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Case Report

Pathology Section

Rheumatoid Nodule Presenting as Symptomatic Swelling of the Oral Cavity: A Case Report

NAMRATHA RAVISHANKAR[1], VIJAYA BASAVARAJ[2], SUSHMA HULIKERE MALLARADHYA[3]

ABSTRACT

Rheumatoid Arthritis (RA) is a multisystem autoimmune condition characterised by destructive synovitis and varied extra-articular involvement. Rheumatoid nodules are the most common extra-articular manifestations of RA. They develop most commonly in the subcutaneous tissue at the elbow and in the finger joints and may occasionally affect internal organs elsewhere in the body. A 65-year-old woman with seropositive RA on treatment with methotrexate presented with an enlarging mass in the buccal cavity. Ultrasonography revealed a well-defined solid lesion in the subcutaneous plane of the right buccinator space. A clinical diagnosis of a benign salivary gland tumour was made and the patient underwent excision of the nodule and histopathological examination showed central areas of necrobiosis surrounded by palisades of histiocytes consistent with a rheumatoid nodule. The diagnosis of rheumatoid nodules in typical locations can be made easily clinically, supported by classic histopathology. In many cases, particularly in unusual locations, the diagnosis can be challenging, requiring extensive examination of the lesion. Although a rare manifestation, clinicians should consider the possibility of a rheumatoid nodule as a possible differential diagnosis of buccal masses in patients with a history of RA or connective tissue disease. Through this case report, we review the pathogenesis, histopathological features, as well as diagnosis and differential diagnosis of rheumatoid nodules while discussing the challenges in distinguishing them from their mimics. A high degree of suspicion will avoid unwarranted surgical intervention.

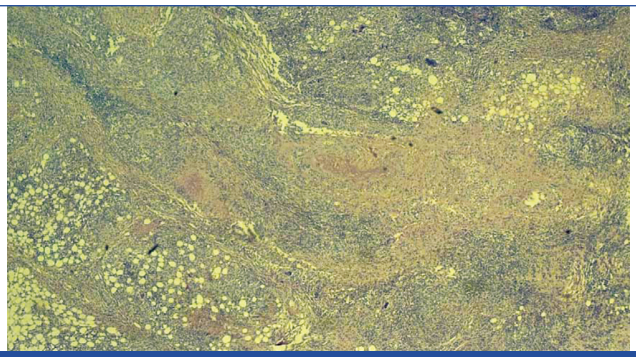
Keywords: Autoimmune condition, Rheumatoid arthritis, Subcutaneous nodule

CASE REPORT

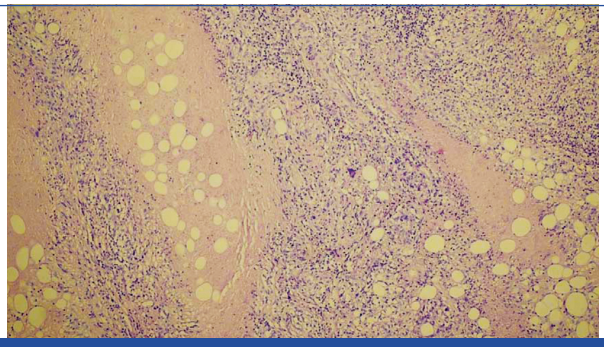
A 65-year-old female presented with an asymptomatic intraoral swelling for four months. The patient was a known case of RA on treatment with methotrexate for the same and was in clinical remission. The patient reported no other systemic diseases in her medical history. The margins of the swelling were well demarcated, and there was no associated neurological deficit and no palpable neck nodes. Ultrasound scan showed a well-defined solid lesion in the subcutaneous plane of the right buccinator space with minimal internal vascularity.

