagnosis of sarcoidosis is established when clinical features are supported by histopathological evidence of typical non-caseating epithelioid granulomas and other laboratory tests (Samtsov, 1992; Newman et al., 1997; Suresh & Radfar, 2005).

4.1 Differential diagnosis

The differential diagnosis of oral soft tissue lesions must consider other granulomatous conditions, such as infections (tuberculosis, leprosy, tertiary syphilis, systemic mycoses, and cat-scratch disease), Crohn's disease, Melkersson-Rosenthal syndrome (including Mieschers cheilitis or cheilitis granulomatosa), Wegener's granulomatosis, foreign body reactions and hairy cell leukaemia (Rybicki et al., 1998).

Patients with CD may present to the clinician with GI symptoms attributed to the disease or non-specific lesions in the oral cavity, nose, or larynx. Some OFG patients have both histopathological and immunopathological features that resemble those observed in CD patients. Some of these clinical manifestations have been found to be consistent with CD, but most have not (Shams et al., 2007). Often an extensive clinical, microscopic, and laboratory evaluation may be required to identify the source of the granulomatous inflammation (Piattelli et al., 1998).

4.2 Evaluation tests

As stated above, clinical microscopic, and laboratory evaluation together may be required to identify the source of the granulomatous inflammation. Negative endoscopy of the GI tract, normal ESR, normal serum albumin, Ca, folate and iron levels will rule out CD.

With regard to sarcoidosis, a normal CXR and ACE level would make sarcoidosis unlikely. Chronic granulomatous disease is ruled out by using the neutrophil nitroblue tetrazolium reduction test (DiAlberti et al., 1992; Mendelsohn et al., 1992; Rybicki et al., 1997; Armstrong et al., 2004; Shams et al., 2007).

Because of the relatively nonspecific clinical findings associated with granulomatous diseases, a microscopic diagnosis of granulomatous inflammation per se often presents a diagnostic dilemma. Clinical, microscopic, and laboratory evaluation may be required to identify the source of the granulomatous inflammation. The serum angiotensin converting enzyme (normal value: 18-55 U/L), blood calcium (normal value: 9-11 mEq/L) and 24-hrs urine calcium (normal value <180 mg) erythrocyte sedimentation rate (1-2 mm/h) should be assessed. Negative endoscopy of the GI tract, normal ESR, normal serum albumin, Ca, folate and iron levels will rule out CD. With regard to sarcoidosis, a normal CXR and ACE level would make sarcoidosis unlikely. Chronic granulomatous disease is ruled out by using the neutrophil nitroblue tetrazolium reduction test.

Another condition that may be associated with granuloma formation is cheilitis granulomatosa (CG). This is a subset of OFG, which presents clinically as persistent lip swelling. It also is a granulomatous inflammation of unknown origin. CG may be part of the triad of the Melkersson-Rosenthal syndrome (MRS). Swelling of the lips along with fissured tongue and facial paralysis constitute this syndrome. Lesions closely resemble nodules of tuberculosis (TB) and the differential diagnosis is often difficult. To make the diagnosis, other appropriate studies (special stains for acid fast bacilli, GMS and PAS stains for fungi, cultures, and so forth) to exclude tubercle bacilli, fungi, foreign bodies, or other causes of the granulomatous condition must be done. When the histopathological findings are compatible with sarcoidosis, in order to confirm the diagnosis, we must proceed with laboratory tests that support the diagnosis for sarcoidosis (DiAlberti et al., 1992; Mendelsohn et al., 1992; Rybicki et al., 1997; Armstrong et al., 2004; Shams et al., 2007).



Fig. 1. Typical swelling of the lips.

5. Histopathology

Histopathologically, OFG lesions closely resemble nodules of tuberculosis (TB) and the differential diagnosis is often difficult. To make the diagnosis other appropriate studies (special stains for acid fast bacilli, GMS and PAS stains for fungi, cultures, etc.) to exclude tubercle bacilli, fungi, foreign bodies, or other causes of the granulomatous condition must be done. Photomicrographs of OFG lesions (Figs.2-8) show edema, scattered and clustered lymphocytes in the connective tissue as well as several well-defined, granulomas consisting of collections of epithelioid histiocytes and multinucleated giant cells (Shams et al.,2007).

