Case Report
Journal of Pierre Fauchard Academy (India Section), *Vol 36(3), DOI: 10.18311/jpfa/2022/30034, September 2022 p. 104-108*
ISSN (Print) : 0970-2199
ISSN (Online) : 2405-772X

Oral Manifestation of Autoimmune Connective Tissue Disease in a 5 Year Old Patient: A Case report

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Abstract

One of the leading causes of morbidity among children includes Connective Tissue Disorders (CTD). Early diagnosis and prompt treatment of any CTD would help identify the associated disorders and is beneficial in preventing severe complications at a later age. Non-specific clinical presentations have made it challenging for both medical and dental practitioners in diagnosing and treating CTDs. Oral manifestations of systemic diseases help in the early diagnosis of certain diseases. Hence it is extremely important for dentists to carefully observe the patient complaints and define the diagnosis. The present case report identifies a CTD condition in a 5-year-old patient, with Hereditary sensory autonomic neuropathy type IV (HSAN -IV).

Keywords: HSAN Type IV, Self-Mutilated Tongue

1. Introduction

The manifestations of Connective Tissue Disorders (CTDs) are rarely reported among children although it has been marked as one of the major causes of morbidity. Despite its minimal prevalence among the child population[1], early diagnosis helps in the identification of associated disorders and in preventing complications at a later stage[1]. The commonest CTD is Systemic Lupus Erythematosus[2] (SLE) while others include: Juvenile dermatomyositis[3], mixed connective disease[4], systemic sclerosis[5], Sjogren syndrome[6] and Juvenile systemic lupus erythematosus[7] with or without the associated anti-phospholipid syndrome. The CTDs most commonly affecting children include sclera-dermiform syndromes, including systemic and localized sclerodermas along with eosinofilic fascitis[8]. The most common characteristics of systemic CTDs include the involvement of multiple organs. Unfortunately, the prevalence of HSAN Type-IV among the Indian Population is not yet clearly known, thereby recommending the need for elaborative research in this field.

Reports from multiple studies on the global forefront have described that the annual incidence rate of 0.37% for systemic lupus erythematosus, 0.30% polymyositis or dermatomyositis, 0.10% mixed connective tissue disease, 0.05% scleroderma, and 47/1,00,000 S-JA among adults. In the entire series of CTD, the prevalence was higher for females as compared to males except for polymyositis or dermatomyositis, where the distribution was similar among both genders[9]. The prevalence of the disease among children is 23% with eleven years as the median age of onset. The youngest patient to have reported CTD was 2 years of age. The gender ratio (female to male) is reported as 6:1[8].

There are literature reports highlighting the oral manifestations of CTDs. These include difficulty in chewing, and swallowing, dysphagia, altered taste sensations, fissured tongue, and lips, increase in the dental caries lesion, and oral candidiasis. Early diagnosis and prompt treatment help to improve the prognosis of the lesion.

The present report is of a rare case of CTD as diagnosed in a five-year child at a dental hospital at Bareilly.

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2. Case Report

A five-year-old female patient reported to the Pedodontia department with the complaint of decayed teeth in the right maxillary and mandibular posterior tooth region. A general examination of the patient suggested that the patient so far was afebrile, with stable vital parameters. The patient was moderately built, well-nourished, and well-oriented, with normal developmental miles.

Extra-oral examination showed no significant finding. Intra-oral examination showed the presence of dental caries in the Maxillary right first and the second molar, maxillary left first molar, and mandibular left first and second molar teeth. A grossly decayed mandibular right first molar tooth was also seen (Figure 1(A)). There was an associated intra-oral swelling with respect to the mandibular right first and second molar. Other associated findings were thickened, fibrous buccal bands on right and left of the first permanent molar region. (Figure 1(B) and Figure 1(C)) the tip of the tongue was bitten and mutilated (Figure 1(D)).