The nodule was totally excised under the clinical diagnosis of either a fibroma or a salivary gland lesion. During the surgical procedure, the specimen presented well-defined borders, with no attachment to any of the surrounding structures and a complete excision was performed. After excision, the specimen was sent to the pathology laboratory for microscopic examination. The specimen was nodular, with a smooth surface and firm consistency

On histopathologic examination, fibro-adipose tissue was seen with histiocytic aggregates around amorphous central fibrinous material at multiple foci [Table/Fig-1,2]. The central necrobiotic areas were palisaded by histiocytes [Table/Fig-3,4]. The surrounding zone of tissue showed perivascular infiltrates of lymphocytes, plasma cells with histiocytes and multinucleate giant cells forming granulomas [Table/Fig-5]. There was no evidence of vasculitis or mucin deposition. The Alcian blue stain was negative in the necrobiotic areas [Table/Fig-6]. Acid-fast stain and stains for fungal elements were negative. The histological diagnoses considered were rheumatoid nodule, an infectious process and sarcoidosis. In the absence of supportive clinical features of sarcoidosis and organisms and in the clinical backdrop of RA, a final diagnosis of rheumatoid nodule was established. The patient had an uneventful postoperative recovery. She had no other subcutaneous nodules. There was no evidence of recurrence in the 10 months following the surgery in this case.



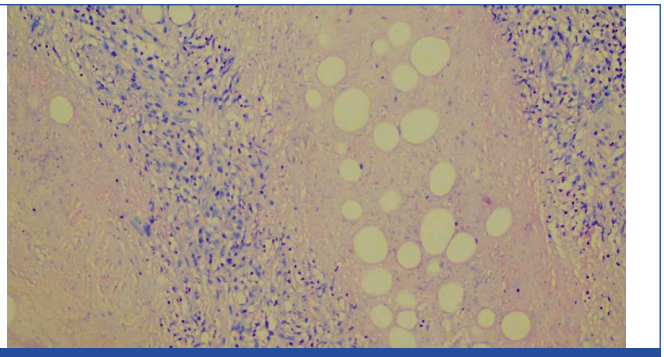
[Table/Fig-1]: Scanner view showing fibro-adipose tissue showing large areas of necrobiosis with eosinophilic material composed of fibrin {Haematoxylin and Eosin (H&E) stain, 4x}.



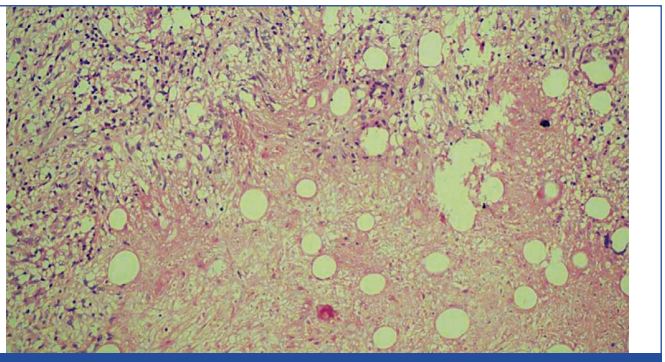
[Table/Fig-2]: Scanner view showing central areas of fibrinoid necrosis surrounded by palisading macrophages and lymphocytes (H&E stain, 4x).

DISCUSSION

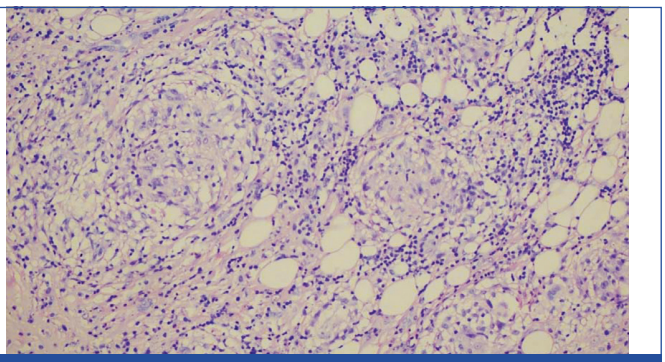
The RA is an autoimmune disease characterised by destructive synovitis and heterogeneous extra-articular manifestations [1]. Rheumatoid nodules are the most common extra-articular manifestations of RA, seen in 20-30% of seropositive individuals [2]. Rheumatoid nodules most commonly occur in pressure areas, such as elbows and finger joints in the subcutaneous plane, but may



