Munchmeyer's Disease – A case report

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Abstract

Fibrodysplasia ossificans progressive (FOP) is a rare autosomal dominant disease. It is also known as Myositis ossificans progressiva, Stone man disease or Munchmeyer's disease. Herein a rare case of Fibrodysplasia ossificans progressive is presented.

Keywords: Fibrodysplasia ossificans progressive, Myositis ossificans, Soft tissue ossifications

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Introduction

Fibrodysplasia ossificans progressive (FOP) is a rare autosomal dominant[1-3] disease. It is also known as Myositis ossificans progressiva, Stone man disease or Munchmeyer's disease[4]. It is characterized by widespread soft tissue ossification and congenital stigmata of the extremities affecting all ethnic backgrounds[5]. It was first described by Patin[6]. The term fibrodysplasia ossificans progressive (FOP) is preferred to myositis ossificans because ectopic osteogenesis occurs in the connective tissue within muscles, fasciae, ligaments, tendons and joint capsules rather than in the muscle fibers themselves[4]. The worldwide reported prevalence is approximately 1/2,000,000. However there is no ethnic, racial, gender or geographic predilection to Fibrodysplasia ossificans progressive[7]. The most common age for FOP occurrence is usually between birth and 10 years with a mean age of three years. Children who have FOP appear normal at birth except for congenital malformations of the great toes. It is pathologically characterized by progressive replacement of muscles, tendons, ligaments, fascia and aponeurosis by bone leading to progressive stiffness of the adjacent joints and particularly the chest wall leading to pneumonia and death. Histological examination of early FOP lesions reveals an intense perivascular lymphocytic infiltrate followed by lymphocyte associated death of skeletal muscle and robust development of fibro proliferative tissue with extensive neovascularity and mast cell infiltration. Tissues from FOP lesions at later stages of maturation exhibit characteristic features of endochondral ossification that support ectopic hematopoiesis[8]. It is particularly disabling in children and is characterized by two cardinal features heterotopic progressive osteogenesis and congenital abnormalities of the great toes[4,9,]. The most characteristic deformity is microdactyly of both halluces due to a single phalanx in valgus position[10,11]. Individuals with Fibrodysplasia ossificans progressive are normal at birth except for having valgus deformity of great toes. Heterotopic ossification is heralded by the rapid appearance of large painful swellings of highly vascular fibro-proliferative tissue involving tendons, ligaments, fascia, and skeletal muscle. These pre-osseous swellings progress along a pathway of endochondral ossification to form mature heterotopic bone[12]. Heterotopic ossification in FOP progresses in specific anatomic and temporal patterns. During the first decade of life, sporadic episodes of painful soft tissue swellings (flare-ups) occur which are commonly mistaken for tumors[13]. These are often precipitated by soft tissue injury, intramuscular injections, viral infection, muscular stretching, falls or fatigue. These flare-ups transform skeletal muscles, tendons, ligaments, fascia, and aponeuroses through an endochondral process into ribbons, sheets and plates of heterotopic bone that span the joints and lock them in place and render movement impossible[14,15]. The early clinical status of FOP is characterized by soft tissue ossification involving neck primarily followed by lower limbs and dorsum[16]. The disease is characterized by frequent edemas as a result of inflammatory processes that cause ossification and subsequently restriction of motility of the affected region. Congenital abnormalities usually associated with short and/or stiff great toes include short thumbs, fifth finger clinodactyly, short broad femoral neck, exostoses of proximal tibiae and abnormal cervical vertebrae with small bodies, large pedicles and large spinous processes. Spine and shoulder stiffness develops by 10 years and restricted hip movements develop by 20 years. The patients affected by FOP are usually confined to bed by the age of 30 years. FOP S primarily involves neck (50%), dorsal paraspinal region (30%),

