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Chronic Arthritis in Juvenile Behcet's Syndrome: A Rare Case

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Running Title: Behcet's syndrome

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ABSTRACT:
Behçet's syndrome is a chronic multisystem vasculitis characterized by mucocutaneous, articular, neurological, gastrointestinal and ophthalmological lesions. Behcet's syndrome is a disease of uncertain etiology. It may be due to immune dysregulation including circulating immune complex, autoimmune cytokines and heat shock proteins are major factor in the pathogenesis of Behcet's syndrome. Patient's positive pathergy test suggests a diagnosis of Behcet's disease. Corticosteroids and immunosupressive drugs are the first line of treatment. This is a case report of juvenile Behcet's syndrome in a thirteen year old girl associated with arthritis.

Key words: Juvenile Behcet's syndrome, Arthritis, Oral ulcer, Pathergy test
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INTRODUCTION:

Behcet's syndrome [BS] is a multi-system disorder, described by Turkish dermatologist Hulusi Behcet in 1937 as a triad of symptoms: recurrent oral ulcer, recurrent genital ulcer and uveitis. [1]. It is a systemic disease, but also involves visceral organs such as the gastrointestinal tract, musculoskeletal, cardiovascular and neurological systems. It is called Behçet's disease, Morbus Behcet, Behcet-Adamantiades syndrome or Silk Road disease [2, 3]. The highest prevalence of BS is seen in young adults between second and third decades and more common in males [4].The first manifestation is usually appearance of oral lesion followed by genital, occular, skin and arthritis. In this article we discussed the clinical, hematological and immunological features of

BS, highlighting culture sensitivity, pathergy test as investigation. The ethical clearance for the publication of this case report was obtained from the university ethics committee.

CASE REPORT:

A 13 year old female patient reported to our dental clinics with a chief complaint of recurrent ulcer on labial aspect of lower lip since five days [Figure 1]. It aggravates spontaneously and regress itself within 7 to 14 days. She had history of similar kind of oral ulcer in the same region three times per month since last one year. It was associated with fever, dry cough, pain, weakness, difficulty in eating, speech and recurrent genital ulcer. She was admitted for the same in Paediatric ward and gave history of itching of left eye, early morning stiffness of metacarpal joints and temporomandibular joints [Figure 2]. She was diagnosed as conjuctivitis and chronic juvenile arthritis from the department of Opthalamology and Orthopedics. Complete blood examination and RA factor for C-reactive protein were carried out. Her Hemoglobin percentage [Hb%] was reduced to 7.9 gm/dl, erythrocyte sedimentation rate [ESR] was increased to 60 mm/1 hour and RA factor for CRP was 23.2mg/l. Her peripheral blood smear showed mild macrocytic anaemia. She was a known case of Hypothyroidism. Patient was under following medication when she reported to dentist [tablet thyroxine 50 mg one and half dose daily since last 1 year]. This was patient's first visit to dentist. Her personal history revealed as she did not have any deleterious habits and cleaned her teeth once daily with tooth brush and tooth paste. She was predominantly a non–vegetarian. On general physical examination, she was conscious and cooperative, moderately built and poorly nourished, well oriented in time, place and person. All vital signs were within the normal limits except temperature which was febrile. There were positive signs of pallor, icterus. On extra oral examination, she had competent lips, with convex profile. No gross asymmetry of the face was seen. Her ears and nose showed no abnormality except for her swollen eyes, multiple papules like erythematous lesion on flexural surface of fore arm, feet and finger nails were brittle. Temporomandibular joint examination revealed tenderness on bilateral temporomandibular joints while opening, no deviation,clicking sound were seen, right submandibular lymph node was tender and palpable. No abnormality was detected on examination of muscles of mastication.On intra oral examination of the soft tissues the buccal mucosa, tongue, floor of the mouth, palate showed no abnormalities except for labial mucosa which showed a solitary ulcer. Examination of the gingival status revealed her oral hygiene status to be fair with moderate stains and calculus deposits. On hard tissue examination she had a normal complement of teeth except some carious teeth were noticed

with respect to maxillary anterior teeth, mandibular right and left posterior premolars and molars. On local examination a solitary ulcer was seen on labial aspect of lower lip which was approximately 3-4 mm in diameter, oval shape surrounded by erythematous halo, sloping edge with yellowish-white floor, no sinus or discharge of pus was evident. Inspectory finding regarding the site, size and location of the lesion were confirmed on palpation. The ulcer was tender, soft in consistency. The adjacent mucosa was normal. Based on history and clinical examination patient was provisionally suspected as Behcet's syndrome along with additional diagnosis were given chronic pulpitis in relation to mandibular right first molar, dental caries in relation to maxillary anterior and mandibular right and left premolars and molars, root stumps in relation to maxillary left second deciduous molar and mandibular left first molar, Chronic generalized gingivitis. Patient was referred to department of pedodontics for restoration of decayed teeth, Root canal treatment, extraction of retained tooth and oral prophylaxis. Patient was advised to use antiseptic gel [Hexigel] in lower labial mucosa twice daily for 7 days and nutrient supplement once daily for 30 days [tablet Neurokind plus] from department of Oral medicine and Radiology. Patient was referred to department of dermatology for further investigation. Pathergy test was performed on flexural surface of left forearm, it showed 2 mm diameter of papules after 48 hours of insertion of 20 gauge of sterile needle which was considered as positive results [from department of dermatology] and advised to apply Diprovate- G ointment twice daily for 15 days.