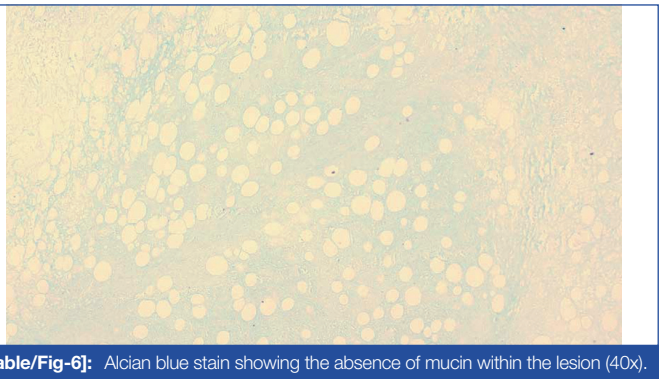
[Table/Fig-3]: Necrobiosis, with fibrin deposition and palisading epithelioid histiocytes (H&E stain, 10x).



[Table/Fig-4]: Necrobiosis with surrounding palisaded epithelioid histiocytes (H&E stain, 40x).



[Table/Fig-5]: Granulomas composed of epithelioid histiocytes identified in the surrounding infiltrate (H&E stain, 40x).



[Table/Fig-6]: Alcian blue stain showing the absence of mucin within the lesion (40x).

rarely be seen in visceral organs such as pleura, lungs, meninges and larynx [3]. These nodules are almost always associated with severe forms of the disease and are an indicator of the presence of rheumatoid factor and anti-Cyclic Citrullinated Peptide (CCP) in the serum [4]. They are resistant to conventional drugs used for the treatment of RA and may even paradoxically aggravate with some therapeutic agents, like methotrexate, which is the mainstay of RA therapy [5]. The patient in the present report was on methotrexate for her arthritis and was in remission.

Reports have shown that the incidence of rheumatoid nodules has reduced substantially from 31% for patients diagnosed between 1985 and 1999 to 16% for patients diagnosed between 2000 and 2014 [6]. The diagnosis of typical rheumatoid nodules in usual locations can be readily made by clinical examination. In many cases, however, when seen in atypical locations, the clinical diagnosis can be challenging, requiring extensive examination of the lesion with histological examination and immunohistochemical markers [7]. The elbow is the most common site for the rheumatoid nodule and 80% of patients with these nodules have at least one nodule at this site. Other commonly affected sites include feet, Achilles tendons, knees, buttocks, knuckles, scalp and bridge of the nose. Unusual locations include choroid, eyelid, vocal cord, lung, aorta, heart valves, myocardium, epicardium, pericardium, pharynx, spinal cord, dura mater, subdural and extradural spaces, peripheral nerves, tendon sheaths, penis, vulva, breast and joints [8,9].

Rheumatoid nodules in the oral cavity are exceedingly rare and are reported infrequently. Only four cases have been reported in the literature [10-13]. Lesions in these sites may lead to significant diagnostic dilemmas in patients with clinical suspicion of malignancy [14]. Although there are no clinical clues that would lead to the preoperative diagnosis of rheumatoid nodules in an unusual location, the index of suspicion should be high in patients with RA with extra-articular swellings. Overt joint symptoms may not necessarily be seen in patients with these lesions [15].