head (10%) or limbs (10%). 70% of FOP patients develop temperomandibular joint ankylosis which used to lead to death by starvation[17]. Other common sites of ossification include joint capsules, ligaments and plantar fascia. However connective tissue of facial and extraocular muscles, intestines, tongue, larynx and skin are not affected. Involvement of dorsal, axial, cranial and proximal anatomic locations precede involvement of ventral, appendicular, caudal and distal areas of the body[18]. Ectopic ossification is hallmark of FOP which occurs during lifespan of a patient, most commonly at mean age of 3 to 5 years[14,17]. Ectopic ossification follows a well-defined pattern, the axial body being compromised first and most. Shoulder and hip regions are affected more than distal segments of the limbs. Deafness and baldness have been reported in up to one fourth of the cases while mental retardation is rare[17]. The other characteristic clinical feature of FOP is acute or chronic limb swelling which is defined as an enlargement of the limb circumference at one or more locations with multifactorial increased tissue turgor[19]. Conductive deafness occurs in 50% of patients having FOP[20,21]. Although the rate of disease progression is variable, most patients are confined to a wheel- chair by their early twenties. Patients with FOP usually succumb later in adulthood at mean age of 40 years to cardiopulmonary complications secondary to thoracic insufficiency syndrome and severe restrictive pulmonary disease due to ossification and ankylosis of the joints of thoracic cage[22,23]. Recently, FOP has been considered a connective tissue disorder due to over expression of a bone morphogenetic protein, BMP4[24,25]. However most studies have concluded that dysregulation in bone morphogenetic protein (BMP) signaling is responsible in the pathogenesis of FOP. A single common heterozygous mutation (617G>A; R206H) has been identified in the cytoplasmic domain of activin receptor IA/activin-like kinase 2 (ACVR1/ALK2), a BMP type I receptor[26]. Exacerbation of FOP may occur spontaneously or can be precipitated by trauma, intramuscular injections including vaccines[19], local anesthesia, especially truncular block near the temporomandibular joint[17], muscle biopsy and careless venepunctur[4]. Trauma is the most important exacerbating factor[17].The differential diagnosis of FOP include Albright hereditary osteodystrophy, pseudomalignant heterotopic ossification, progressive osseous heteroplasia and osteosarcoma.

Case Report

A 10 year old female patient **(Fig. 1)** reported to the outpatient Department of Oral medicine and Radiology with a chief complaint of progressive inability to open mouth since past 1 year. The patient also complained of multiple swellings on the back and right scapular area **(Fig. 2 & Fig. 3).** Multiple bony hard swellings are also noted in posterior occipital area**(Fig. 4).** On whole body examination, she had laterally deviated short first toes of both feet **(Fig. 5).** Firm round subcutaneous swellings were present on vertebral region, right scapula and right occipital region of the skull. There was marked restriction of movements of the right shoulder and right temporomandibular joint. The patient had no difficulty in neck rotation, sitting and walking. Bilateral temporomandibular joint has decreased mobility on palpation. After a through history it was revealed that swellings had been appearing and subsiding since the patient was 6 years old. On palpation all the swellings appeared firm, non-tender with normal overlying skin. Multiple aspirations of the swelling had been done previously with negative results. Hemogram, erythrocyte sedimentation rate, serum calcium, alkaline phosphatase, creatine phosphokinase, alanine and aspartate transaminases, routine urinalysis, and creatinine clearance were within normal limits. An orthopantogram and whole body radiographic examination was advised. Panoramic radiograph shows decreased right temporomandibular joint space with enlarged maxillary tuberosity. Multiple retained deciduous teeth are also noted in maxilla and mandible(**Fig. 6**). Chest posteroanterior (PA) view including abdomen and arms shows extensive focal and cord-like ossification of muscles and soft tissue of back, chest, abdomen and visualised right arm giving pattern of branching tree(**Fig. 7**). AP radiograph of feet showed microdactyly of the great toes and bilateral hallux valgus(**Fig. 8**). Lateral view of thorax and abdomen shows cord-like ossifications of muscles of back(**Fig. 9**). Axial CT image of thorax shows ossification of back and chest muscles(Fig. **10a, 10b, 10c**). The 3D CT shows posterior view of trunk and neck exhibiting excellent demonstration of soft tissue and muscle ossifications mimicking tree branching pattern(**Fig. 11**). On the basis of clinical and radiographic features, the resent case is diagnosed as Fibrodysplasia ossificans progressive. Parents were advised to make child avoid sporty games, I.M injections, arterial puncture and physiotherapy and avoid any surgery to prevent such episodes.