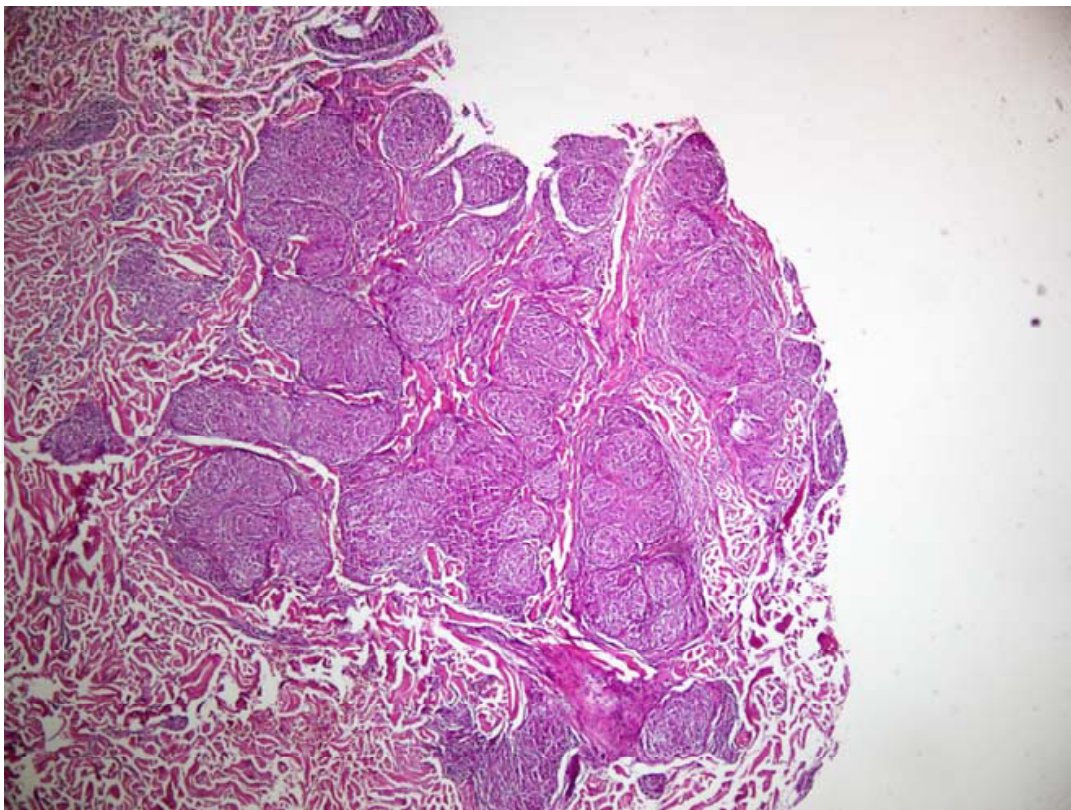


Fig. 2. Confluent noncaseating granulomatous inflammation (H&E low power view).

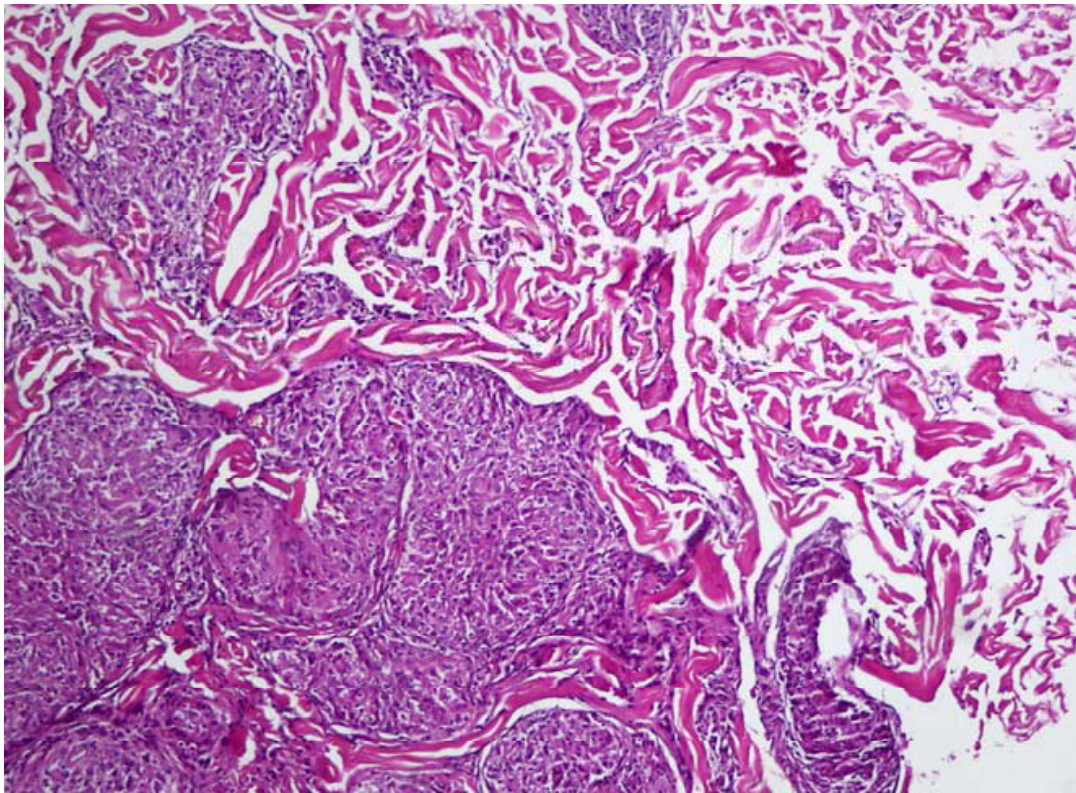


Fig. 3. Confluent noncaseating granulomatous inflammation (H&E medium power view).