The most widely accepted hypothesis for the pathogenesis of rheumatoid nodules is that they are mediated by immune complexes. Fibrin deposits are secondary to complement activation due to aggregation of IgM-RF complexes on the endothelial surface of the cell after vascular injury, causing an immune complex formation [16]. Injury to the endothelial cells may result in deposition of IgM immune complexes on the vessel walls, which activate macrophages. Proinflammatory cytokines secreted by macrophages, such as Interleukin-1β (IL-1β) and tumour necrosis factor-α, are hypothesised to play a pivotal role in the induction of these nodules [17]. Secreted cytokines, mediators, growth factors, proteases, and collagenases all culminate in inflammation, angiogenesis, necrobiosis, and granuloma formation [18].

Occasional case reports exist, describing aspiration cytology of a rheumatoid nodule, where smears demonstrated fragments of amorphous necrotic debris surrounded by spindle cells, foamy macrophages, histiocytes, plasma cells, and occasional giant cells [14].

Rheumatoid nodules have a highly characteristic microscopic appearance and represent a granulomatous immune response [19]. On microscopy, a rheumatoid nodule shows a homogenous central eosinophilic area of necrobiosis in the subcutis or dermis surrounded by a well-developed palisade of elongated histiocytes, with occasional lymphocytes, neutrophils, mast cells, and foreign body giant cells [20]. The necrobiotic area shows eosinophilic degenerated collagen, and elastic fibres admixed with fibrinoid material and cellular debris and in some cases, Hale's colloidal iron stain may be positive within the necrobiotic areas [21]. Older lesions may show cystic degeneration of the necrotic component. The outer zone of chronic inflammatory cells may show numerous plasma cells [22]. Eosinophils may be present and occasionally, fibrinoid necrosis of the blood vessels associated with nuclear fragments or sparse neutrophils may be seen in the areas of necrobiosis. Nodules that are superficial may rarely perforate the epidermis [20].

The mononuclear cells surrounding the necrobiotic areas stain strongly positive for ferritin and the macrophages in the nodule show a characteristic lack of cytoplasmic antiprotease with a strong expression of ferritin [23]. Immunohistochemical studies have also shown that the palisading cells surrounding the necrobiotic centre are HLA-DR-positive histiocytes and the associated plasma cells show predominantly IgG positivity [24].

Many histopathologic features of RN overlap with those of other granulomatous lesions, including infectious necrotising granulomas and correlation with clinical context, serologic and microbiologic studies, as well as careful evaluation of special stains, is crucial in making the

diagnosis [25]. Mucin deposition is usually negligible in rheumatoid nodules, which helps to differentiate it from its closest histological mimics - granuloma annulare and necrobiosis lipoidica. The latter entities are more superficial in location and have abundant mucin and less fibrin deposition compared with the rheumatoid nodule [26].

The histopathological differential diagnosis of rheumatoid nodules includes several entities that share overlapping features like necrobiosis or granulomatous inflammation and the distinguishing features are summarised below [Table/Fig-7] [7].

Asymptomatic nodules typically do not require any specific treatment. Management of rheumatoid nodules is conservative unless surgical excision is indicated in the presence of secondary infection, ulceration, or disabling symptoms [27]. In the present case, surgical excision was necessary for diagnosis owing to the unusual location of the nodule, leading to a lack of clinical suspicion.

Entity	Key histological features	Distinguishing features
Rheumatoid nodule	Central area of fibrinoid necrosis surrounded by palisading histiocytes, peripheral granulation tissue with chronic inflammatory cells	Usually subcutaneous, central fibrinoid necrosis and associated with RA seropositivity
Necrobiosis lipoidica	Palisading, necrobiotic granuloma with a large confluent area of necrobiosis centred in the superficial dermis and subcutaneous fat	Often on the shins and linked with diabetes. Lacks classic fibrinoid necrosis Plasma cells are almost always present
Granuloma annulare	Degenerated collagen (necrobiosis), palisading histiocytes and mucin deposition (Alcian blue+)	Usually seen in the dermis Abundant mucin and no fibrinoid necrosis
Foreign body granuloma	Granulomatous inflammation with foreign body type of multinucleated giant cells surrounding exogenous material	Presence of foreign material, which may polarise. Lacks central fibrinoid necrosis
Infectious granulomas (TB, fungal)	Caseating necrosis (in TB), epithelioid histiocytes and Langhans giant cells. Organism identification is possible with special stains	Acid-fast bacilli on Ziehl-Nielsen (TB) with caseation necrosis Fungal hyphae on PAS/GMS for fungi
Sarcoidosis	Non-caseating granulomas. Tight clusters of epithelioid histiocytes and giant cells. Minimal or no necrosis	No central necrosis or palisading Hilar lymphadenopathy