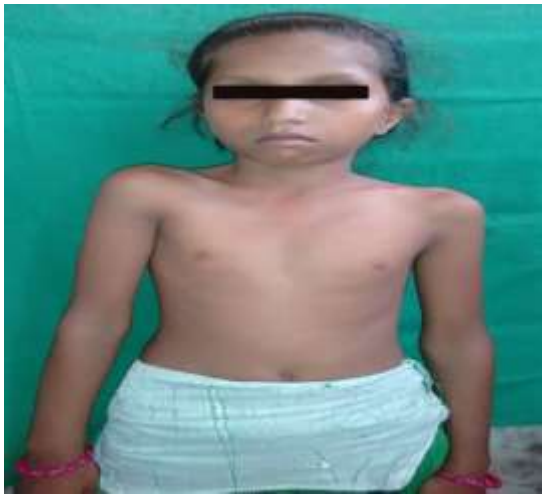

Fig. 1: Patient photograph

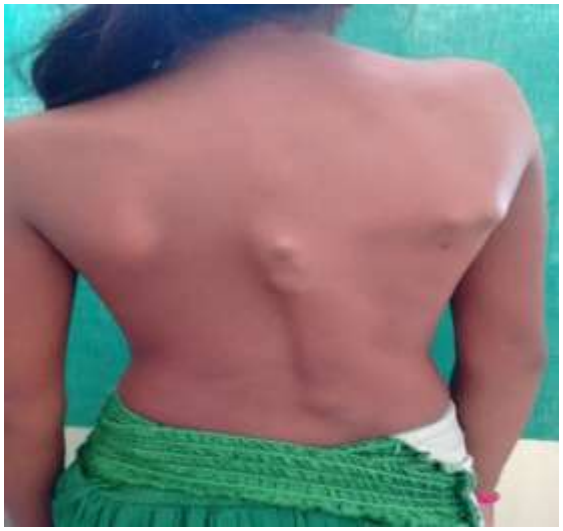

Fig. 2

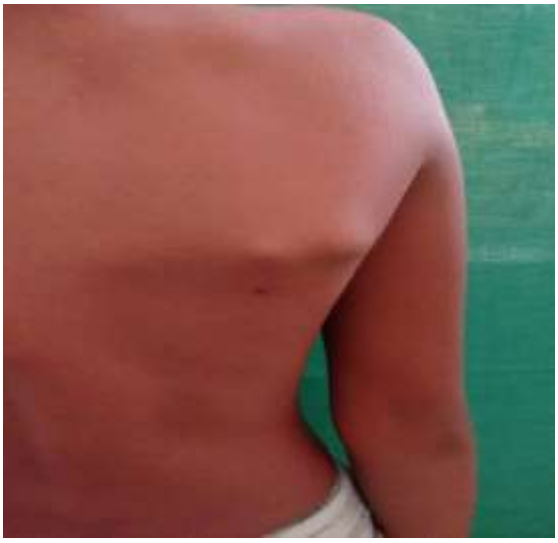

Fig. 3

Fig. 2 & 3: Photograph of back showing multiple swellings on the back and right scapular area

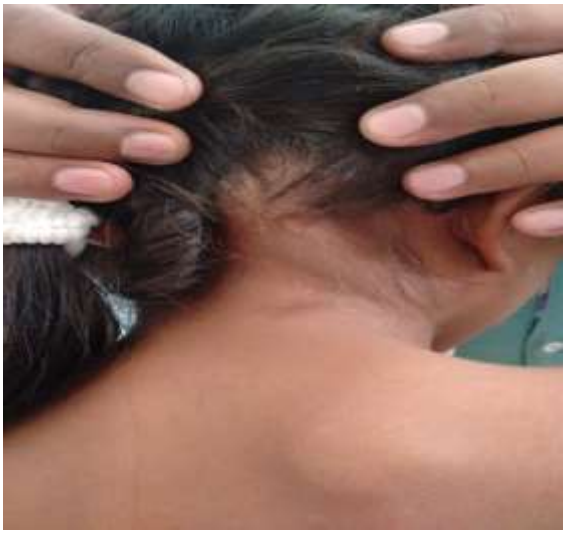

Fig. 4: Photograph of Head showing multiple bony hard swellings in posterior occipital area

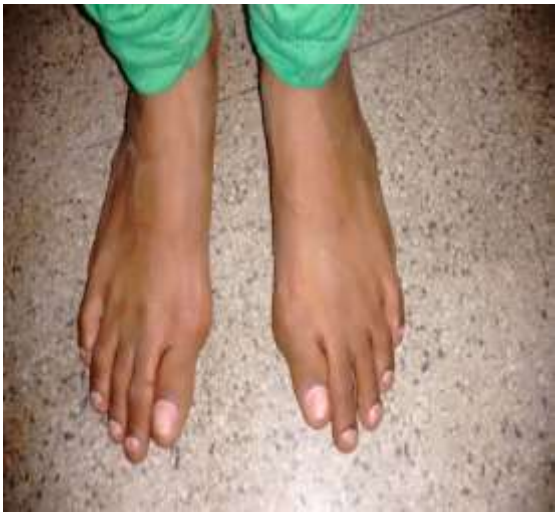

Fig. 5: Photograph of feet showing laterally deviated short first toes of both feet