The patient gave a history of diarrhea, hemoptysis, and hematuria at the age of four months. This was accompanied by hospital admission, FFP, and Vit K transfusions. Another incident that the parents reported was at the age of 10 months. The pediatrician was approached with the complaint of oral ulcer, tongue biting, and hand (self-amputation). The patient was not irresponsive to pain-inducing pinch, very mildly responsive to pricks, and the pain sensation was grossly lost. With the suspicion of autoimmune connective tissue disease, specialized investigations were done. ANA testing {antinuclear-AB IFA, HEP2, SERUM} showed positive with endpoint titre 1:80 and positive CRP values. The details of the blood parameters have been mentioned in Table 1. Intra-oral radiographs were recorded (Annexure). A provisional diagnosis of congenital sensory neuropathy was made from the clinical presentation and serological investigations.

Patient was kept on antibiotics (Roxithromycin syrup 5ml given thrice daily for 7 days) and a topical steroid (Triamcinolone oro-mucosal 0.1% w/w) was advised for local application and referred to a tertiary care centre for further treatment.

The patient was admitted to and blood investigation showed raised PT and APTT. From the narrated history, the probable diagnosis of HSAN TYPE IV was made and the patient was discharged. The patient had a negative family history of the reported illness. The child was born through consanguineous marriage. Because of logistic constraints, the patient's family refused to undergo karyotyping.

Dental treatment included GIC restoration with respect to the maxillary right and left first molar, maxillary



Figure 1. **(A).** Dentition stage. **(B)**. Fibrous band on right buccal mucosa. **(C)**. Fibrous band on left buccal mucosa. **(D).** Self mutated tongue.

Table 1. Complete blood report of the patient

Complete Blood Count	
Hemoglobin	12.4
WBC Count	6.3
RBC Count	5
Neutrophil	62
Lymphocyte	33
Eosinophil	05
Monocyte	00
Basophil	00
Others	00
Platelet Count	229
HCT	35.2
MCV	70.8
MCH	24.9
MCHC	35.2
RDW-CV	22.9
RDW-SD	38.1
Prothrombin Time (Sec)	69.1
Active Partial Thromboplastin time (APTT)	40.6
Kidney Function test	
Creatinine	0.69
Blood Urea	46

right second molar, Mandibular left first and second molar teeth. An extraction of 84 was done, followed by a Pulpectomy of 85. An incisional biopsy sample was made from the left buccal mucosa and skin from the left thigh taken under Local Anesthesia. Histologic features of both samples suggested connective tissue fibrosis.

The patient was on a regular follow-up. Intra-oral findings showed thickening of the bands, with the aging of the child.

The patient was advised to genetic testing to confirm mutation of NTRK1 (genetic coding of the neurotropic Tyrosine Kinase Receptor). For the self-mutilation behavior, the patient was referred to a child psychologist and counseling was done to distract and to get engage in other activities. The genetic tests were not performed by the patient because of their financial instability.

3. Discussion

CTD is a rare but alarming condition among children which overlaps with copious autoimmune disordered mentioned earlier in the report. Clinically CTD among children ranges from an acute severe illness impersonating serious infection and sometimes to a deceptive onset of gradually progressive lesion developing over weeks and months. It is difficult to diagnose a CTD because of its diverse clinical presentation in the majority of the cases[10]. Some cases present with Malar and Gottron's rashes, Lymphadenopathy, alopecia, Raynaund's phenomenon, renal involvement, photosensitivity, and oral ulcers suggestive of CTD. Other signs and symptoms vary from polyarthritis, myalgia, malaise, poly-arthralgia, myositis, fatigue, and febrile conditions. The involvement of multiple systems, the presence of inflammation, and lack of some obvious etiology provokes a clinician for a CTD diagnosis.

Hematological findings include the presence of anti-U1 RNP antibody and also a rheumatoid factor. Increased anti-nuclear antibodies count, and anti-ds DNAs direct towards the diagnosis of CTD. As CTDs mainly affect the connective tissue components, including collagen, elastin, muco-polysaccharides, etc. Major defects in the collagen components of the oral cavity have been noted as the disease manifests. The collagen components in the oral cavity include Type 1 collagen in the alveolar bone, dentin, and cementum, and Type 1 and Type 111 collagen in the periodontal ligament and the pulp. Type 1 and type 1V collagen in the gingiva and Type 1, 11, and 111 collagen in the TMJ[11].

