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Oral submucous fibrosis: is it a collagen disease? A study in search for its aetiology

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ABSTRACT

Background: The aetiopathogenesis of oral submucous fibrosis (OSMF), though not an uncommon disease, is not yet well established. OSMF is prevalent in the geographical area of study. These were the driving factors to conduct this study. This haematological study in patients with oral submucous fibrosis was conducted to find out some definite causative features so that an effective treatment regime could be evolved.
Methods: This prospective hospital-based observational study was conducted in the Department of Otorhinolaryngology (ENT) and Pathology in a tertiary care medical college hospital. The 150 clinically diagnosed patients were enrolled for the study. Routine laboratory tests were done to identify markers which would suggest autoimmune conditions.
Results: In 124 cases (83%), mild to moderately anaemia was observed while 75 cases (50%) showed raised ESR. Lymphocytosis and eosinophilia were observed in 42 cases (28%) and 48 cases (32%) respectively. Hyperglobulinaemia was observed in 45 cases (30%). In 18 cases (12%) leukocytosis was observed. In 30 cases (20%), pus cells were seen in urine, while ova and cysts were found present in 42 cases (28%).
Conclusions: The present study could not establish the commonly claimed theory of collagen disease. The exact aetiology of OSMF is not yet known. Some genetic factors seem to play a role, which make some people predisposed to react abnormally to chronic masticatories of different forms of areca nut, tobacco and areca leaves. Therefore further research in the direction of genetic studies will perhaps reveal the exact cause of OSMF.

Keywords: Oral submucous fibrosis, Aetiology, Autoimmune disease, Collagen disease

INTRODUCTION

Oral submucous fibrosis (OSMF) though prevalent throughout the Indian subcontinent, its aetiopathogenesis is still an enigma. The disease frequently leads to severe trismus and ankyloglossia that make patients' life miserable. The collagen theory regarding its aetiology is supported and disagreed by many workers. Rowell described OSMF as an autoimmune disorder.[1-7]

Joshi named the disease as "submucous fibrosis of palate and pillars" in 1953 and reported its clinical features.[8] Su designated the same condition as "idiopathic scleroderma of the mouth".[1] Most of the patients with OSMF have the complaint of long standing gradually progressive painless difficulty in opening the mouth (trismus) and fibrosis of the soft palate, faucial pillars and buccal region. Other common features include intolerance to spicy food and recurrent vesicles and ulceration in oral cavity and oropharynx.[9]

The leading and well reported and accepted predisposing factor of OSMF is chewing of different forms of betel nuts, betel leaves and tobacco.[1,4,10-12] Several other factors

are also incriminated for the aetiology of OSMF such as taking excessive spicy foods, chillies, excessive hot and cold drinks.[5,13,14] Some consider OSMF as collagen disease and many immunological studies have been done with diverse results.[1,6,15-17] OSMF is also incriminated as a precancerous lesion as it is frequently associated with leukoplakia and oral cancer.[18-20] The reported histopathological findings of OSMF include: 1) Epithelial atrophy, 2) acanthotic and paracanthotic changes, 3) fibroelastotic changes transformation of connective tissue in the lamina propria, 4) round cells infiltration and decreased vasularity.[21] As the exact cause of this disease is yet not certain there is no well accepted effective treatment.

Joshi performed the Kahn test and gastric juice analysis in OSMF patients and found them normal.[8] Infection is never considered as the cause of the disease because patients never present with any pain and fever. Pindborg and Singh analyzed the fluid of vesicles by incising them which was found sterile on culture.[22] Phatak observed the increase in the absolute null cell population and reduction in T-lymphocytes population.[17] In his another study, he found a strong fibrin precipitating factor (PPF) in the saliva of OSMF patients.[23]

Since a good number of patients had been observed to attend ENT OPD and the aetiology of the disease was not proved, author considered it worthwhile to study the haematological findings of OSMF to find out some definite causative features so that an effective treatment regime could be evolved. Findings of present study could open fresh avenues for further research.

METHODS

The present hospital-based observational study was carried out in 150 clinically confirmed patients of OSMF in the Department of Otorhinolaryngology Head and Neck Surgery of P.B.M. Group of Hospitals Bikaner from March 1979 to February1981.

Inclusion criteria

All the patients with OSMF presented in the Department of Otorhinolaryngology Head and Neck Surgery of P.B.M. Group of Hospitals Bikaner during the study period were enrolled for the study.

Exclusion criteria

The patients who were not willing and did not give their informed consent were excluded from the study. There were no other exclusion factors.

Routine laboratory tests are useful to identify markers which may suggest autoimmune inflammatory conditions. All the 150 clinically diagnosed patients of OSMF were subjected to following investigations:

- Blood:
  - Complete blood cells count (CBC) including Haemoglobin (Hb) estimation and erythrocytes sedimentation rate (ESR) to look for any inflammation and autoimmune conditions
  - Venereal Disease Research Laboratory test (VDRL) for syphilis
  - Serum proteins
  - Rose-Waller factor in patients with chronic arthralgia
- Urine: Albumin, sugar and microscopic.
- Stool: Ova and cyst.
- X-ray chest PA view.

Statistical analysis

As this hospital-based observational study was descriptive and not analytic, no statistical analysis was employed.

