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Case Report

Mixed connective tissue disease in young Saudi patient with recurrent dental abscess: A case report

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ABSTRACT

Mixed connective tissue disease (MCTD) or overlap syndrome is a rare disease. It has overlapping features of more than one autoimmune disease with high titer of anti-ribonucleoprotein antibodies against U1. We present a 12-year-old Saudi male patient who was presented to the dental clinic complaining from non-healing oral ulcers and multiple periapical abscesses that not responsive to extractions and the use of oral antibiotics, these symptoms were accompanied with persistent fever, headache, muscle weakness, general malaise, and painful bilateral cervical lymphadenopathy. After a thorough investigation, he was diagnosed with (MCTD) and was managed dentally and medically accordingly.

Keywords: Dental abscess, dermatomyositis, mixed connective tissue disease, polyarthritis, rheumatoid, systemic lupus erythematosus

Introduction

Mixed connective tissue disease (MCTD) is a rare systemic autoimmune disease characterized immunologically by the presence of high-titer autoantibodies anti-U1 ribonucleoprotein (RNP) against the U1 small nuclear RNP auto-antigen.[1-4] Clinically, it has overlapping features with juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), systemic sclerosis, dermatomyositis (DM), and polymyositis. The most common clinical manifestations in children with MCTD are polyarthritis/polyarthralgia, Raynaud's phenomenon, and myositis.[5] MCTD can begin with any clinical manifestations of rheumatoid arthritis, SLE, or DM.[1]

The early manifestation of this disease is not specific. It can start with malaise, arthralgia, myalgia, and fever. Although MCTD is a rare condition, 23% of cases present in childhood, and 11 years old is the median age of onset;[5] the youngest patient diagnosed with MCTD was 2 years old.[6] The female to male ratio is 6:1,[5,6] and in the United States, 0.3–0.6% of pediatric rheumatology patients have MCTD.[6,7] Oral manifestations associated with MCTD include difficulty in chewing and swallowing, changes in taste, the presence of a fissured tongue and lips, increased dental decay, and oral candidiasis.[8] MCTD has a good prognosis, given the low prevalence of serious renal disease and life-threatening neurologic problems.[1,2]

Case Report

A 12-yearold Saudi child presented in the dental clinic (College of Dentistry/King Saud University) with intraoral swelling in lower left molar area with purulent discharge accompanied by non-healing oral ulcers and multiple periapical abscesses that are not responsive to extractions of primary teeth nor the use of oral antibiotics, after obtaining the patient's father consent for presenting the clinical pictures of his child and the publication of the case in a scientific journal, the following clinical figures will show the extent of the intra/extra oral lesions of the case [Figures 1 and 2].

Figure 1shows the extraoral swelling in the left cheek due to the periapical infection of the lower left teeth.

Figure 2 shows an intraoral swelling of the lower left area of the jaw due to the periapical infection and fever was up to 39.5°C for 7 days. This swelling was associated with pain, headache, malaise, and loss of appetite. These symptoms developed immediately after his dental appointment. The patient has a history of developing all of the above-mentioned signs and symptoms after each dental visit where he needed an extraction of his primary 1st and 2nd molars. He also presented with delayed healing at the extraction wound site. On examination of his oral cavity, the patient was found to have an ulcerative,

