Use of Curcumin for management of Oral Submucous Fibrosis in Pediatric patients- A case report and literature review

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ABSTRACT
Oral Sub-Mucous Fibrosis (OSMF) has been conventionally defined as “An insidious, chronic disease that affects any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by, or associated with, the formation of vesicles, it is always associated with a juxtaepithelial inflammatory reaction followed by fibroelastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat”. Patients with OSMF clinically present with burning sensation on eating spicy foods, limitation of mouth opening, ulceration, difficulty in tongue protrusion, shrunken uvula. Chewing of Areca nut and its derivatives such as Gutkha, Pan masala, Mawa, Betel quid, Sweet Supari and other formulations has been the main causative factors but also use of smokeless tobacco, nutritional deficiencies, excessive consumption of chillies, immunological factors, and genetic predisposition have been the contributing

KEY WORDS – OSMF, Paediatric, Curcumin, Areca Nut.

ABSTRACT-
Oral Sub Mucous Fibrosis (OSMF) is a potentially premalignant disease of the oral cavity with areca nut consumed in various forms being the main etiologic agent. Considering its irreversible nature, high malignant transformation rate and complexity of treatment options, early diagnosis backed with affirmative habit control, effective multi-targeted treatment approach and regular follow up is of utmost importance. Increase in the cases of pediatric Oral Sub Mucous Fibrosis warrants prompt attention towards both, its management and its prevention by effectively curbing the initiation of the habit of tobacco in different forms in the pediatric age group and finding an efficient replacement to the traditionally used steroids for management in these patients.

In this article we report a case of OSMF in a 12 year old boy with habit of eating pan masala who was successfully managed by using topical curcumin.

Key Messages – OSMF, Paediatric, Curcumin, Areca Nut.

Key Messages –

- Management of OSMF cases specially in the paediatric age group can be successfully managed by topical curcumin which has shown to effectively alleviate all the clinical symptoms of the patient without any side effects as compared to conventional steroids and other surgical modalities.
- Well-designed clinical trials with adequate sample size and long term follow up to assess the longevity of the results specially for paediatric patients is recommended.

MAIN TEXT-
Oral Sub-Mucous Fibrosis(OSMF) has been conventionally defined as “An insidious, chronic disease that affects any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by, or associated with, the formation of vesicles, it is always associated with a juxtaepithelial inflammatory reaction followed by fibroelastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat”. Patients with OSMF clinically present with burning sensation on eating spicy foods, limitation of mouth opening, ulceration, difficulty in tongue protrusion, shrunken uvula. Chewing of Areca nut and its derivatives such as Gutkha, Pan masala, Mawa, Betel quid, Sweet Supari and other formulations has been the main causative factors but also use of smokeless tobacco, nutritional deficiencies, excessive consumption of chillies, immunological factors, and genetic predisposition have been the contributing
factors towards development of OSMF. Owing to the multifactorial etiology the management of this condition is complex and includes counselling of the patients to stop the habit combined with pharmaceutical management modalities like topical steroids, intra-lesional injection of steroids, chymotrypsin or hyaluronidase, nutritional supplements, lycopene, CO2 laser, interferon gamma, turmeric, placental extracts, etc. For severe cases surgical interventions like myotomy, coronoidectomy, or excision of fibrous bands are performed. Along with this physiotherapy, local heat therapy, and mouth opening exercises are also advised.

The most commonly affected group is 20-40-years-although few paediatric patients are also reported to have this condition due to the increase in consumption of tobacco products in this age group. A systematic review conducted by Jain and Taneja in 2019 reported in total 10 cases of paediatric (below 10 yrs. age) OSMF with female preponderance and with areca nut chewing habit found in all the patients. Some articles have also reported OSMF cases in the age range of 11-20 yrs. In all these cases the habit of areca nut consumption in some or the other form has always been present.

This article reports a case of OSMF and its successful management using curcumin in a 12-year-old boy with habit of eating pan masala.

CASE PRESENTATION

A 12-year-old boy reported to the Department of Oral Medicine and Radiology with complain of decrease in mouth opening and burning sensation on eating medium spicy food since 5 to 6 months. He complained of slight loss of weight due to inability to eat food. Personal history revealed consumption of pan masala 4 times a day since 4 to 5 years.

General examination revealed a boy with a lean appearance. Vital signs were normal. Extra oral examination revealed a symmetrical face with slightly sunken cheeks. Mouth opening was reduced – 21.2mm.[Fig1] Intraoral examination revealed blanching and fibrosis of right and left buccal mucosa and posterior aspect of the palate and the pterygomandibular raphe. [Fig 2,3,4]. No ulceration or vesicle formation was noted. Oral hygiene was fair with slight stains but no calculus on teeth. Tongue showed areas of depapillation and uvula was slightly shrunken. On palpation, all the findings were confirmed. The buccal mucosa was inelastic and rubbery to palpate, with presence of fibrous bands. Considering the clinical presentation along with presence of pan masala habit a provisional diagnosis of Oral Sub-mucous fibrosis stage II was made according to clinical and functional classification of OSMF given by Kerr et al.