[Table/Fig-7]: Histopathological differential diagnosis of rheumatoid nodule.

CONCLUSION(S)

Rheumatoid nodules are well-characterised common extra-articular manifestations of RA. However, the occurrence of a rheumatoid nodule in the oral cavity is extremely rare. These unusual presentations may cause problems leading to a delay in the diagnosis and to mistaking them for other lesions or tumours. Their appearance can be confused with many clinical conditions when seen in atypical locations. It is prudent to be aware of uncommon locations of rheumatoid nodules and consider them as possible differential diagnoses for any soft tissue mass in patients with RA in order to prevent unnecessary surgical intervention.

REFERENCES

[1] Yachoui R, Ward C, Kreidy M. A rheumatoid nodule in an unusual location: Mediastinal lymph node. Case Rep. 2013;2013:bcr2013009516.
[2] Cadório MJ, Teixeira J, Oliveira J, Santiago T, Gonçalo M, Duarte C. Beyond rheumatoid nodules in rheumatoid arthritis. ARP Rheumatol. 2024;3(3):240-42.
[3] Upile T, Jerjes W, Sipaul F, Singh S, Hopper C, Wright A, et al. Rheumatoid nodule of the thyrohyoid membrane: A case report. J Med Case Reports. 2007;1(1):123.
[4] Talotta R, Atzeni F, Batticciotto A, Ditto MC, Gerardi MC, Sarzi-Puttini P. Accelerated subcutaneous nodulosis in patients with rheumatoid arthritis treated with tocilizumab: A case series. J Med Case Reports. 2018;12(1):154.
[5] Bulbin B, Kramer N, Rosenstein ED, Rosenstein RK. JAK inhibitors for the treatment of rheumatoid nodules. JAAD Case Rep. 2025;59:113-16.
[6] Kimbrough BA, Crowson CS, Davis JM, Matteson EL, Myasoedova E. Decline in incidence of extra-articular manifestations of rheumatoid arthritis: A population-based cohort study. Arthritis Care Res. 2024;76(4):454-62.
[7] Fareez F, Moodley J, Popovic S, Lu JQ. Rheumatoid nodules: A narrative review of histopathological progression and diagnostic consideration. Clin Rheumatol. 2023;42(7):1753-65.
[8] Kaye BR, Kaye RL, Bobrove A. Rheumatoid nodules. Review of the spectrum of associated conditions and proposal of a new classification, with a report of four seronegative cases. Am J Med. 1984;76(2):279-92.
[9] Lynch JM, Barrett TL. Collagenolytic (necrobiotic) granulomas: Part II--the "red" granulomas. J Cutan Pathol. 2004;31(6):409-18.
[10] Tay GCA, Sauer DA, Andersen PE. Rheumatoid nodule presenting as a buccal submucosal nodule: A rare presentation of a common disease. Head Neck. 2017;39(1):E12-E14.
[11] Ogi K, Miyazaki A, Shimizu S, Abe M, Genba R, Miyamoto S, et al. A case of rheumatoid nodules in the buccal subcutaneous: A novel case report of review and the literature. J Oral Maxillofac Surg Med Pathol. 2018;30(3):290-93.
[12] Skov BG. Rheumatoid nodule in the oral mucosa. A case report with immunohistochemical study. J Oral Pathol. 1987;16(8):403-05.