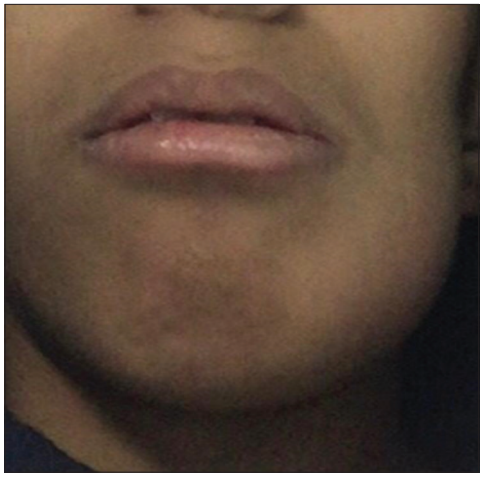

Figure 1: Extraoral swelling

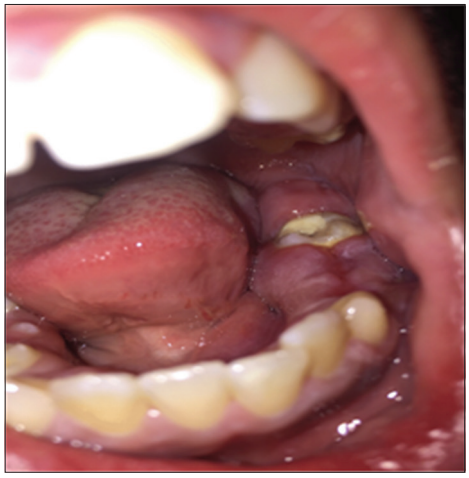

Figure 2: Intraoral swelling

reddish, edematous, and localized swelling with purulent discharge in the left mandibular area near the molars and was diagnosed with an acute dental abscess.

He was admitted to the extended-release (ER) and was given amoxicillin/clavulanate (1 g twice a day for 2 days) by the dentist, which was not effective, after which, therapy was changed to clindamycin intravenously, followed by oral clindamycin. The swelling subsided over a period of 5 days, and the patient was discharged.

Within few weeks, he returned to the ER with persistent fever up to 40°, headache, malaise, photophobia, neck stiffness, epigastric pain, dry cough, and bilateral painful axillary, and cervical lymph node adenopathy, as well as sudden generalized skin rash involving the upper and lower extremities. His physical activity was decreased as well.

On admission, a computed tomography scan of the brain and a lumbar puncture was taken, and the reports were normal. He received ceftriaxone 2 g IV Q24 h, vancomycin (480mg IV Q6), paracetamol (480 mg PO Q6), and azithromycin (250 one capsule twice per day for 3 days). The results of his laboratory evaluation are shown in Table 1.

After 3 days, he awakened in the morning with severe muscle weakness, such that he was unable to get out of bed and could not dress or hold a cup or spoon, and had difficulty swallowing. In addition, he complained of a raised rash on his cheek, redness of his ear [Figure 3],

hair loss, and painless red oral ulcers in his palate. He gave a history of pain in multiple small and large joints with morning stiffness before his admission to the hospital.

The patient had a history of cutaneous leishmaniasis 2 years before this presentation; there is no history of developmental delay. Antenatal history was not significant. Family history revealed that his parents are 1st cousins, and his sister has celiac disease.

The patient was ill-appearing, with a discoid rash of his face, mild tenderness in several joints with no evidence of restricted joint movement, and muscle weakness measuring 3 out of 5 in the lower limbs.

The results of his laboratory evaluation at the second admission are presented in Table 2.

The patient also had an electromyograph, which revealed proximal myopathy. A magnetic resonance imaging study was unremarkable, and a bone marrow biopsy and an ultrasound of the abdomen were normal. The patient was treated with methylprednisolone (IV), followed by oral prednisolone, and hydroxychloroquine sulfate, 200 mg per day, the patient was discharged after 2 weeks of hospitalization with a good response. Follow-up visits for 1-year showed improvement of patient weakness, hair loss, joint pains, and skin rash.