Culture sensitivity for urine showed heavy mixed bacterial growth of E.coli after 48 hours of aerobic incubation which were sensitive to broad spectrum antibiotics except Ampicillin and Ceftazidime. Liver function test showed increased in total protein level to 9.3gm/dl, serum globulin to 5.9gm/dl and albumin/globulin ratio was decreased to 0.6. Serum calcium level was decreased to 8.4 mg/dl. Renal function test showed decreased in blood urea level to 11mg/dl and creatinine level to 0.4 mg/dl. Based on clinical examination, laboratory tests, pathergy test, patient was finally diagnosed from department of dermatology as chronic arthritis in juvenile Behcet's syndrome. Patient was prescribed the following medication after confirmation from different departments including Dermatology, Medicine, Ophthalmology and Endocrinology: Tablet Dapsone - 100mg half dose daily, Folic acid - 5mg, Neurokind plus once daily, Naproxen - 250mg twice daily, Methotrexate - 5mg, Capsule Indomethacin - 25mg, prednisolone eye drops along with Tablet thyroxine - 50mg one and half dose once daily. Patient was discharged from the hospital after 7days and was followed up to three months.

During this duration she had a mild recurrence of joint symptoms, oral ulcer, which responded well to medication. [Tablet Methotrexate and Antiseptic gel].

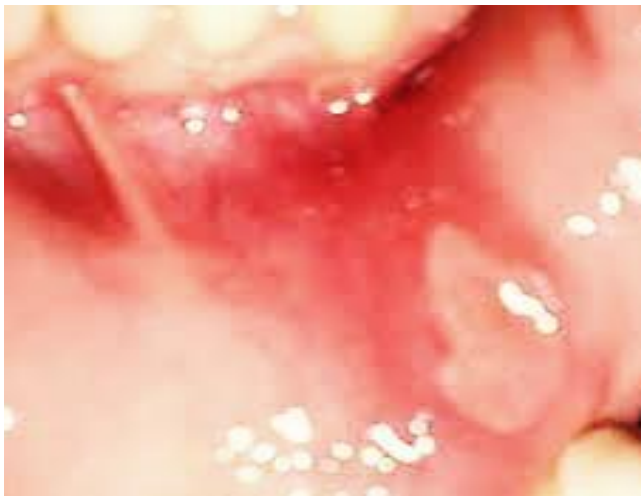

Figure 1: Recurrent apthous ulcer in vermillion border of lower lip

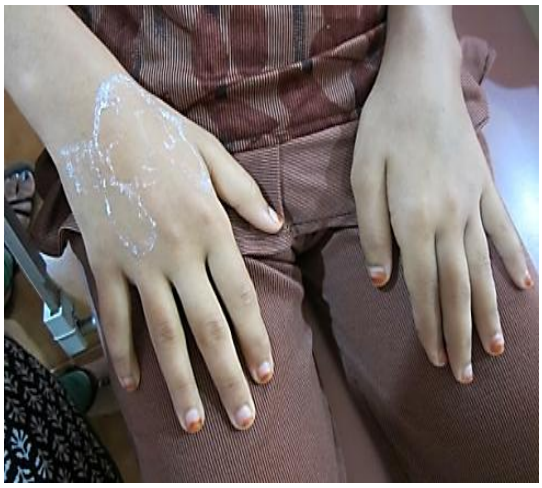

Figure 2: Phalangarthritis of carpal and metacarpal joint

DISCUSSION:

Childhood - onset, Behcet's syndrome is uncommon, accounting for 3-7% of all cases. Our patient had a classical triad of Behcet's syndrome: recurrent apthous ulcer, genital ulcer and conjuctivitis [4, 14]. The highest incidence occurs in the Middle East and Japan, with a lower frequency in northern Europe, United States. The exact etiology has not been established. Behcet's syndrome has an immunogenic basis because of strong association of certain Human leukocyte antigen types [HLA]. HLA B-51 genotype is most frequently linked to BS especially in Asia [5]. However in our case E.coli bacteria was found and it was not related to genetic predisposition.

