An unusual Oral physiological presentation of any clinical case needs an immediate referral to oral diagnosis which helps in early diagnosis, good prognosis and more life expectation. This is a case report of a 4 year old girl who was referred to oral physician due to unresolved persistent facial swelling which was later diagnosed as Langerhans cell Histiocytosis. This is a reminder and suggestion for early referral to prevent extensive clinical manifestation, extended regime of treatment protocol, suffering from ailment and financial burden.

INTRODUCTION:
Langerhans cell histiocytosis is a rare disease of unknown cause characterised by oligoclonal proliferation of bone marrow derived antigen presenting histiocytes (Langerhans cell) which affect single system at single/multiple site or may represent itself as a multisystem disease 1-3. The disease usual occurrence is in childhood.1 May be seen in young adults and also in later part of life with male pre dominance 2,3. The incidence is 1 in 200,000.6 and 1 in 560,000 18 per year in children and adults respectively. The etiology remains obscure but the evocative origin from environmental, infectious, immunologic, reactive,10 and even neoplastic still remains a debatable factor.4 Localised Langerhans cell histiocytosis of bone is a chronic focal benign tumor like condition with an unpredictable clinical course.5,10 We present a case of Langerhans cell histiocytosis with multifocal Eosinophilic granuloma of maxillofacial skull bones with typical radiologic features.

CASE REPORT:
A four year old female child, referred to the department of Oral medicine and radiology through a dentist due to an unresolved swelling on the left side of the face since 8 months. Initial presentation for dental care from child parents was pain and mobile teeth in the lower left back teeth region since a month. 2-3 days later a sudden progressive facial swelling was noticed. Medical history revealed antigen presenting histiocytes (Langerhans cell) which helps in early diagnosis, good prognosis and more life expectation. This is a case report of a 4 year old girl who was referred to oral physician due to unresolved persistent facial swelling which was later diagnosed as langerhans cell Histiocytosis. This is a reminder and suggestion for early referral to prevent extensive clinical manifestation, extended regime of treatment protocol, suffering from ailment and financial burden.

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No history of fever, weight loss, tooth infection, trauma or any swelling in other parts of the body.

On examination, Patient was febrile and had hyperextension of right knee joint. Level II B left submandibular lymphnode was 2.5 cm, solitary, movable, soft to firm in consistency and tender.

Extraorally three different tender solitary swellings, one on the occipital bone, second, on the left middle and lower third of the face and the third on the left submandibular region noted (Fig.1).

Occipital swelling was 4 cm in diameter, definite and hard (Fig 1B). The facial diffuse swelling was 7x5 cm; smooth, slightly erythematous surface with softness and mild local rise of tem-perature (Fig1B). An additional sagging swelling was 2x3 cm in size from submental to submandibular area with local rise of temperature (Fig1C).

Intraorally, comparative asymmetry on right and left side of maxillary and mandibular arch was due to five different solitary swellings (Fig 2). One on left anterior palate of 3x2x1 cm, solitary, diffuse, soft in consistency and tender (Fig 2A). Second oval shaped diffuse swelling of 2.5x1 cm, on the left Retromolar trigone (RMT) area, soft to firm in consistency and tender (Fig 2C). The third doomed shaped definitive swelling of 1 cm over left lower edentulous ridge of primary second molar with firmness and tender (Fig 2B). The fourth swelling of 3x2 cm was appreciable due to medial migration of left plica lingualis, soft to firm in consistency and tender (Fig 2B&C). The fifth swelling was diffuse, extending bilaterally involving buccal and lingual vestibule in edentulous area of 74, 75 soft, tender and decorticated (Fig 2D). The overlying mucosa of all these swellings was smooth and normal to pale pink coloration.

In addition, the gingiva was soft, swollen and edematous wrt 54, 63, 64, 65, 72, 73. Gingival recession wrt 55, Grade III mobility wrt 55, 63, 65, 84, 85 (Fig 3) and dry saliva (Fig 2A&B) was noted. The multiple unusual, nonphysiological, nonregressive clinical presentations in a 4 year old child made to arrive at a provisional diagnosis of Langerhans cell histiocytosis.

Radiologic investigation with Panoramic, Lateral skull, PA skull view and occlusal cross sectional view revealed active rarifying osteitis with epicentre of bone destruction at middle one third of root(Fig 4A), destructive skull morphology(Fig 4C&D), and bi-cortical expansion(Fig 4B&D) with decortication in edentulous area(Fig 4B&D) respectively. The skeletal survey was non contributory. Bilateral, Bimandibular with occipital bone involvement suggested multifocal aggressive disease radiographically. Jaw lesion biopsy gave an impression of Langerhans cell histiocytosis (Fig 7). Confirmatory diagnosis of LCH was made with Immunohistochemistry which showed the neoplastic cells positive for CD1a and S100.
Before treatment in higher centres, Hematologic investigations revealed Microcytic hypochromic anaemia, raised ESR of 35mm with normal blood glucose levels. Kidney function test revealed reduced serum creatinin and Blood urea nitrogen, urine osmolality. Liver function test, chest and skeletal survey radiography appeared normal. Computed Tomographic examination (Fig5ABC) revealed same features as conventional radiographs with an additional extra osseous soft tissue involvement in the occipital bone and minimal soft tissue bulge towards the epidual aspect (Fig5D&E). Ultrasound of Thorax and abdomen revealed normal study. Hbs Ag, Anti HCV antibodies was negative and non reactive Anti HIV 1 and 2 antibodies.