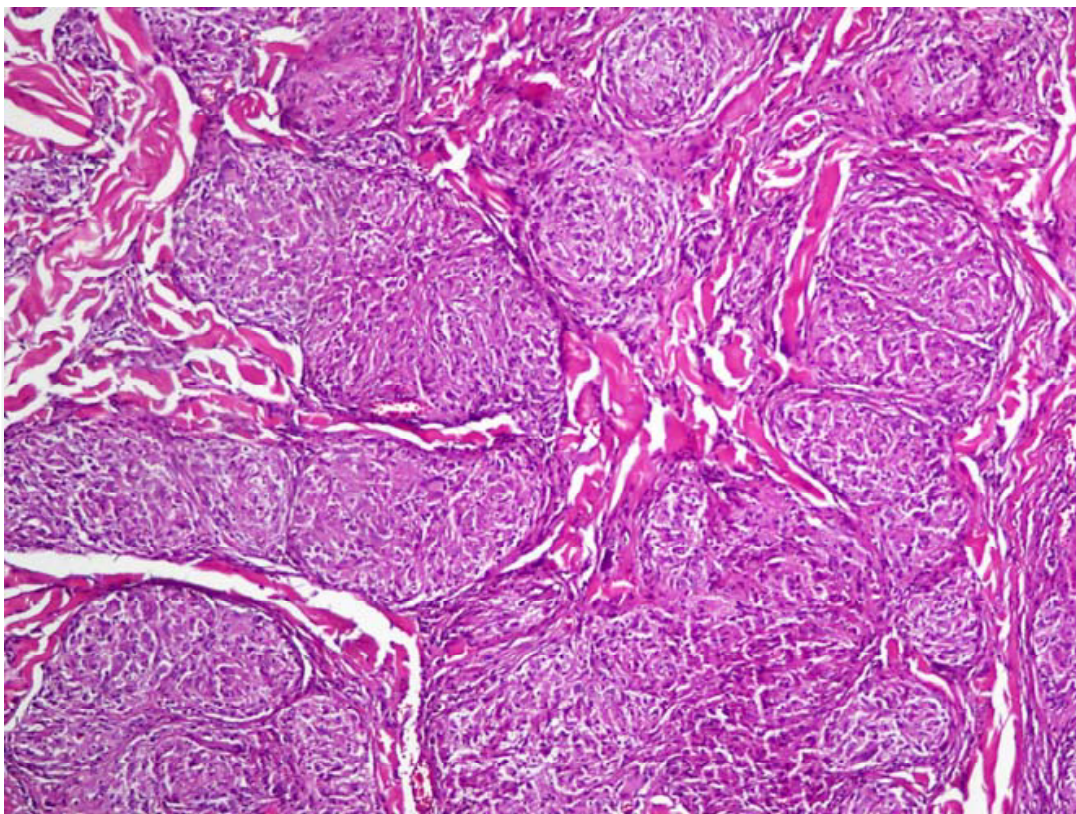


Fig. 4. Confluent noncaseating granulomatous inflammation (H&E high power view).

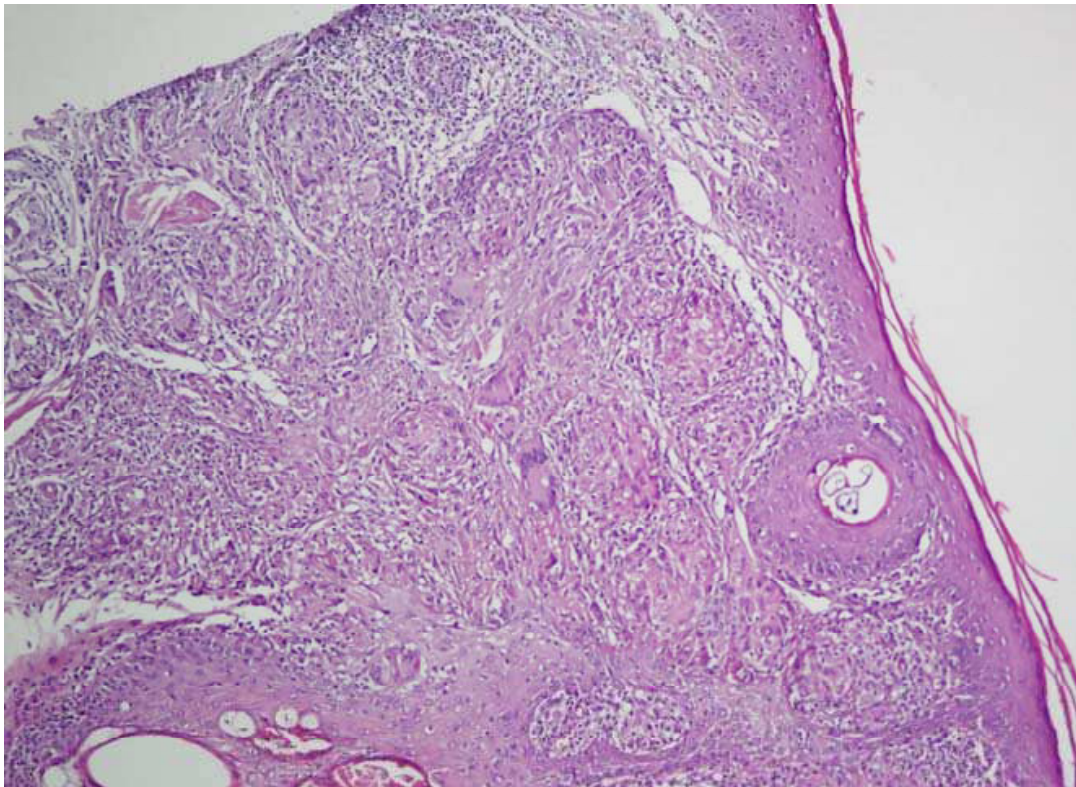


Fig. 5. Sarcoidosis of skin, noncaseating granulomatous inflammation (H&E low power).