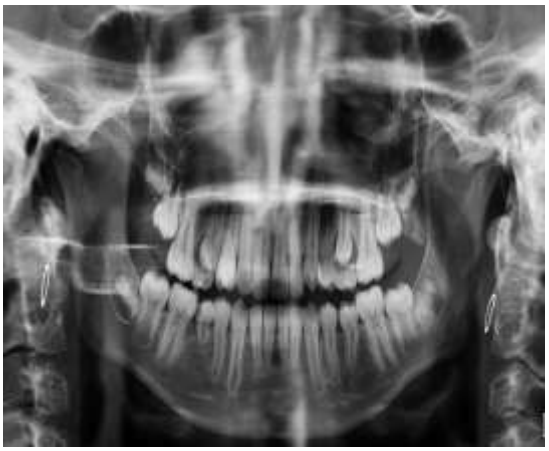

Fig. 6: Panoramic radiograph showing decreased right temporomandibular joint space with enlarged maxillary tuberosity. Multiple retained deciduous teeth are also noted in maxilla and mandible

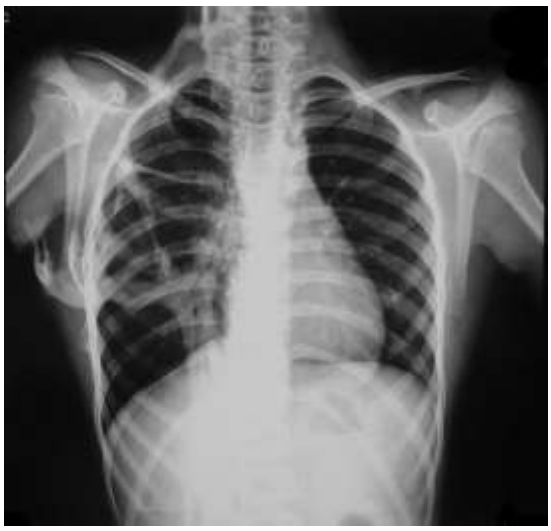

Fig. 7: Chest posteroanterior (PA) view including abdomen and arms showing extensive focal and cord-like ossification of muscles and soft tissue of back, chest, abdomen and visualized right arm giving pattern of branching tree

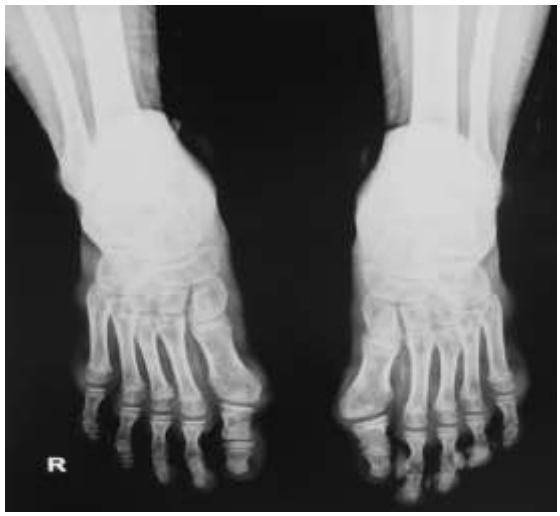

Fig. 8: AP radiograph of feet showing microdactyly of the great toes and bilateral hallux valgus

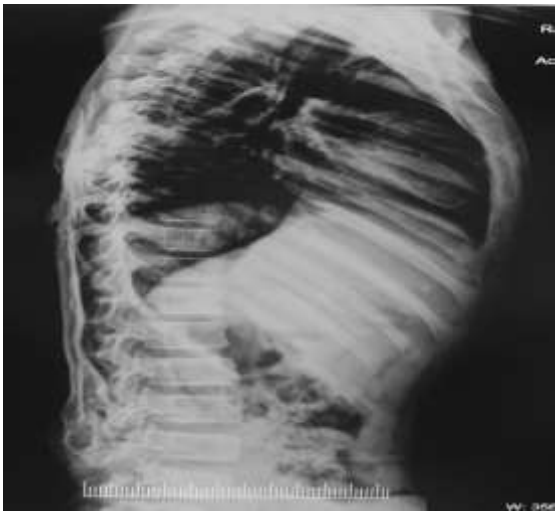

Fig. 9: Lateral view of thorax and abdomen showing cord-like ossifications of muscles of back