Combined Chemotherapy and Radiotherapy was the choiced modality of treatment. The class and course of medication depended on the nature of progression of the disease. Etopside, vinblastin, prednisolone and cytoblastin were administered in our case. On fourth month course of treatment, fever, lip ulceration and mucositis appeared which regressed with conservative treatment ef- fectively. Prognostic follow up showed regression of all mucosal lesions clinically (Fig5ABCD) and PET scan (Fig5E) revealed normal study at the end of fourteenth month. Currently, after 21st month, patient is absolutely healthy with complete regression of bony and soft tissue lesion and is under periodic regular follow-up.

DISCUSSION:
Langerhans cell Histiocytosis (LCH), conventionally termed as Histiocytosis X is dendritic cell associated reticuloendothelial syndrome disease.6 It is an exceptional disease potentially ensu- sing in death or permanent sequelae or can resolve spontane- ously.6,7,9 The Langerhans cells are usually present in bone and skin. The same proliferative intrinsic worth of these immune cells is found in epidermis, mucosa and other organs.6

90% of LCH affects Head and neck region.24 10% of Head and neck LCH have oral lesions.10 35% of Stomatologic features can be the first and the only clinical feature initially. Of which 30% are associated with cervical lymphadenopathy.2,6 77% is the incidence of oral lesions in LCH,2,10.

Microscopically, LCH appears as yellowish granulomatous les- ion.6 Presence of Birbeck granules or racket body can be the opinion of LCH under electron microscope except in sclerosing cholangitis and Cirrhosis due to progression of Langerhans cells.6,7,9 Kidney or coffee bean,6,7,17 shaped nucleated Histiocytic cells are usually present in bone and skin. The same proliferative intrinsic worth of these immune cells is found in epidermis, mucosa and other organs.6

As Histiocytic disorder manifests itself with multiple presentations, it often leads to incorrect diagnosis. But by correlating the chief com- plaint, signs and symptoms with clinical manifestation in association with radiographic features LCH can be diagnosed earlier clinically,7

It is traditionally classified by Lichtenstein as Eosinophilic Gran- uloma, Hand-shuler-Christian disease and Letterer-Swoe dise- ease.10 The clinical picture of this disease depends on its type, compromised body or organ. Thus Eosinophilic granuloma is a syndrome of multiple lytic lesions of hematopoietic active bone with good prognosis.6 But the total number of bone involve- ment and the extent of adjacent soft tissue destruction decide the disease termination.9 This was the suggested cautionary feature for early referral in our case. Hand-shuler-Christian disease is a chronic disseminated form with multiple compromised organs related with general physical expressions commonly seen in 3-6 years of age.6 Letterer-Swoe disease is a acute and disseminated form commonly seen in less than 2 years of age with negative prognosis.6,7

Usually Patient chief complaints are, pain, swelling and tender- ness.10 Gingiva, teeth, angle and body of the mandible are the common intraoral sites of involvement.6,11 Clinical presenta- tions are gingival inflammation, bleeding, necrosis, Hyperpla- sia17,20 and Hypertrophy.4,10,18 Timefraction over the gingi- val area indicates Langerhans cell accumulation secondary to ‘cytokine storm’, leading tissue destruction resulting in necrotic ulceration.4,6,20 This happens only if the disease destroys the bone.10 The epicentre of the disease usually initiates in the posterior region of the lower jaw at the periapical area. Ultimately results in mobility and premature exfoliation of deciduous teeth with rariyloss of ositis. This is an eloquent sign of LCH which was the chief complaint in our case. Premature exfoliation of ante- rior teeth is rare and results in negative prognosis.6 Precocious eruption of permanent teeth are also an added feature in chil- dren with excess crestal bone loss.4,12,17

Other added clinical features are nonspecific pain, dry mouth, halitosis,6 candidiasis, edematous and inflamed attached ginga- giva together with erosions, ulcerations covered with peeling pseudomembrane.4 Oral mucosal ulceration appears oval or round or diffuse,20 erythematous border with tenderness.2,20

Clinical oral presentations in young adults or elderly people are unusual mobility, early exfoliation of teeth,8 post extraction de- layed healing,12 post extraction hyperplastic growth,12 burning sensation,8 chronic mucosal Erythema, Pebbled surface of Palatal mucosa,10 exophytic large ulcerative mass,10 Ulcerations of Oral mucosa,8 Halitosis, pathologic fracture,23 osteoposes- is and amenorrhea8 in females.8,12,23

Disease involvement of Occipital bone and Bilateral partaking of maxilla and mandible is rare, which were of expressions in our case. Extension of osteolytic lesions of Occipital bone may result in difficulty in swallowing and hoarseness of voice secondary to involvement of Jugular foramen.17,19 This is a noted point in our case as oral swelling was unnoticed by both parents as well as general dental practitioner.