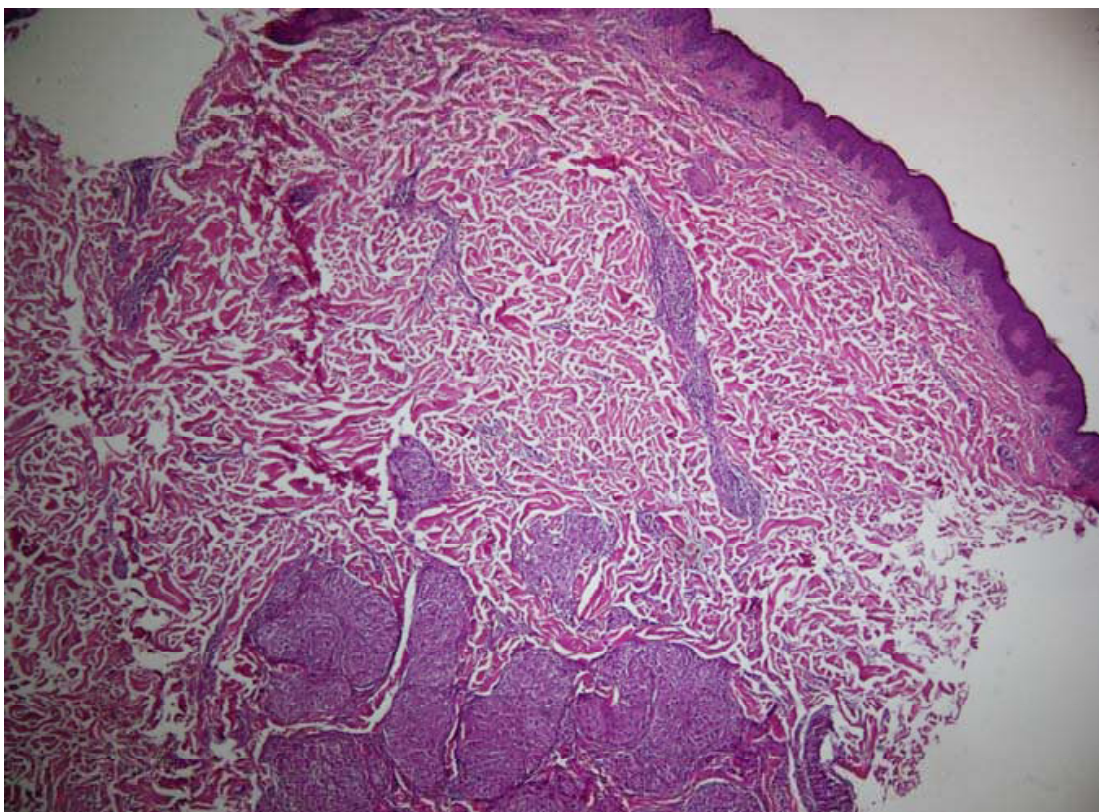


Fig. 6. Sarcoidosis of skin, noncaseating granulomatous inflammation (H&E low power view).

