A 28-year-old man reported to the Department of Periodontics, Mahatma Gandhi Missions Dental College and Hospital, Navi Mumbai, with a chief complaint of swollen gums involving the entire upper and lower jaws. History revealed appearance of gingival enlargement at 10 years of age. With slow progression, the condition became increasingly severe and generalized, causing unaesthetic appearance together with difficulties in speaking and mastication [Table/Fig-1a] besides these, no other complaints were present, such as pain, bleeding or halitosis. The patient reported a history of prior surgical excision seven years ago which was followed by orthodontic intervention during which the gingival overgrowth recurred. Medical history was not contributory as the patient was not on any medication that could be associated with gingival hyperplasia, such as phenytoin, cyclosporine, or calcium channel blockers.

Family history revealed, the sister (33-year-old) [Table/Fig-1b], niece (7-year-old) [Table/Fig-1c], and mother (60-year-old) [Table/Fig-2a-c] all exhibited signs of gingival enlargement. The sister gave a similar history as the patient with appearance of enlargement at 10 years of age, with gradual increase in size and extent of severity. In the niece, gingival enlargement was noticed early at the age of four years, and by the age of seven had gradually increased in size to cover the crowns of all the teeth. The mother reported development of isolated areas of gingival enlargement at the age of 16 which gradually increased in severity involving all the teeth, resulting in aesthetic disfigurement and deranged occlusion. At the age of 24, she underwent full mouth extraction in an attempt to eliminate the enlargement, and has been wearing complete denture prosthesis since then.

Extra oral examination revealed a dysmorphic face with evident protrusion of the lips. The patient was unable to close his lips completely because of the gingival overgrowth. Other features noticed were macrocephaly, hypertelorism, bushy eyebrows with synophrys (unibrow), hypoplastic nares and cupid’s bow mouth [Table/Fig-1]. Intra-orally, the examination found generalized, severe gingival overgrowth involving both buccal and lingual regions in the maxillary and mandibular arches [Table/Fig-3,4]. The enlarged gingiva was pink, firm, and smooth. No acute inflammatory signs were present. The patient’s dentition suffered from serious malocclusion, involving displacement, rotation, and diastemas. Other features noticed were a highly arched palate, and v-shaped maxillary and mandibular arches. The extra and intra-oral features were remarkably similar in the patient’s mother, sister (underwent cosmetic correction of synophrys), and niece. Intra-oral examination of the mother revealed...
severely resorbed residual alveolar ridges. The ridges were covered by significant amounts of loose flabby tissue, which resulted in a poorly fitting prosthesis. Panoramic radiographs [Table/Fig-5] of the patient indicated moderate to severe alveolar bone resorption around multiple teeth indicating presence of chronic generalized periodontitis.

Based on the symptomatology and family history, a diagnosis of Gingival fibromatosis with distinctive facies was arrived at (see discussion below), which was confirmed by a preoperative biopsy. The treatment envisaged of an external bevel gingivectomy at all quadrants, the treatment plan was explained to the patient and informed consent obtained. The surgical intervention was carried out under general anaesthesia, using a combination of electrosurgery and scalpel. Thedecision to operate under general anaesthesia was taken based on the following considerations; reduction of treatment time from 4 sittings to 1 sitting, secondly in the maxillary tuberosity region, the gingival enlargement was in close proximity to the greater palatine foramen, as such there was an anticipated risk of accidental perforation of the greater palatine vessels, and the management of this would have been easier under general anaesthesia. Lastly, the sheer bulk of the gingiva needing removal would have resulted in significant patient discomfort and difficulty in feeding. To counter this it was decided to monitor the patient on an in-patient basis with ready tube feeding if required. Taking into consideration the amount of heat generated while using electrosurgery, an 8 to 15 seconds cooling period was advocated between successive incisions or recontouring of the gingiva. Teeth no. 12, 27, 37, 36, 31, 41, 42, 45, 46, 47 were extracted during the procedure due to diastemas, malpositioning of teeth, prolonged retention of primary dentition, delayed eruption, cross and open bites, prominent lips, and open lip posture [7, 8].

The gingiva in HGF displays normal colour, exaggerated stippling, and firm consistency. The tissue is densely fibrotic (bony hard on palpation) and displays a nodular or pebbled surface. Both attached and free gingiva is involved but does not extend beyond mucogingival junction [9, 10]. The histologic appearance of HGF is non-specific and is characterized by a well-structured epithelium with elongated and thin papillae inserted in fibrous connective tissue that is rich in collagen fibers [11]. Due to this, the definitive diagnosis of HGF should be based on family history and clinical findings. HGF can develop as an isolated disorder or more rarely it is associated with other manifestations as part of a syndrome or some chromosomal abnormality [Table/Fig-8]. Accordingly, HGF has been divided into two forms: non-syndromic and syndromic. The syndromic characteristics seen in association with HGF range from hypertichrosis [12], mental retardation [13], epilepsy [14], progressive hearing loss [15], and abnormalities of fingers and toes [16]. Of these, hypertichrosis is the most commonly associated feature. HGF has predominantly an autosomal dominant mode of inheritance; however, autosomal recessive modes of inheritance has also been reported in the syndromic variant [17].