If LCH involvement is in condyle, then chronic localised throbbing pain followed by Preauricular swelling, limited mandibular movements, gradual disappearance of TMJ sounds, trismus, de- viation and loss of maximum intercuspatation of teeth on affected side are usual clinical presentations.13,25,26

Involvement of ear, eye, and oral lesions with combined cranio- facial lesion have risk of developing Diabetes insipidus and CNS manifestations.7,9,15 In our case pre and post treatment caution was taken to evaluate the patient for Diabetes and ruled out neurodegeneration.

Radiographic typical feature presents as solitary or multiple lytic lesions,6,10 This can be described as Punched out lesions19, scooped-out alveolar lesions, Floating teeth appearance8 and button sequestrum5 on skull radiographs.2,5,10 But initial jaw lesion appears as definitive radiolucency which represents gran- ulomatous tissue.6 This is responsible for displacement of tooth bud, mobility of teeth and later jaw fracture.6,23 The epicentre of bone destruction can also be at furcal level or at middle one third of radicular portion which was noted in our case.2 In primary condylar LCH in addition to osteolytic areas, condylar displacement can be appreciable on TMJ open and closed mouth view.13

Due to its multisystem involvement, Multidisciplinary approach is the management principle. Single system unifocal bony lytic lesion less than 2cm is suited for curettage. 2-5cm lesions for biopsy and partial curettage. Greater than 5cm or critical anatomic site involvement is suited for systemic therapy.7

Single system multifocal bone LCH has higher incidence with 100% survival rate irrespective of mode of treatment but high tendency for disease reactivation and permanent conse- quences.7,15 The minimum duration for treatment response is 6 weeks which can be extended in case of involvement of long or bone.9 Even in disseminated form with early referral have shown good prognosis.21 According to proposed clinical score to determine disease activity by Histiocytite society, Patients with scores >6 have a poor outcome.22 The present case inspite of belonging to stage II or Group A LCH, the clinical score of dis-
ease activity was 6 and hence qualified for aggressive chemotherapy.14,21,22 Medical management took 13 weeks for the clinical response to appear better9 and was extended to LCH III maintenance protocol duration. There is also risk of secondary malignant tumor from radiotherapy.2,9 This all could have been prevented by early referral.

In case of reactivation of single system LCH, the suggested management is ‘wait and watch, local therapy, NSAID for bone lesion, vinblastin and steroid.9 Detailed clinical examination, Biochemical investigation and imaging evaluation is mandatory at the time of diagnosis and at each revisit for better prognosis.7 which all was followed in our case.

The acceptable time of follow up is 5 years after last therapy or last reactivation.9 The routine consultation should be 4 in first year, 2 in second and third year and 1 each in fourth and fifth year.9

The disease prognosis depends on its age of initial initiation, number of affected teeth and degree of organic dysfunction.6 Patients with isolated bone located lesion bears excellent prognosis but poor prognosis in children below 2 years of age.6 So it is imperative to observe and follow up children until growth is completed and additional up to adult life.7,9

CONCLUSION:
Langerhans cell histiocytosis is a heterogenic versatile mimicker involving multisystem. So diagnosis is usually delayed. The living distinction of these patients mainly depends on early detection and management. In this regard, Oral diagnostician can play a vital role in early diagnosis and early referral when this entity appears initially as a sole oral manifestation which can be overlooked by clinicians. In the present case, the disease could have been diagnosed at an earlier stage and referral to oral Physician, would have helped in early management, adequate treatment, and better outcome in less span of time helping in future quality life.

ILLUSTRATIONS:

Fig 1: Extraoral swellings. A. Facial swelling B. Profile of Occipital & sagging swelling C. Sagging swelling

Fig 2: Intraoral swellings. A. Palatal swelling, B. Doom shaped and oval swellings, C. Bicortical expansion due to swelling in relation to edentulous area of 74, 75. D. Swelling on left floor of the mouth with migration of plica linguaris.

A&B. Ropy saliva

Fig 3: Soft swollen edematous gingiva with recession

Fig 4: A. Panoramic Radiograph B. Occlusal radiograph C. Lateral skull view radiograph D. PA mandible view radiograph. All showing aggressive osteolytic lesions.

Fig 5: A. Coronal section B. Axial section C. Sagittal section of CT showing osteolytic lesion and with soft tissue enhancement in D&E