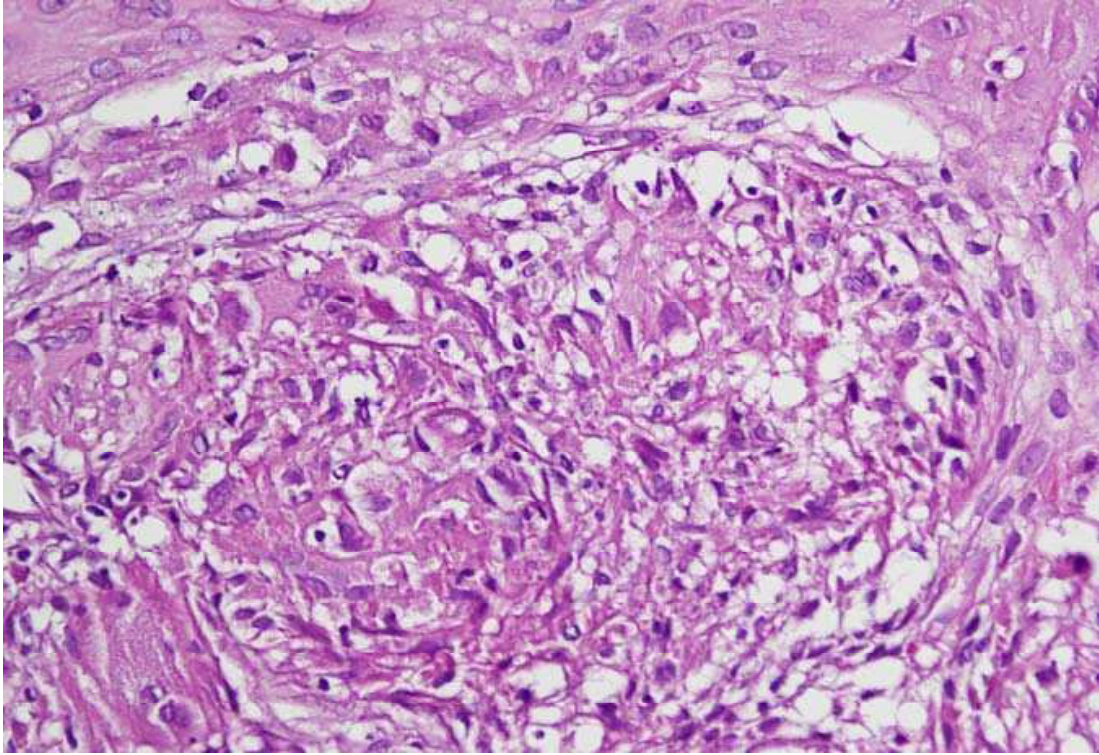


Fig. 7. Sarcoidosis – asteroid bodies and multinucleated giant cells (H&E high power view).

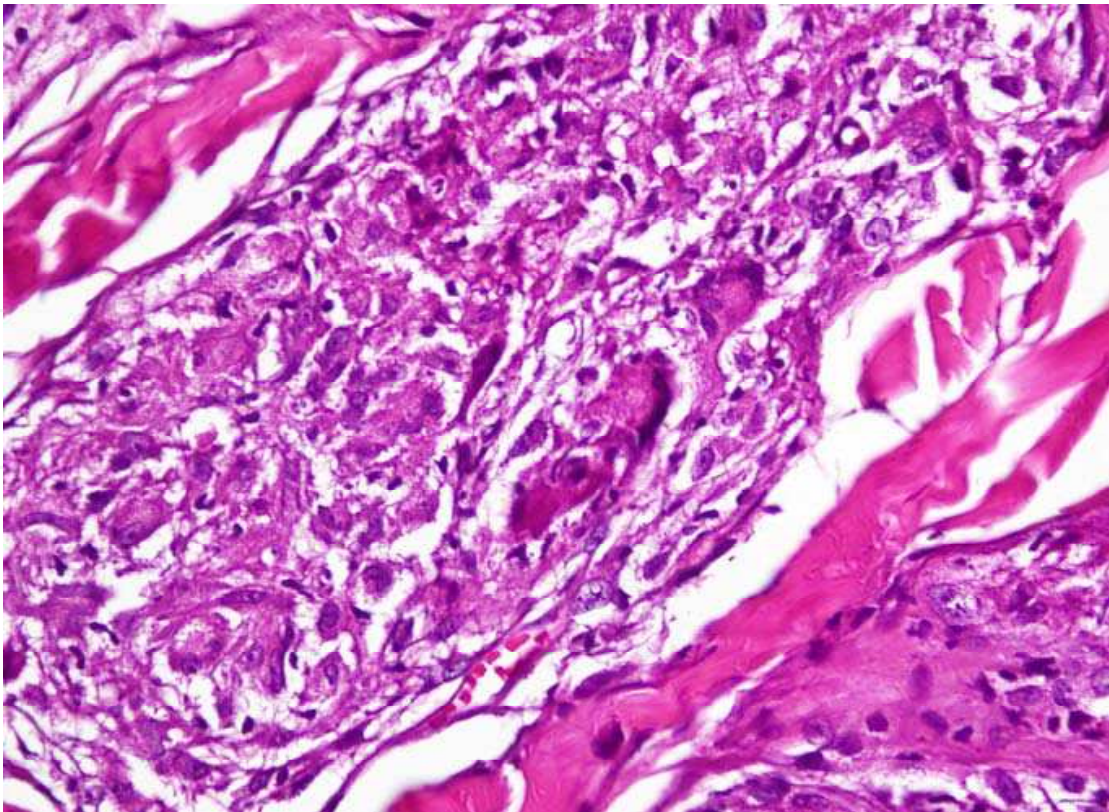


Fig. 8. Sarcoidosis – asteroid bodies and multinucleated giant cells (H&E high power view).

6. Treatment

Oral glucocorticoids are the first-line treatment. Other medications include cytotoxic drugs such as methotrexate, azathioprine, chlorambucil, cyclosporine and cyclophosphamide. Some authors suggest the surgical excision for treatment of oral soft tissue or jaw lesions. A variety of drugs have been tried in treatment of OFG including corticosteroids. Surgery in these patients is usually unnecessary as treatment is primarily pharmacological. Systemic corticosteroids are considered the best treatment. Glucocorticoids effectively suppress the activated T-helper-induced cell processes occurring at the site of disease in 50 percent of the patients. The usual therapy is prednisolone 1 mg/kg for 4 to 6 weeks followed by a slow tapering over 2 to 3 months. This is repeated if the disease again becomes active. Intralesional steroid injections are also an alternative treatment method that one might also consider. The prognosis is generally favourable (Shams et al., 2007).