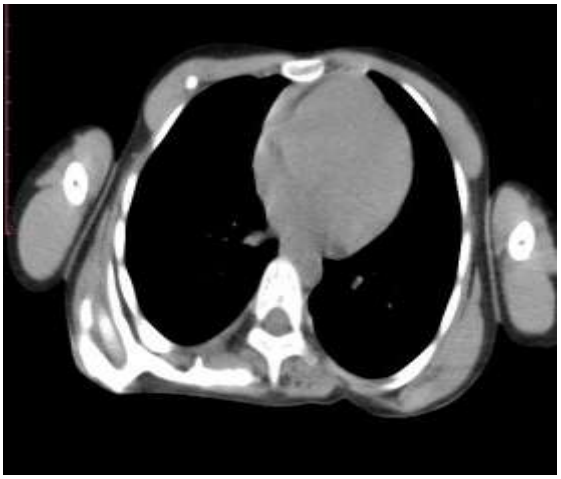

Fig. 10 a

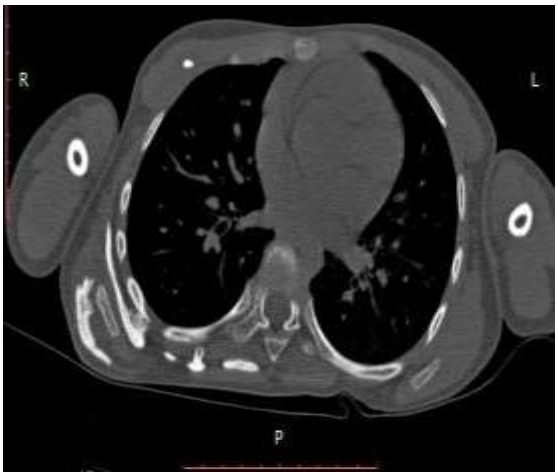

Fig. 10 b

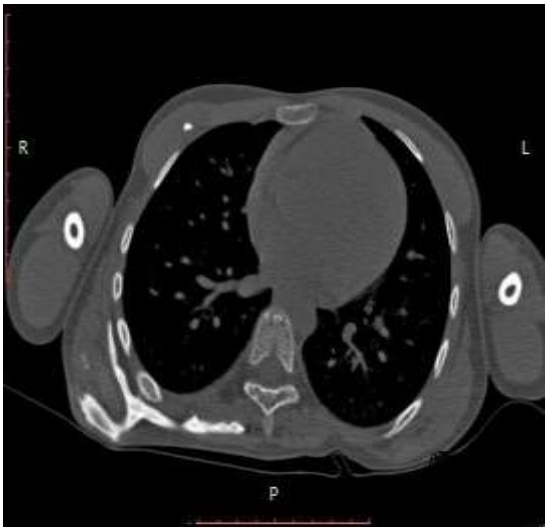

Fig. 10 c

Fig. 10a, 10b, 10c: Axial CT images of thorax showing ossification of back and chest muscles

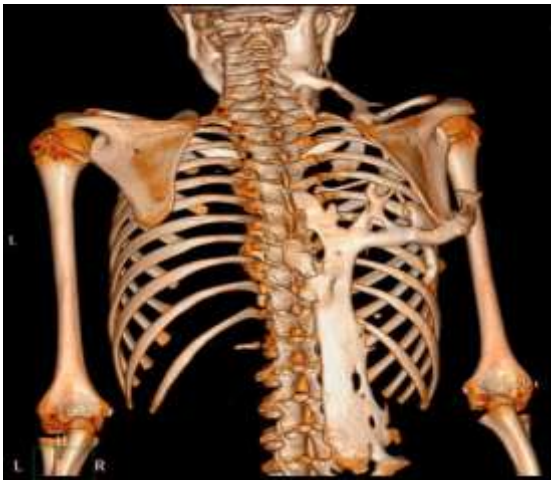

Fig. 11: The 3D CT shows posterior view of trunk and neck exhibiting excellent demonstration of soft tissue and muscle ossifications mimicking tree branching pattern