Behcet's syndrome is a clinical diagnosis based on the International study group criteria: An international group of physicians have established a set of guidelines to aid in the diagnosis of Behçet's patients. The criteria put forth by the study group include [6]:

Recurrent oral ulcerations (apthous or herpetiform) at least three times in one year; In addition, a patient must also meet two of the following: Recurrent genital ulcerations, Eye lesions (uveitis or retinal vasculitis) observed by an Ophthalmologist, Skin lesions (erythema nodosum, pseudo folliculitis, papulopustular lesions, acneiform nodules) adult patients not on corticosteroids, Positive "pathergy test" read

by a physician within 24 - 48 hours of testing. Synovitis / Capsulitis (Rare findings)

Oral lesion is the most important criteria for BS and it is the first manifestation in 25% to 75% cases of the BS. Oral ulcer commonly involves the soft palate, oropharynx and labial mucosa of lips. The lesions vary in size with ragged borders and surrounded by erythematous halo [1, 2]. In our case she had an oral ulcer.

The genital lesions are the second manifestation, seen in 75% of the patients. Lesions appear on the vulva, vagina, glans penis, scrotum, and perianal area. The genital ulcerations cause more symptoms in men than in women [2]. In present case patient had a recurrent genital ulcer.

Ocular involvement is the third manifestation, seen in 70% to 85 % of the cases. The most common findings are posterior uveitis, conjunctivitis, corneal ulceration [2]. In our case patient had conjuctivitis.

Other cutaneous manifestations like erythematous papules, vesicles, pustules and erythema nodosum-like lesions.These skin lesions seen in 40 % to 88 % of cases of BS. One of the most important diagnostic points of skin manifestations is the presence of positive “pathergy test” [2]. Our case had an erythema nodosum like lesions on flexural surface of forearm, feet and also pathergy test positive.

Arthritis is one of the more common minor manifestations of the disease and is usually self-limiting and non-deforming. It is seen in around 3-7% of cases. The knees, wrists, elbows and ankles are affected most frequently. [1, 2].

In present case she was diagnosed as chronic juvenile arthritis in metacarpal joints. Cardiovascular, Central nervous system (CNS) involvement is uncommon. Around 10% to 25 % of the patients show CNS involvement. Gastrointestinal, renal systems involvements are common [2]. Our patient had alterations in urine analysis, Hb%, ESR, C-reactive protein, liver and renal function test.

The differential diagnoses were considered Reiter’s syndrome (RS), Magic syndrome and Erythema multiforme. RS includes urethritis, arthritis, cutaneous lesions, seen in young adult men but BS mostly seen in children to young adults and oral ulcer is the first manifestation.

Laboratory findings for BS and RS almost similar but genetic markers for RS and BS are HLA B-27 and HLA B-51. However these tests were not done in present case.

Magic syndrome includes oral ulcer, genital ulcer with inflamed cartilage, mostly seen in older individuals with decreased strength in all extremities but BS mostly seen in children to young adults and oral ulcer is the first manifestation. Erythema multiforme target like oral lesion but in BS lesion appears as apthous ulcer. [7]

MANAGEMENT and PROGNOSIS:

As Behcet's syndrome is a multi-system disorder, patient was referred to different departments before starting treatment like dermatology, genitourinary medicine, gynecology, internal medicine, ophthalmology, oral medicine and rheumatology. [8]The management of BS depends on the severity and site of involvement. Patient with eye involvement or CNS lesions require more aggressive therapy with drugs. The oral and genital ulcerations respond well to potent topical corticosteroids: [8] Betamethasone (0.1% cream applied twice daily and 0.5mg 2-4times as a mouth wash) [9].

Patients fail this initial conservative approach often require Thalidomide (Tablet Thalomid 100-300mg daily with water at bed time), low-dose Tablet Methotrexate 5mg /day daily [2, 12]. Severe ocular or systemic diseases combined use of immuno suppressive agents: Azathioprine (Tablet Imuran 1-3mg/kg/day combined with prednisolone).

Contraindicated in pregnancy, concurrent malignant disease, allergic reaction, renal and hepatic insufficiency [7, 10]. Other medication includes levamisole, cyclophosphamide and chlorambucil [9, 10]. Recently the agents that are active against the cytokine TNF-α such as infliximab and ethanercept have found potential effectiveness against mucocutaneous and ocular lesion of Behcets syndrome. [8, 13]

CONCLUSION:

The occurrence of BS in children should be recognized. Awareness of its clinical features in children combined with appropriate investigations will help to delineate this group of children from other forms of chronic inflammatory joint diseases. Behcet's syndrome showed no signs of remission for 3 months in our case. The major features recurrent apthous ulcer, genital ulcer, conjuctivitis, arthritis and skin lesions were noted in present case. In this case the doctor/patient relationship had been under strain for 3 months as BS requires only symptomatic treatment.

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