Investigations -

Complete blood count, Hb was advised. The report suggested a Hb level of 11g/dL. Scaling and polishing was performed.

Treatment plan-

The patient was asked to stop the habit of consuming pan masala and a detailed counselling session was performed for the same in which the harmful effects of consuming pan masala and its malignant potential was emphasized. Keeping in view the stage of OSMF in the present case and the young age of the patient a conservative medicinal management strategy using topical curcumin instead of the mono targeted symptomatic relief provided by steroids was advocated. The patient was advised to apply commercially available topical curcumin three times a day for a period of three months. The patient was asked to apply the topical medication with a help of cotton swab and was advised to dab a sufficient amount so as to cover the lesion and then rinse after five minutes. Physiotherapy exercises namely ballooning exercise and use of ice cream sticks or fingers was mouth opening were advised daily for at least 10-15 times. Multivitamin capsule containing lycopene, Betacarotene, selenium, zinc sulphate, alpha- lipoic acid, alpha tocopheryl acetate was advised to be taken once daily and dietary modifications for including more green leafy vegetables with combination of grains, fruits were suggested in view to increase the Hb level. Scaling and polishing was performed.

The degree of pain / burning sensation was recorded on a Numeric Pain Rating Scale(NPRS) which is a segmented numeric version of the Visual Analog Scale. The quality of life assessment was done using EORTC QLQ-H &N 35 questionnaire. Patient was asked to regularly use the topical medication as advised along with multivitamins and physiotherapy exercises and parents were also...
advised to keep a proper check on the boy for any use of pan masala and supervise the application of medication. Regular follow up every 15 days was instructed.

RESULTS/ OUTCOME
At each follow up visit, clinical examination was performed and pain and burning sensation on the NPRS was recorded while at the end of 2 months EORTC QLQ-H&N 35 was recorded. The patient reported improvement in his pain and burning sensation with the NPRS score improving considerably at the end of 2 months and consistent thereafter. The EORTC questionnaire taken at the end of 4 months also reflected upon the betterment of quality of life as compared to what it was initially both in social and functional aspects. The mouth opening was increased from 21.2mm to 36.3mm after 4 months. [Fig 5] The patient is still called for regular follow up visits.

DISCUSSION
Oral sub mucous Fibrosis is insidious in origin and is an irreversible collagen metabolic disorder with malignant potential of 7-30%. Numerous etiological factors contributing towards causing this disease have been suggested but Areca nut consumption is regarded as the most important and noteworthy etiologic agent. Areca nut/ betel nut is easily available and used in various forms like paan, paan masala, Khaini, Mishri, Zarda, Gudakhu. In the case described in this article the patient had habit of eating paan masala since 4 to 5 yrs almost 4 times a day. Paan masala is mixture of areca nut with slaked lime, catechu and other flavouring agents and other than the oral cavity where it causes OSMF, pan masala has also shown to have deleterious effects on gastrointestinal system and Genito-urinary tract. In the past few years the consumption of areca nut and its various commercially available forms has been on an increase in the school going age group and is mainly seen in children of low socio-economic status who are uneducated and lack cognizance of its harmful effects and fall prey to it under peer pressure. Younger the patient more the magnitude of deleterious effects of consuming pan masala is noted.

Keeping in view the stage of OSMF in the present case and the young age of the patient a conservative medicinal management strategy which was directed towards avoidance of mono targeted symptomatic relief which the conventional steroids offers a better multi-targeted modality was adopted by using topical curcumin. Medicinal herbs, since ages have been successfully used for treating various human diseases. Various studies have shown the successful use of one such naturally occurring polyphenol curcumin which is isolated form the ground rhizomes of the plant curcuma longa to be very effective in treating OSMF owing to its anti-oxidant, anti-inflammatory, anti-septic, anti-carcinogenic, chemo-preventive, anti-tumor, antibacterial, anti-fungal and anti-viral activities. Both systemic and topical forms of curcumin have been used in various studies for effective treatment of OSMF. Studies have also shown effectively the mechanisms of action of curcumin which give these positive results in OSMF.

Reviewing the literature till date table I shows all the reported cases of OSMF in paediatric patients and the management modality used for their treatment. Table I- All reported cases of OSMF in children below 14 years of age. To the best of our knowledge ours is the first paediatric case where we have successfully used topical curcumin in improving the patient’s symptoms. The successful management with the use of curcumin is well reflected in the change in clinical signs of mouth opening and also in symptoms of patients as measured by the NPRS scale and the improvement in the quality of life as recorded by the EORTC questionnaire.