Discussion

Based upon history and clinic-radiological findings, FOP should be diagnosed as early as possible and noninvasively. The hallmark of diagnosis of FOP is bilateral great toe anomaly present from birth. The bilateral great toe is reported in 79% to 100% of patients having FOP[17,27,28,29]. Early and correct diagnosis of MOP is fundamental for indication of proper management of the disease. The classical clinical presentation of FOP is highly suggestive and it can allow for diagnosis without unnecessary biopsy and surgical procedures and intra-muscle and intravenous injections which can deteriorate prognosis for the disease. Radiologically Myossitis Ossificans Progressiva can be identified approximately two to four weeks after the onset of the process. The calcifications in FO starts on the extremities and progresses towards the center. This characteristic differentiates MOP from osteosarcoma. In MOP, Computed tomography can be used to delineate the central radiolucency encompassed by peripheral density[30]. Routine laboratory tests including serum calcium and serum phosphorus are usually normal or non-contributory in FOP. Roentgenograms may aid in documenting minor osseous dysmorphism. Bone scintigraphy with 99mTc-MDP demonstrates early heterotopic ossification and aid in the assessment of the extent and progression of the FOP. Intramuscular vaccines such as diphtheria-pertussis tetanus, measles, hepatitis B and other injectables can be applied subcutaneously[31]. Dental treatment should be carried out with utmost care peculiarly avoiding anesthesia in the mandible in order to prevent temporomandibular joint ankylosis[17]. Prophylaxis of dental cavities is essential to avoid need for more aggressive procedures. The diaphragm, tongue, and extra-ocular muscles are spared from HO. Cardiac muscle and smooth muscle is also spared in FOP. Neck stiffness is an early finding and can precede the appearance of HO at that site. Cervical spine abnormalities include large posterior elements, tall narrow vertebral bodies, and fusion of the facet joints between C2 and C7[32]. The cervical spine often becomes ankylosed early in life. Other skeletal features associated with FOP are short malformed thumbs, clinodactyly, short broad femoral necks, and proximal medial tibial osteochondromas[33,34,35]. In addition to progressive immobility, other life-threatening complications include severe weight loss following ankylosis of the jaw, as well as pneumonia and right-sided heart failure resulting from thoracic insufficiency syndrome (TIS)[36]. Since curative therapy is not available, management is based on the principle of primum non nocere, particularly at preventing abnormal ossification. Biopsy of calcified nodules is to be avoided if the diagnosis of FOP is clear on clinical and radiological grounds which may result in recurrent ossification of the site, sometimes worse than the original lesion[37]. So far no effective treatment for FOP is known. All management is conservative that is, of avoiding conditions potentially provocative of abnormal ossification. Several types of treatment have been tried such as administration of calcium chelators such as sodium etidronate. In acute flare ups, oral corticosteroids and intravenous etidronate can be used simultaneously. Early diagnosis and high index of suspicion will not only prevent the itrogenic harm but may also slow the disease progress and avoid rapid and early deterioration in patient's quality of life[38]. Misdiagnosis may lead to inadvertent managements like manipulations, biopsies and surgery. Kitterman et al reported incidence of misdiagnosis to be >90%, with 68% receiving inappropriate treatment which lead to permanent disability in about 50% of cases[39]. Corticosteroids are indicated as first-line treatment at

beginning of flare-ups. A brief 4 day course of high-dose corticosteroids, started within the first 24 hours of a flare-up, may help reduce the intense inflammation and tissue edema seen in the early stages of the disease. The use of corticosteroids should be restricted to treatment of flare-ups that affect major joints, the jaw, or the submandibular area. A typical dose of prednisone is 2 mg/kg/d, administered as a single daily dose. When prednisone is discontinued, a non-steroidal anti-inflammatory drug (NSAID) or cox-2 inhibitor (in conjunction with a leukotriene inhibitor) may be used symptomatically for the duration of the flare-up.Palhares[40] observed that high doses of ascorbic acid controlled progression of the disease. Decrease in ossifications during the inflammatory process has been attributed to the action of ascorbic acid on modulating synthesis of procolagen type III. In cases of severe MOP with restriction of movements and gastric intolerance, the use of intravenous diphosphonate can be indicated and present good results, as reported by Alpigiani et al[41]. The median lifespan is approximately 40 years of age. Most patients are wheelchair-bound by the end of the second decade of life and commonly die of complications of thoracic insufficiency syndrome[42].

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