7. Prognosis

Oral lesions may be the first or the only sign of sarcoidosis in an otherwise healthy patient. Although, oral involvement of the disease is very rare and often localized, however, the prognosis of orofacial sarcoidosis correlates with mode of onset, initial clinical course, characteristics of the host and extent of the disease. However, this multisystem disorder may never be completely cured. Moreover, it is important to endorse a periodic follow-up of patients in order to evaluate the status of the patient and course of the disease. Many of those affected remain asymptomatic and remission sometimes occurs spontaneously (Shams et al., 2007).

8. Discussion

The nomenclature of OFG lacks specificity. Recently, a question has been posed to determine whether OFG is a manifestation of a separate and specific inflammatory bowel disease. Other authors also suggested that OFG is a descriptive term and the specific cause of these lesions is unknown (Shams et al., 2007).

Some authors (Edmondstone & Wilson, 1985; Hills et al., 1987; Edmondstone, 1988; Bardinas et al., 1989; Panayreas et al., 1991; Rybicki et al., 1997) have reported a familial, (i.e. among people in the same household), seasonal and occupational clustering of sarcoidosis, suggesting a multifactorial origin that includes genetic predisposition, infectious organisms and environmental exposures as probable underlying mechanisms.

8.1 Organ involvement

Sarcoidosis is known to affect a wide array of organs and tissues, including the lung, heart, liver, spleen, bones, skin, eyes, lymph nodes, parotid glands and, on occasion, the oral cavity (Cahn et al., 1964; Tilman, 1964). The extent of the disease and its complications vary, ranging from mild symptoms in some patients to major incapacitation in others (Tilman, 1964; Steinberg & Mueller, 1994). Many patients experience no symptoms and are identified incidentally. The most prominent manifestations of the disease involve the lungs, as evidenced clinically by the presence of dyspnea in patients. Lung volumes and diffusing capacity often are reduced, and chest radiographs reveal bilateral hilar lymphadenopathy, diffuse parenchymal infiltrates or both (Reed, 1988; Steinberg & Mueller, 1994; Quernheim, 1998; Hong & Farish, 2000).

8.2 Disease course

The pattern of onset in sarcoidosis, the site involved determines the course and prognosis of the disease. Skin, eyes and lymph nodes are the most frequent sites of extrapulmonary involvement. Cutaneous sarcoidosis has been reported to occur in 25 percent of patients, and it may suggest chronicity and poor prognosis (Hong & Farish, 2000). Similarly, one of four patients is affected with ocular sarcoidosis with the potential for progression to blindness (Steinberg & Mueller, 1994). Cardiac sarcoidosis and neurosarcoidosis are uncommon, but they may lead to fatal complications such as dysrhythmias and conduction block, as well as seizures and encephalopathy. Other possible systemic effects include liver and spleen enlargement, thrombocytopenia, abnormal calcium metabolism, renal dysfunction, arthropathy and skeletal deformities (Hillerup, 1976; Johns, 1988 ; Reed, 1988 ; Steinberg & Mueller, 1994).

8.3 Diagnosis of exclusion

Owing to the absence of a diagnostic gold standard, sarcoidosis is a diagnosis of exclusion (Quernheim, 1998 ; Hong & Farish, 2000). First, the clinician establishes a compatible clinical picture based on symptomatology and physical and radiographic findings. Next, the clinician performs a biopsy of the most accessible organ, such as skin or lymph nodes, to obtain histologic evidence of noncaseating granulomas. These structures are composed of focal aggregates of lymphocytes, macrophages and multinucleated giant cells, but they are not unique to this disease. Therefore, it is necessary to exclude other sources of granulomatous inflammation, such as foreign-body implantation, tuberculosis, Crohn's disease and deep fungal infections (Israel & Sones, 1964; Reed, 1988 ; Steinberg & , Mueller, 1994).

8.4 Comprehensive assessment

Clinicians confronting patients with oral granulomatosis must perform a comprehensive assessment of potential target organs in patients suspected of having sarcoidosis, with special attention paid to the lungs, heart, central nervous system (CNS), eyes, skin and lymph nodes. A chest radiograph and a thorough ophthalmic evaluation are required, even for patients without specific pulmonary or ocular complaints. Baseline laboratory tests include complete blood cell counts, erythrocyte sedimentation rate, liver and renal function tests, serum calcium and SACE levels, pulmonary function tests, electrocardiography and tuberculin testing. Periodic follow-up is essential for the clinician to evaluate the progression of the disease and to detect new organ involvement (Reed, 1988; Steinberg & , Mueller, 1994 ; Rybicki et al.,1996; DiAlberti et al.,1997 ; Rybicki et al.,1998).