CONCLUSION
The results of the present paediatric OSMF case suggests that curcumin shows effective improvement in the overall symptoms and is a safe and promising treatment modality owing to its anti-oxidant, anti-inflammatory, anti-septic, anti-carcinogenic, chemo-preventive, anti-tumor property especially in paediatric cases where possible adverse effects of other drugs conventionally used for OSMF could be
a concern. Numerous studies done on adult OSMF patients have shown successful results with curcumin and hence well designed clinical trials with adequate sample size and long term follow up to assess the longevity of the results specially for paediatric patients is recommended.

REFERENCES


Figure 1: pre-treatment inter-incisal mouth opening

Figure 2: blanching and fibrosis of the pterygo-mandibular raphe area and of the posterior palate.

Figure 3: Blanching of the left buccal mucosa

Figure 4: Blanching of the right buccal mucosa

Figure 5: post –treatment inter-incisal mouth opening.
<table>
<thead>
<tr>
<th>Sr No</th>
<th>Year</th>
<th>Age / Gender</th>
<th>Author/s</th>
<th>etiology</th>
<th>Mouth opening</th>
<th>Management</th>
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<tr>
<td>1</td>
<td>1985</td>
<td>4yrs/F</td>
<td>Patzer A Hayes[31]</td>
<td>Areca Nut</td>
<td>11</td>
<td>Systemic and local corticosteroid therapy, Fibrotic tissue surgery, Graft</td>
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<td>2</td>
<td>1993</td>
<td>12/F</td>
<td>Anil S[14]</td>
<td>paan supari</td>
<td>17</td>
<td>Placentrex Injection</td>
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<td>3</td>
<td>1999</td>
<td>8/F K Mundra[32]</td>
<td>Betel Nut</td>
<td>20</td>
<td>Microwave diathermy, Local corticosteroids injection, Excision of fibrotic bands, Supportive treatment (vitamins and minerals)</td>
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<td>6</td>
<td>2010</td>
<td>9/F Sumeet Setia[33]</td>
<td>Smokeless tobacco</td>
<td>25</td>
<td>Zinc acetate syrup, Ferrous fumarate tablet, Oral physiotherapy, Vitamin A tablet, Vitamin E capsule</td>
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<td>7</td>
<td>2010</td>
<td>2.3/F Mohaideen Sitheeque[34]</td>
<td>Areca Nut</td>
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<td>Not reported</td>
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<td>3/M Mohaideen Sitheeque[34]</td>
<td>Betel Nut with Areca Nut</td>
<td>-</td>
<td>Not reported</td>
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<tr>
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<td>3/F Mohaideen Sitheeque[34]</td>
<td>Betel Nut with Areca Nut</td>
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<td>2011</td>
<td>9/F Anuradha Agarwal[35]</td>
<td>Sweet supari</td>
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<td>14</td>
<td>2012</td>
<td>12/F Richa Dharwal[36]</td>
<td>Pan Masala</td>
<td>19</td>
<td>Zinc acetate syrup, Vitamin A tablet/Zinc acetate syrup, Vitamin A tablet, Vitamin E capsule</td>
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<td>2013</td>
<td>14/F Anshula Deshpande[37]</td>
<td>Areca nut and tobacco</td>
<td>30</td>
<td>Medical therapy (vitamin B complex capsule-antioxidant capsulier iron tablet), Oral physiotherapy</td>
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<td>16</td>
<td>2013</td>
<td>11/F Vinay Gupta[38]</td>
<td>Areca Nut</td>
<td>14</td>
<td>Oral physiotherapy</td>
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<tr>
<td>17</td>
<td>2013</td>
<td>10/M Vinay Gupta[38]</td>
<td>Areca Nut</td>
<td>13</td>
<td>Oral physiotherapy</td>
<td></td>
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<td>2015</td>
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<td>Pan chewing, gutkha</td>
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<td>21</td>
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<td>12/M Mamta Kamat[41]</td>
<td>Roasted tamarind seeds</td>
<td>21</td>
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<td>23</td>
<td>2018</td>
<td>10/M Sahand Samiread [42]</td>
<td>--</td>
<td>10</td>
<td>Fibrotic tissue surgery, Buccal fat pad graft, Custom made prosthesis, Corticosteroids therapy, Local Triamcinolone, Oral physiotherapy, Supportive treatment, Vitamin B tablet</td>
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<td>24</td>
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<td>5/M Pratik Kariya[43]</td>
<td>Betal Nut</td>
<td>6</td>
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