[13] Kato K, Segami N, Fukuda H, Minato H. Rheumatoid nodule in the lower lip of a patient with rheumatoid arthritis: A novel case report and review of literature. J Oral Maxillofac Surg. 2014;72(8):1532.e1-1532.e5.
[14] Kalugina Y, Petruzzelli GJ, Wojcik EM. Fine-needle aspiration of rheumatoid nodule: A case report with review of diagnostic features and difficulties. Diagn Cytopathol. 2003;28(6):322-24.
[15] Friedman BA. Rheumatoid nodules of the larynx. Arch Otolaryngol Chic Ill. 1960. 1975;101(6):361-63.
[16] Lora V, Cerroni L, Cota C. Skin manifestations of rheumatoid arthritis. G Ital Dermatol E Venereol Organo Uff Soc Ital Dermatol E Sifilogr. 2018;153(2):243-55.
[17] Hessian PA, Highton J, Kean A, Sun CK, Chin M. Cytokine profile of the rheumatoid nodule suggests that it is a Th1 granuloma. Arthritis Rheum. 2003;48(2):334-38.
[18] Kato Y, Yamamoto T. Sacral rheumatoid nodule mimicking inflammatory atheroma. Indian J Dermatol. 2016;61(1):127.
[19] Aróstegui Aguilar J, Diago A, Carrillo Gijón R, Fernández Figueras M, Fraga J, García Herrera A, et al. Granulomas in dermatopathology: Principal diagnoses - Part 1. Actas Dermo-Sifiliográficas Engl Ed. 2021;112(8):682-704.
[20] Weedon's Skin Pathology [Internet]. 2009 [cited 2025 Jun 4]. Available from: https://shop.elsevier.com/books/weedons-skin-pathology/weedon/978-0-7020-3485-5.
[21] Ghazarian D, Al Habeeb A. Necrobiotic lesions of the skin: An approach and review of the literature. Diagn Histopathol. 2009;15(4):186-94.
[22] Blacksin MF, Ha DH, Hameed M, Aisner S. Superficial soft-tissue masses of the extremities. Radiogr Rev Publ Radiol Soc N Am Inc. 2006;26(5):1289-304.
[23] Aherne MJ, Bacon PA, Blake DR, Gallagher PJ, Jones DB, Morris CJ, et al. Immunohistochemical findings in rheumatoid nodules. Virchows Arch A Pathol Anat Histopathol. 1985;407(2):191-202.
[24] Athanasou NA, Quinn J, Woods CG, Mcgee JO. Immunohistology of rheumatoid nodules and rheumatoid synovium. Ann Rheum Dis. 1988;47(5):398-403.
[25] Klaisuban W, Su C, Koslow M, Ryu JH, Tazelaar HD, Jenkins SM, et al. Revisit of histopathology in rheumatoid lung nodules. Am J Surg Pathol [Internet]. 2025;49(6):588-93.
[26] Weidner N, Cote RJ, Suster S, Weiss LM. Modern Surgical Pathology E-Book. Elsevier Health Sciences; 2009. 1294 p.
[27] Murthy PS, Malik AK, Rajagopal R, Aggarwal SK. Benign rheumatoid nodules. Indian J Dermatol Venereol Leprol. 2002;68:365.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, JSS Medical College and JSS AHER, Mysore, Karnataka, India.
2. Professor, Department of Pathology, JSS Medical College and JSS AHER, Mysore, Karnataka, India.
3. Senior Resident, Department of Pathology, JSS Medical College and JSS AHER, Mysore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Namratha Ravishankar,
Assistant Professor, Department of Pathology, JSS Hospital, Mahatma Gandhi Road, Fort Mohalla, Mysuru-570004, Karnataka, India.
E-mail: namrathar@jssuni.edu.in

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