8.5 Laboratory markers

The SACE level has been studied extensively as a laboratory marker in sarcoidosis. Secretion of ACE by granuloma-forming epithelioid cells results in high serum levels in 80 to 90 percent of patients with sarcoidosis. However, because of the lack of specificity, an elevated SACE level is only suggestive of, rather than diagnostic for, sarcoidosis. The reported false-positive and false-negative rates for the SACE level as a laboratory marker of sarcoidosis are 10 and 40 percent, respectively. (Schultz et al., 1979 ; Chesnutt & Enigmas, 1995 ; Shah et al., 1997 ; Rybicki et al.,1998)

8.6 Pattern of onset

The pattern of onset in sarcoidosis determines the course and prognosis of the disease, as well as the patient's therapeutic response. Although spontaneous resolution is common in

cases of acute sarcoidosis, chronic disease often is associated with a gradual onset, a progressive course and many potential complications. Poor prognostic indicators include older age at onset, black race, hypersplenism and advanced pulmonary involvement. It is uncommon for patients to die of sarcoidosis and death often is attributed to terminal fibrosis of critical organs such as the lungs, heart or CNS (Steinberg & , Mueller, 1994; Mana et al., 1994; Newman et al., 1997; Quernheim, 1998).

8.7 Head and neck involvement

Sarcoidosis typically is diagnosed before orofacial sequelae appear. Sarcoidosis may affect the head and neck lymph nodes, osseous and soft oral tissues, as well as the major and minor salivary glands. Parotid glands are affected in 4 to 6 percent of cases of sarcoidosis, with a self-limiting or permanent enlargement as the outward presentation. Enlargements often are bilateral, asymptomatic, firm and smooth on palpation, with no changes in size when eating. Associated xerostomia may or may not be present. Although these clinical features are characteristic of Sjögren's syndrome, occasionally they may be associated with sarcoidosis. A labial gland biopsy is a highly sensitive and specific diagnostic test in the histologic assessment of Sjögren's syndrome, but it also can assist in the differentiation of Sjögren's syndrome from sarcoidosis when clinical presentations are similar (Greenberg et al., 1964; Gold & Sager, 1976; James et al., 1976; Giotaki et al., 1986; Melsom et al., 1988; Drosos et al., 1999; Levy et al., 2001).

Sarcoid lesions of the jaw bones may appear as diffuse, poorly defined radiolucencies on dental radiographs, and they can result in tooth mobility on clinical examination.

Several studies have shown sarcoid infiltration of the minor salivary glands with or without clinical involvement of the major salivary glands. Therefore, when accessible and clinically involved tissues are not available, the clinician can perform a biopsy of normal-appearing tissue to confirm the histologic diagnosis in a patient with compatible clinical findings (Hughes & Gross, 1972; Tarpley et al, 1972; Rasmussen & Neukirch, 1976; Nesson & Jacoway, 1979).

8.8 Labial minor salivary gland biopsy

Several cases of sarcoidosis-induced parotid enlargement confirmed via biopsy of the labial minor salivary gland have been reported in the literature. This technique has a lower diagnostic yield in sarcoidosis compared with biopsies of the liver, lung, lymph node or parotid gland, perhaps because of the uncommon, delayed (after other clinical signs develop) and less intense histologic involvement of the minor salivary glands. On the other hand, this procedure is simple, minimally invasive and associated with significantly less morbidity than is a parotid gland biopsy. In addition, the tissue is readily accessible from the lower labial mucosa, and the clinician can perform the procedure under local anesthesia at chairside (Chisholm et al., 1971 ;Tannenbaum et al., 1974 ; Siltzbach, 1980 ; Marx et al., 1988).

Owing to the complexity of disease manifestation, clinicians tailor therapy to each patient. Many patients experience temporary or long-term remission without medical therapy. Therefore, treatment often is deferred for three to 12 months to assess the overall disease progression. Immediate medical treatment is reserved for patients with neurological, cardiac, severe ocular, advanced pulmonary and disfiguring cutaneous disease, as well as persistent hypercalcemia (Turiaf et al., 1976 ; van Maarsseveen et al., 1982; Nagata et al., 1999). Clinicians focus treatment on the suppression of the immune system, and corticosteroids are the mainstay of therapy. Topical, inhalational, intralesional or systemic steroids may be used to control the disease, depending on its severity. Physicians closely

monitor patients receiving long-term systemic steroid therapy for potential adverse effects of these medications. They also can consider steroid-sparing immunosuppressive agents for patients with critical organ involvement that is poorly controlled with systemic steroid therapy. Implanted cardiac defibrillators or heart and lung transplantation may be indicated for patients with cardiac and pulmonary sarcoidosis in which the organs are not salvageable. Splenectomy may be necessary to treat sarcoidosis-induced splenomegaly associated with a risk of rupture (Russo & Millikan, 1994; Baughman, 1997; Judson, 1998; Crystal, 1998; Pietinalho et al., 1999).

8.9 Dental considerations

Dentists need to consider a number of issues regarding the dental care of patients with sarcoidosis. Sarcoid lesions of the jaw bones may appear as diffuse, poorly defined radiolucencies on dental radiographs, and they can result in tooth mobility on clinical examination. Approximately 1 to 6 percent of patients with sarcoidosis may have an obstruction of the nasal passages or chronic sinusitis. Steroid supplementation before major oral surgery may be indicated for patients with adrenal suppression secondary to long-term steroid therapy. These patients also may be susceptible to infection and require prophylactic antibiotics before undergoing invasive dental procedures (Clayman, 1998).

