Volume : 3 | Issue : 7 | July 2014 • ISSN No 2277 - 8179

Research Paper

Langerhans Cell Histiocytosis-A Case Report With Oral Diagnostic Perspective And Review

Medical Science

KEYWORDS : Langerhans cell histiocytosis, Eosinophilic Granuloma, Skull, Oral manifestation, aggressive, multifocal

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ABSTRACT

An unusual Oral physiological presentation of any clinical case needs an immediate referral to oral diagnostician 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 disease1-3. The disease usual occurrence is in childhood.1 May be seen in young adults and also in later part of life with male predilection.2,3 The incidence is 1 in 200,0004,6 and 1in 560,00018 per year in children and adults respectively. The etiology remains obscure but the evocative origin from environmental, infectious, immunologic, genetic4, reactive10 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. Medication gave relief from pain and swelling for a month. But the recurrence and persistent of swelling for next 4 months made the dentist to extract 74 & 75. Inspite of extraction and medication, the intermittent pain and swelling persisted for the next two months made the dentist to refer to our Institution.

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 2.5cm, 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 4cm in diameter, definitive and hard (Fig1B). The facial diffuse swelling was 7x5cm; smooth, slightly erythematous surface with softness and mild local rise of temperature (Fig1B). An additional sagging swelling was 2x3cm 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 3x2x1cm, solitary, diffuse, soft in consistency and tender (Fig2A). Second oval shaped diffuse swelling of 2.5x1cm, on the left Retromolar trigone (RMT) area, soft to firm in consistency and tender (Fig2C). The third doom shaped definitive swelling of 1cm over left lower edentulous ridge of primary second molar with firmness and tender (Fig2B&C). The fourth swelling of 3x2cm was appreciable due to medial migration of left plica linguaris, soft to firm in consistency and tender (Fig2B&C). The fifth swelling was diffuse, extending bilaterally involving buccal and lingual vestibule in edentulous area of 74, 75 soft, tender and decorticated (Fig2D). 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 (Fig3) and ropy saliva (Fig2A&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(Fig4A), defective skull morphology(Fig4C&D), and bicortical expansion(Fig4B&D) with decortication in edentulous area(Fig4b&D) respectively. The skeletal survey was non contributory. Bilateral, Bimaxillary with occipital bone involvement suggested multifocal aggressive disease radiographically. Jaw lesion biopsy gave an impression of Langerhans cell histiocytosis (Fig7). 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 anemia, 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 epidural 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. Etopiside, vinblastin, prednisole and cytoblastin were administered in our case. On fourth month course of treatment, fever, lip ulceration and mucositis appeared which regressed with conservative treatment effectively. Prognostic follow up showed regression of all mucosal lesions clinically (Fig8ABCD) and PET scan (Fig8E) 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 dentritic cell associated reticuloendothelial system disease.6 It is an exceptional disease potentially ensuing in death or permanent sequelae or can resolve spontaneously.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 organs6.

90% of LCH affects Head and neck region.24 10% of Head and neck LCH have oral lesions10. 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 LCH2,10.

Microscopically, LCH appears as yellowish granulomatous lesion.6 Presence of Birbeck granules or racket bodies validate the opinion of LCH under electron microscope except in sclerosing cholangitis and Cirrhosis due to regression of Langerhans cells.6,7,9 Kidney6 or coffee bean6,17 shaped nucleated Histiocytic cell is a mandated Histopatologic feature for diagnosis except in 'special site' cases where biopsy outweigh risk in earlier disease manifestation.7,9,15 Immunohistochemistry with positive lesional cell staining for CD1a and CD207(langerin) is a confirmatory diagnostic test for Langerhans cell Histiocytosis.7,9 In highly characteristic clinical and radiologic features even Fine needle aspiration cytology has proved useful diagnostic tool.11

As Histiocytic disorder manifests itself with multiple presentations, it often leads to incorrect diagnosis. But by correlating the chief complaint, 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 Granuloma, Hand-shuller-Christian disease and Letterer-Siwe disease.10 The clinical picture of this disease depends on its type, compromised tissue or organ. Thus Eosinophilic granuloma is a single or multiple lytic lesions of hematopoietic active bone with good prognosis.6 But the total number of bone involvement 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-shuller-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-Siwe disease is an acute and disseminated form commonly seen in less than 2 years of age with negative prognosis.6

Usually Patient chief complaints are, pain, swelling and tenderness.10 Gingiva, teeth, angle and body of the mandible are the common intraoral sites of involvement.6,11 Clinical presentations are gingival inflammation, bleeding, necrosis, Hyperplasia17,20 and Hypertrophy.4,10,18 Tumefaction over the gingival 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 rarifying osteitis. This is an eloquent sign of LCH which was the chief complaint in our case. Premature exfoliation of anterior teeth is rare and results in negative prognosis6.Precocious eruption of permanent teeth are also an added feature in children with excess crestal bone loss.4, 12,17

Other added clinical features are nonspecific pain, dry mouth, halitosis6, candidiasis, edematous and inflamed attached gingiva together with erosions, ulcerations covered with peeling pseudomembrane.4 Oral mucosal ulceration appears oval or round or diffuse20, 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 delayed healing,12 post extraction hyperplastic growth,12 burning sensation8, chronic mucosal Erythema, Pebbled surface of Palatal mucosa,10 exophytic large ulcerative mass,10 Ulcerations of Oral mucosa,8Halitosis,pathologic fracture,23 osteoporosis 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 occipital swelling was unnoticed by both parents as well as general dental practioner.