This paper documents a family spanning 3 generations with individuals manifesting the syndromic form of HGF – Gingival fibromatosis with distinctive facies in which the transmission occurs through an autosomal recessive trait. This syndrome was described by Goldblatt and Singer [7]. Although familial aggregation of HGF

**DISCUSSION**

One of the rare causes of gingival overgrowth is hereditary gingival fibromatosis (HGF), also known as familial or idiopathic gingival fibromatosis. HGF is a characterized clinically by gradual and progressive enlargement of keratinized gingiva, which is of normal colour, firm in consistency, non-haemorrhagic, and asymptomatic [1]. The first case was described by Gross in 1856 and the prevalence has been estimated at 1:750000 [2]. Oral manifestations of HGF are highly heterogeneous and can vary from isolated areas of gingival enlargement typically seen around the maxillary tuberosities and the labial gingiva around the lower molars to generalized involvement

[Table/Fig-8]: Syndromes associated with HGF (Adapted from Coletta RD and Graner E) [17]
has been widely reported in the literature [1,6,7,18], to the best of the authors knowledge, this is the first 3 generational case report of gingival fibromatosis with distinctive facies.

The exact pathogenesis of HGF currently remains unknown, however a review of the literature reveals the following pertinent mechanisms; genetic analysis of HGF has revealed several chromosomal mutations, the most studied of which are 3 different gene loci associated with chromosome 2 and 5 (GINGF on2p21-22, GINGF2 on 5q13-22 and GINGF3 on 2p22.3-p23.3). Among these loci, the SOS1 (son of seven less one) gene has been recognized as being an essential part of the GINGF locus [19]. The SOS1 protein is a guanine nucleotide exchange factor which plays an essential role in signal transduction during cell growth and differentiation. The mutation linked to HGF causes a single base insertion, which as a result of the ensuing frameshift, generates a premature stop codon. This truncated SOS1 protein production leads to enhanced activity of the SOS1–Ras–MAPK pathway which enhances the activity of type I collagen, transforming growth factor (TGF)-β, and tissue inhibiting factor of matrix metalloproteinases (TIMPs), whereas it decreases the expression of matrix metalloproteinases (MMPs). The net result of which is increased gingival connective tissue synthesis coupled with inhibition of connective tissue breakdown, leading to excessive connective tissue accumulation [17]. It has also been demonstrated that fibroblasts from HGF patients produce 30% to 50% more collagen than normal gingival fibroblasts [20]. This is thought to be due to the excessive local production of TGF-β, which also brings about myofibroblast differentiation, which has been demonstrated in HGF patients [21]. Myofibroblasts are seen in abundance in fibrotic lesions, and their presence in HGF lesions points to a possible role in the pathogenesis of HGF. However, it should be mentioned, the pathogenic cascade as described above is based on piecemeal evidence, and the true pathogenesis remains to be elucidated.

HGF cannot be definitively treated but may be managed with varying and unpredictable degrees of success. The sheer bulk of excessive gingival tissue necessitates surgical intervention in most cases. The choice of technique used is dictated by the clinician’s acumen and experience as well as the extent and degree of gingival enlargement. Techniques that have been used for the excision of the enlarged gingival tissues, including external or internal bevel enlargement. Techniques that have been used for the excision of the enlarged gingival tissues, including external or internal bevel gingivectomy in association with gingivoplasty, an apically positioned flap, electrocautery, and CO2 laser [12,15,17,18]. The patient though still has to deal with the risk of recurrence. The risk of recurrence though, should be weighed against the benefit of psychological well-being, improved function, and improved plaque control. Recent reports also attest to the fact that regular follow up and meticulous plaque control can prevent or minimize recurrence for up to two years following treatment [22-24]. Recently, a novel non surgical therapy for HGF has been proposed wherein antibodies that target the C-terminal telopeptide of the α2 chain of collagen I, are used to inhibit extracellular collagen fibril formation [25]. This research is still in the in vitro phase, but may be of potential future benefit.

CONCLUSION

A family with three generations affected with HGF in which the disease is transmitted by an autosomal recessive mode of inheritance is described in this study. Efforts are underway to elucidate the pathogenic mechanism of HGF. This can further illustrate the correlation between gene mutations, molecular changes, histology, and the clinical situation. Further information has the potential of providing not only novel methods for disease prognosis and differential diagnosis, but also targets for disease prevention and treatment.

ACKNOWLEDGEMENTS

The authors wish to thank the MGM Medical College and Hospital, Navi Mumbai for their assistance towards the surgical management of the case. The authors report no conflicts of interest related to this case report.

REFERENCES