RESULTS

In the present study, which was carried out in 150 patients with OSMF, some the features were found suggestive of collagenous aetiology of the disease. In majority of cases (124/83%), mild to moderately anaemia was observed (Table 1) while half of the cases showed raised ESR (Table 2). The findings of other investigations are shown in Table 2. Lymphocytosis and eosinophilia were observed in approximately one-third of the cases, 42 (28%) and 48 (32%) respectively. Total serum proteins were within normal limits (6-7.5 gm%) in most of the cases except 9 (6%), although hyperglobulinaemia was observed in approximately one-third of the cases (45/30%). In 18 cases (12%) leukocytosis (count >11,000/mm^3) was observed. In 30 cases (20%), pus cells were seen in urine, while ova and cysts were present in 42 cases (28%). VDRL and Rose-Waller test were found normal in all the cases. X-ray chest PA view revealed old tubercular lesion and chronic bronchitis in 3 cases (2%) each.

Table 1: Haemoglobin (Hb) in gm% in 150 patients of OSMF.

Hb in gm%	Number of patients			Percentage (%)
	Male	Female	Total	
7.1-9.0	6	14	20	13.33
9.1-11.0	10	34	44	29.33
11.1-13.0	20	40	60	40.0
13.1 and above	20	6	26	17.33
Total	56	94	150	100
Mean	11.92	10.82	11.37	

Table 2: Investigation findings in 150 patients of OSMF.

S. No.	Investigations' findings	Number of patients	Percentage (%)
1	Anemia	124	82.66
2	Raised ESR	75	50.00
3	Eosinophilia	48	32.00
4	Lymphocytosis	42	28.00
5	Hyperglobulinaemia	45	30.00
6	Ova and cysts in stool	42	28.00
7	Pus cells in urine	30	20.00
8	Leukocytosis (count >11,000/cumm)	18	12.00
9	Old tuberculosis X-ray chest	3	2.00
10	Chronic bronchitis X-ray chest	3	2.00

DISCUSSION

Collagen vascular disease is an autoimmune disease that affects connective tissue so also called connective tissue disease. Collagen, which has great tensile strength, is a protein-based connective tissue that is main component of the tissues. The features suggestive of collagenous aetiology of OSMF, observed in various studies, were as follows:

- Hyperglobulinaemia.[5,7,24,25]
- Increased in mononuclear cells and lymphoid and plasma cells infiltration and eosinophilia.[3,7]
- Significant increase in dense collagen and hyaline degeneration of connective tissues.[3]
- Dense hyalinised juxta epithelial connective tissues showing metachromasia with alcoholic toluidine blue and constricted blood vessels.[11]
- Findings resembling scleroderma.[26]
- Raised levels of mucopolysaccharides and mucoprotein.[27]
- Bone marrow showing allergic reaction with hypercellularity and eosinophia.[15]
- Blood eosinophilia.[11,24,28]
- Raised antistreptolysin 'O' titre.[27]
- Response with corticosteroids.[7,14-16]

In the present study, which was carried out in 150 patients of OSMF, the findings in support of the theory of collagen disorder were not conclusive. The features found in present study, suggestive of collagenous aetiology of the disease were as follows:

- Blood eosinophilia in 48 cases (32%)
- Serum hyperglobulinaemia in 45 cases (30%)
- Association of the disease with scleroderma and leukoderma in 1 case (0.66%).

Desa did not agree with the theory of collagen disease as he found no abnormality of either exposed or protected skin or gastro-intestinal tract.[5] He argued that scleroderma (collagen disease) preliminary affected the cutaneous connective tissues with occasional involvement of oral mucosa, while in the OSMF, there had never been any cutaneous or visceral spread of this condition.

However, Su suggested that hypersensitivity was an important aetiological factor in the entire group of disease.[1] Sirsat and Khanolkar reported that in submucous fibrosis of the palate, the degenerated collagen and hyalinised areas seen with H&E were identified with areas of staining abnormality with the differential connective tissue stain.[24] Rowell also suggested that OSMF is of an autoimmune aetiology, as he observed hypergammaglobulinaemia in his patients of OSMF.[7]

About 83% of the patients (124) of OSMF in present study were mild to moderately anaemic (Hb – 7.1 to 13 gm%). Similar findings were observed in several studies.[11,15,16,24] The cause of anaemia does not seem to be related to the severity of OSMF, as the Hb gm% was relatively more in patients who had more advanced lesion. Factors like poor nutrition seem more responsible for such anaemia. In 42 cases (28%), ova and cysts were observed in the stool, which explained the anaemia in the cases, furthermore that could also cause some allergic manifestation.

ESR was found raised in 50% of the cases (75). The same observations were reported in several other studies.[5,29] Twelve percent of the patients were having leukocytosis (count more than 11,000/mm^3). Lymphocytosis and eosinophilia were observed in 42 (28%) and 48 (32%) cases respectively, as also reported by other workers.[11,24]

Paymaster observed positive serological test for syphilis in 9% of the patients with OSMF.[18] In contrast to this, VDRL test was found non-reactive in all the cases of present study. Rao and Raju reported the same fact of negative Kahn's test in their patients.[16] The patients who had chronic arthralgia were subjected for Rose-Waller test but none showed positive results.

Almost all patients (146/96%) of the present study were exposed to chronic irritation of oral mucosa by areca nuts (Kircha and Sopari). Most of the people in the geographical area of study are addicted to Kircha and Sopari as masticatory many since decade's together, bur all of them do not suffer from OSMF. So author presumes, there might be some genetic factor which is causing the abnormal response to tissue trauma caused by different forms of masticatory irritants, chewing of various forms of areca nut, areca leaves and tobacco, however these genetic factors are yet to be studied.

CONCLUSION

The present study could not establish the commonly claimed theory of collagen disease. So, the exact aetiology of OSMF is not yet known. So there has been no uniform therapeutic remedy. Some genetic factors seem to play a role, which make some people predisposed to react abnormally to chronic masticatories of different forms of areca nut, tobacco and areca leaves. Therefore further research in the direction of genetic studies will perhaps reveal the exact cause of OSMF.

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