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

Involvement of ear, eye, and oral lesions with combined craniofacial lesion have risk of developing Diabetes insipidus and CNS manifestations.7,9,15 So 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 lesions6,10.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 granulomatous 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 consequences.7,15 The minimum duration for treatment response is 6 weeks which can be extended in case of involvement of lung 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 Histiocyte society, Patients with scores >6 have a poor outcome.22 The present case inspite of belonged 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 revist 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 1each 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 2years 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:

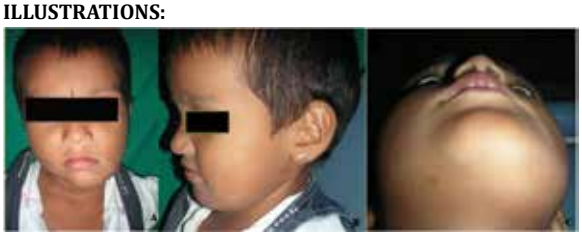

Fig 1: Extraoral swellings. A. Facial swelling B. Profile of Occipital &sagging swelling C.sagging swelling

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

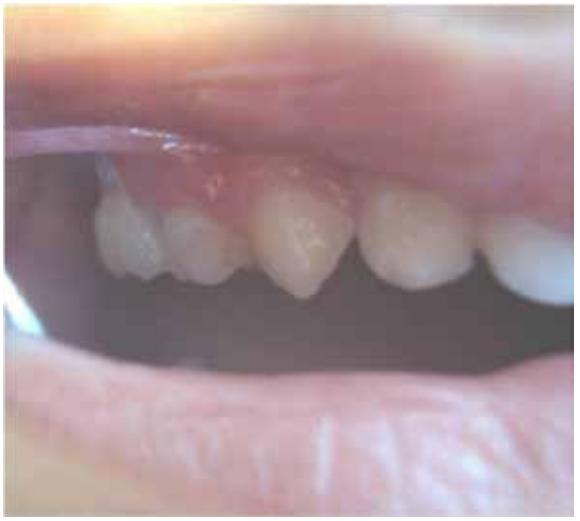

Fig 3: Soft swollen edematous gingiva with recession

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. Sagital section of CT showing osteolytic lesion and with soft tissue enhancement in D&E

Volume : 3 | Issue : 7 | July 2014 • ISSN No 2277 - 8179

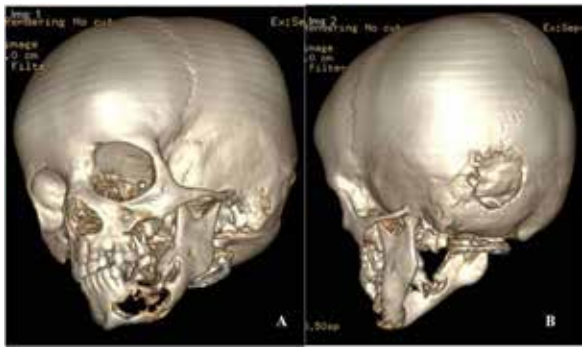

Fig 6: Three dimensional reconstructive images of computed tomography showing osteolytic lesions in mandible (A) and occipital bone (B).

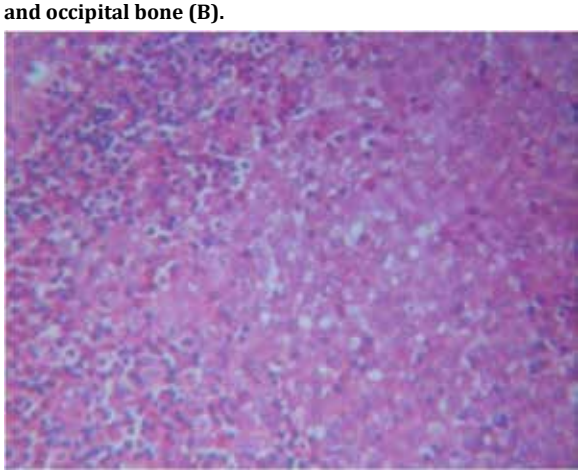

Fig 7: Histopathology showing Kidney or coffee bean shaped nucleated

Histiocytic cell

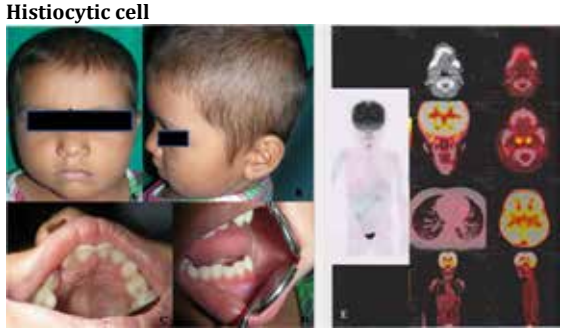

Fig 8: A, B, C, D Clinical and E PET scan follow up showing regressive LCH lesions

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