In addition, platelet retention associated with hypersplenism may lead to occasional thrombocytopenia, necessitating preoperative blood count studies. Anemia and other hematologic changes also may result from granulomatous infiltration of bone marrow (Yanardag et al., 2002). Practitioners also need to evaluate patients for leukopenia, anemia, thrombocytopenia and oral mucositis secondary to the administration of drugs that are toxic to bone marrow. Clinicians should defer dental procedures performed in hospitals under general anesthesia until a patient's medical status and degree of vital organ dysfunction have been evaluated. Sarcoid infiltration of major salivary glands and subsequent xerostomia predispose patients to caries, periodontal disease and candidiasis, highlighting the need for frequent recall appointments and aggressive preventive measures with salivary stimulants, topical fluoride and anti-fungal medications (Yanardag et al., 2002).

9. Conclusion

Orofacial granulomatosis is a generic term applied to manifestations of several diseases including sarcoidosis, Crohn's disease, Melkersson-Rosenthal syndrome, cheilitis granulomatosa of Miescher and foreign-body reactions. What bonds these diseases together is the presence of noncaseating granulomas. A typical clinical manifestation of orofacial granulomatosis is recurrent labial swellings that eventually persist (Kim & Lee, 2010; Martini, 2010).

Orofacial granulomatosis (OFG) is the presence of persistent enlargement of the soft tissues of the oral and maxillofacial region, characterized by non-caseating granulomatous inflammation in the absence of diagnosable systemic Crohn's disease (CD) or sarcoidosis. Over 20 years have passed since OFG was first described and an extensive review of the literature reveals that there is no consensus whether OFG is a distinct clinical disorder or an initial presentation of CD or sarcoidosis. Furthermore, the precise cause of OFG is still unknown although several theories have been suggested including infection, genetic predisposition and allergy. OFG is a rare granulomatous disorder, characterized by persistent enlargement of the soft tissues of the oral and maxillofacial region. Recurrent facial swelling, with/without intraoral manifestations, is the single most common presentation at onset.

Several prior studies have suggested different treatment modalities for oral CD, ranging from the use of mouthwash with corticosteroids to intravenous infusions of an infliximab. Consistent with the findings of previous reports, a favourable outcome in our patient, using intralesional triamcinolone, is suggestive that this can be used as a treatment option for patients with CD that have oral lesions. The symptoms associated with CD usually show a clinical course that waxes and wanes. If patients with CD complain of symptoms associated with these oral lesions during the course of their disease, treatment of the oral lesions with intralesional triamcinolone can improve the quality of life of the patients by ameliorating associated disease symptoms.

In conclusion, patients presenting with an OFG should be carefully evaluated for gastrointestinal signs and symptoms such as diarrhea, hematochezia and abdominal pain. Even in cases with no presenting gastrointestinal symptoms, intestinal disease might exist on closer examination, thus investigation of the GI tract is highly suggested. Intralesional triamcinolone injections can be successful in relieving symptoms associated with oral lesions in a CD patient. (Kim & Lee, 2010; Martini, 2010).

The clinical outcome of OFG patients continues to be unpredictable. Current therapies remain unpredictable. Regular clinical review is indicated to identify the development of gastrointestinal or systemic involvement. The aim of this review was to analyze the developments in our understanding of the aetiology, pathogenesis and treatment protocols, with particular emphasis on management and outcomes of this disease.

10. Acknowledgments

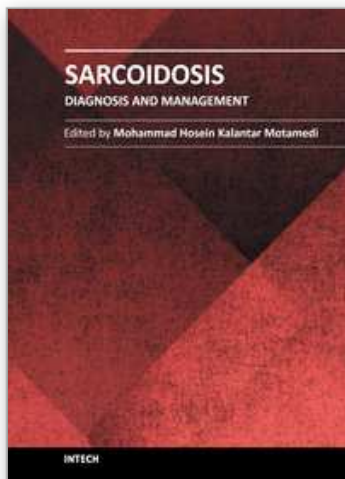
The authors are professors at the Baqiyatallah University of Medical Sciences and would like to thank the faculty and staff of the Trauma Research, Maxillofacial and Pathology departments of the Baqiyatallah Medical Center.

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Edited by Prof. Mohammad Hosein Kalantar Motamed

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Sarcoidosis is a type of inflammation that occurs in various locations of the body for no known reason. Normally, when foreign substances or organisms enter the body, the immune system will fight back by activating an immune response. Inflammation is a normal part of this immune response, but it should subside once the foreign antigen is gone. In sarcoidosis, the inflammation persists, and some of the immune cells form abnormal clumps of tissue called granulomas. The disease can affect any organ in the body, but it is most likely to occur in the lungs. It can also affect the skin, eyes, liver, or lymph nodes. Although the cause of sarcoidosis is not known, research suggests that it may be due to an extreme immune response or extreme sensitivity to certain substances. It also seems to have a genetic component as well, and tends to run in families. Sarcoidosis most commonly develops in people between 20 and 50 years of age. African Americans are somewhat more likely to develop sarcoidosis than Caucasians, and females are somewhat more likely to develop sarcoidosis than males. The symptoms of sarcoidosis depend on the organ involved. This book deals with the diagnosis and treatment of this mysterious disease of unknown etiology.

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University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
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Fax: +385 (51) 686 166
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InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

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