Discussion

MCTD in children is a rare systemic autoimmune disease requiring at least two overlapping immunological diseases[3] such as (SLE), (DM), scleroderma, and (JIA), and evidence of an anti-U1 RNP antibody, which is a key laboratory finding of MCTD. A high antinuclear antibody (ANA) and rheumatoid factor may be present.[2, 3, 5]

Common features of pediatric-onset MCTD include polyarthritis and polyarthralgia, Raynaud phenomenon, myositis, fever, and fatigue,[5] but it can begin with any clinical manifestations of JIA, SLE, or DM. Less common manifestations include lymphadenopathy, malar rash, alopecia, or renal involvement.[1] Our patient presented with an oral abscess that was slow to resolve, followed by severe polyarthritis, cervical and axillary lymphadenopathy, and muscle weakness. The muscle weakness in MCTD mainly involves the proximal muscles, with mild to

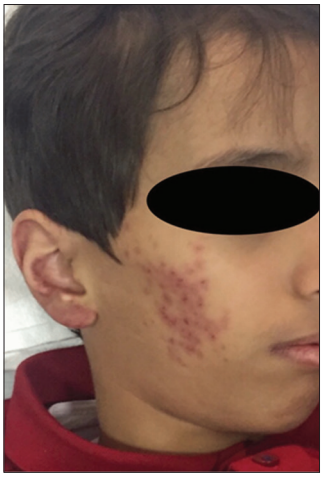

Figure 3: (Discoid rash) This clinical picture shows the skin rash on the face of the patient

Table 1: Initial laboratory studies

Investigation	Value	Normal range
WBC	3	(4–1×10⁹/L)
Neutrophils	1.4	(1.8–7.5×10⁹/L)
Lymphocytes	1.3	(1.5–4×10⁹/L)
Monocytes	0.1	(0.2–0.8×10⁹/L)
HGB	12.1	(12.5–18 g/dL)
MCV	73	(75–95 fL)
UARBC	23	(0–3) HPF
Urine cast	51	(0–2) LPF

Urine culture had no growth after 24 h. WBC: White blood cells; HGB: Hemoglobin, MCV: Mean corpuscular volume, UARBC: Urine red blood cell, HPF: High-powered field, LPF: Low-powered field

moderate weakness and high muscle enzymes.[1] Our patient presented with moderate to severe muscle weakness involving the upper and lower limbs, with a muscle strength of 3 out of 5. Electromyography revealed proximal myopathy. In most patients, the myositis may present acutely and may come with a fever.[1]

SLE features can be found in a 3rd of patients with MCTD, and include serositis, malar rash, hypo-pigmentation, and hyper-pigmentation, photosensitivity,[5] malar rash, and discoid skin lesions.[2] Our patient presented with a discoid rash, photosensitivity, a generalized macular skin rash, and an oral palatal ulcer. In MCTD, mucous membranes can be involved, including nasal septal perforation, orogenital ulcerations, and buccal ulcerations.[2]

In children, MCTD may present with hematologic complications, such as leukopenia, anemia, and thrombocytopenia;[5] our patient had evidence of leukopenia and anemia [Table 2]. One report found that 75% of patients with MCTD had leukopenia, whereas thrombocytopenia is infrequent.[9] Anemia and leukopenia usually come with disease activity and improve with treatment.[1]

Table 2: Laboratory studies at the second admission

Investigation	Value	Normal range
WBC	2.7	(4–1×10⁹/l)
Neutrophils	1.2	(1.8–7.5×10⁹/l)
HGB	10.4	(12.5–18 g/dl)
MCV	73	(75–95 fl)
C-reactive protein	26	(0–6 mg/L)
Erythrocyte sedimentation rate	38	(0–15 mm/h.)
ANA	Positive	
Anti-scleroderma70	Negative	
Anti-J0-antibodies	Negative	
Anti-centromere Abs	21 units weak positive (20–30) units	
Anti-ENA-RNP	123 units	(0-20) Units
Anti-ENA-smooth muscle	109 units	(0-20) Units
Creatine kinase	41	(50-190 U/L)
Anti-nucleosome	29 units moderately positive (20–60)	
Aspartate transaminase	46	(5–40 U/L)
Alanine transaminase	42	(0–41 U/L)
Anti-myeloperoxidase Abs	Negative	
Anti-proteinase 3 Abs	Negative	
CMVG (Cytomegalo Virus IgG), CMVM (Cytomegalo Virus IgM)	Negative	
Hepatitis C and B	Negative	
Virus 1, EPV (IGG), EPV (IGM)	Negative	
Ds DNA	212 equivocal (201–300 IU/mL)	