In the present study, the patient presented with intra-oral swelling diagnosed to be a slow-resolving oral abscess. This was a squeal for the underlying dental carious lesion. There have been reports by clinicians where dental caries was a secondary finding for patients with CTDs. The patient was reported to be febrile with myalgia and muscular weakness majorly in the proximal muscles which were documented to be a common finding for CTD patients. Most patients were found to have the acute manifestation of myositis accompanied by fever.

Hematological changes accompanied among children diagnosed with CTDs include leukopenia, anemia along with thrombocytopenia. A similar blood picture was reported by the present patient. A study reported that 75% of CTD patients had leukopenia while thrombocytopenia was comparatively uncommon. Disease activity determined the presence of anemia and leukopenia and alterations were seen with treatment. The preset patient had a positive titre count and raised CRP levels. This is an indicative of treatment and studies have reported the same

for child patients reporting with CTDs. A 60% increase in rheumatoid factor levels has also been reported among CTD patients.

Patients have also reported having gatro-intestinal symptoms including diarrhea, gastric upsets, and dysphagia along with malabsorption symptoms. The present patient complained of diarrhea. Ulcerations in the gastric tract might be associated with hemorrhagic diarrhea[12].

Serological tests include ANA, and anti-U1 RNP which have been reported to be 100% positive in CTD patients. Anti-cyclic citrullinated peptide antibodies are present in 50% of the patients with CTD. Copious tests including anti-Sm, anti-double-stranded DNA, anti-Ro/SS-A, and anti-single-stranded DNA show positive results in CTD patients.

She also reported delayed responses, mostly due to lateral neural responses as reported by some authors[13].

There have been recommendations for different diagnostic criteria. Some authors including Sharp *et al.*, Kasukawa *et al.*, and Alarcón-Segovia *et al.*[1,10,11]. Among these the most commonly used criteria for diagnosing pediatric patients include the Kasukawa criteria. Due to varied clinical presentations, the classification could be based on the presence of at least three clinical criteria and three serological criteria for confirmation.

A couple of investigatory aids have been put forward in recent times including several imaging techniques and blood picture analysis. Other advancements in genetic and immunologic factors help understand the etio-pathogenesis of the disease better thereby providing an opportunity to improve prognostication and targeted therapy. The treatment of CTDs mostly includes immune-suppressive drugs[11]. Unpredicted clinical manifestations increase the need to treat and handle in a comprehensive manner with treating the local presentations of the disease. For moderate symptoms, antimalarials including hydroxychloroquine, NSAIDs (Non-steroidal anti-inflammatory drugs), and corticosteroids are the treatment of choice. If there is involvement of the Central Nervous system (CNS) and kidneys, immunosuppression agents like cyclophosphamide could be used[13–15].

Copious studies reported that the majority of the patients with CTD have favourable prognosis if diagnosed early with a prompt treatment plan.[16,17] If the patients develop pulmonary hypertension, renal involvement such as glomerulonephritis, or neurological involvement the prognosis turns poor[1]. The mortality rate as reported in the literature from 10 to 12 years ago ranges from 16% to 28%[2]. A recent study reported the pediatric mortality rate to be 3–4 per 1000, and the adult mortality is 12–23/1000[6]. The commonest causes of death include pulmonary hypertension and cardiac involvement[2].

Reviewing the literature stated that there was no established relationship or any diagnostic confirmatory oral manifestation of CTDs. The multiple clinical and serological factors have knocked the need to investigate more on the clinical and serological markers of CTD.

4. Conclusion

As oral cavity is an important junction for the diagnosis of underlying systemic conditions. Therefore, it should be examined carefully and with responsibility by the dentists at any point in time. This need was transparently presented in the current case report where the oral findings called for a systemic medical examination which helped the clinician and the patient guardians towards a confirmatory diagnosis thereby improving the prognosis of the disease.

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