WBC: White blood cells; HGB: Hemoglobin, MCV: Mean corpuscular volume, ANA: Anti-nuclear Abs, RNP: Ribonucleoprotein

Our patient presented with generalized arthritis and a positive rheumatoid factor, which have been reported to be present in 60% of MCTD patients.[2] One study found that a positive rheumatoid factor could be an early sign of MCTD around the time of presentation, and MCTD may lead to joint deformity.[1]

Patients with MCTD can present with *gastrointestinal* symptoms such as heartburn, diarrhea, dysphagia, and malabsorption symptoms.[2] Our patient complained of heartburn, which was managed with a proton pump inhibitor, as well as dysphagia, which improved with prednisolone.

Renal involvement is one of the major complications of MCTD. It has been observed in some studies in approximately 25% of patients, and it is often asymptomatic.[1]

The most important serology in MCTD is anti-U1 RNP, but there are many other serology tests that can be positive in MCTD, like ANA, which is positive in 100% of patients with MCTD.[2] Rheumatoid factor, which is positive in 70% of patients with MCTD, and anti-cyclic citrullinated peptide

antibodies, which are positive in 50% of patients with MCTD.[4] Additional tests that can be positive in MCTD include anti-Sm, anti-double-stranded DNA, anti-Ro/SS-A, and anti-single-stranded DNA [1]. Our patient had a positive ANA, anti-U1 RNP, and anti-Smith antibodies [Table 2].

There are different criteria for diagnosis MCTD, such as Sharp *et al.,* Kasukawa *et al*., and Alarcón-Segovia *et al*.[1,10,11]

However, the most important and widely used criteria for diagnosing pediatric patients with MCTD are the Kasukawa criteria.[6,7] If the classification criteria are not met like in this case, patients can be diagnosed based on clinical manifestations and serology.[1] At present, the most common way to diagnose MCTD is to have at least three clinical criteria and serological criteria.[1]

There is no specific treatment for pediatric MCTD. However, nonsteroidal anti-inflammatory drugs, anti-malaria drugs such as hydroxychloroquine and corticosteroids are the treatment of choice for mild to moderate symptoms.[7,12] Immunosuppression using agents like cyclophosphamide is required if internal organs are involved such as the *central nervous syste*m and kidneys.[12] Our patient was treated with high dose corticosteroids and hydroxychloroquine to maintain remission.[5]

Many studies showed that most patients with MCTD have a good prognosis with treatment, though some may have a poor prognosis, especially if they develop pulmonary hypertension, renal involvement such as glomerulonephritis, or neurological involvement.[1] The mortality rate in studies from 10 to 12 years ago ranges from 16% to 28%.[2] A more recent study found that the pediatric mortality is 3–4 per 1000, whereas the adult mortality is 12–23/1000.[6] The most common causes of death are pulmonary hypertension and cardiac involvement.[2]

Patients with MCTD with polymyositis or scleroderma have a worse prognosis.[2] However, some patients with SLE features in their disease course with positive anti-U1-RNP antibodies may shift from MCTD to SLE.[1]

In the literature (up to our knowledge) there was no direct relationship between any oral/dental manifestations and MCTD, but in this case, the un-responded/persistent dental infection occurrence raised the issue of early oral/dental manifestation and MCTD. It has been documented in many other diseases that oral manifestations proceed the systemic signs and symptoms as in the case of Pemphigus Vulgaris, Crohn's Disease.

Conclusion

The oral cavity must be examined by a dentist as an integral component of the human body, which provides critical information regarding some systemic diseases. This need was clear in this case, which presented with multiple periapical abscesses not responsive to extractions or the use of oral antibiotics, with persistent fever and malaise. Such information should be considered and appreciated to assist in reaching the proper diagnosis and delivering effective management to the patient.

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