Fibrodysplasia ossificans progressiva: case report

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Abstract: Fibrodysplasia ossificans progressiva (FOP) is a rare genetic disease characterized by widespread soft tissue ossification and congenital stigmata of the extremities. We report the case of a 33-year-old woman with clinical and radiological features of FOP. She was born with bilateral hallux valgus and at the age of 10 presented swelling and ossification of the left scapula. During the course of the disease numerous crises were observed. In this patient authors noticed FOP exacerbation after a surgical operation.

Key words: calcinosis, etidronate sodium, fibrodysplasia ossificans progressiva

INTRODUCTION

Fibrodysplasia (myositis) ossificans progressiva (FOP) in Polish literature [1,2] is referred to as progressive muscle ossification or myositis ossificans progressiva, is a very rare genetic connective tissue disease eventually leading to significant disability [3]. The disease process involves ectopic production of osseous masses in intramuscular and perimuscular connective tissue, in tendons and joint capsules. The osseous masses form bridges that abnormally connect sections of the skeleton, causing disfiguration and inhibiting normal motor functions [4,5].

There are some congenital defects of hands and feet that can suggest this disease. These defects include: short hallux and hallux valgus, short thumbs, synostosis and hypoplasia of digital phalanges [6]. The first symptoms of disease usually develop in the first decade of life, and appear as painful swelling of soft tissues with subsequent formation of bony tissue. These lesions usually affect the areas of spine, shoulder and pelvic girdle. The disease follows a course of bouts separated by variable intervals. Consecutive bouts can be triggered by intramuscular injections and surgical operations, however they usually appear independently of extrinsic factors, with unpredictable frequency.

CASE REPORT

A 33-year-old female patient was admitted to the Clinic in May 2001 in order to establish further therapeutic management. From 1 to 3 years of age she was under care of the outpatient Orthopaedic Clinic of the Institute of Orthopaedics of the University of Medical Sciences in Poznań due to congenital skeletal malformations. She was then diagnosed with significant hallux valgus deformity (90%) (fig. 1) and short thumbs. After the initial medical treatment surgery followed at the age of 3 years, namely bilateral correction of hallux valgus. During the 3-year follow up in the outpatient clinic she was also diagnosed with left-sided torticollis. At the age of 8 years a diagnosis of bilateral hypoacusis was established.

Clinical signs of the disease such as swelling of soft tissues with the subsequent ossification around the left shoulder blade was first documented in 1978 (at the age of 10) during hospitalisation in the Clinic of Rheumatology, of the Paediatric Rheumatological Institute in Warsaw. Laboratory tests failed to demonstrate elevated inflammatory markers and radiological studies showed a round calcification in the true pelvis. The clinical picture and ancillary studies made it possible to exclude a systemic connective tissue disease. The patient was discharged and followed up for signs of myositis ossificans progressiva. During another hospitalisation of the patient in the Institute of Paediatrics of the University of Medical Sciences in Poznań in 1979, the diagnosis of FOP was confirmed by radiograms of the cervical and thoracic spine. Changes were described as band-like shadows of soft tissues around the spine and chest. Results of laboratory studies were normal except for leucocyturia and E. coli bacteria in the urine. Prednisone and sodium edetate were used in the therapy. In 1980 the patient was hospitalised in the Medical Department of the Children’s Health Institute, where in addition to FOP she was diagnosed with epilepsy, urinary incontinence and acne simplex. Radiological evaluations demonstrated calcifications around shoulder joints and in the left axillary fossa. Functional studies of the respiratory tract revealed mild restrictive/obstructive ventilation disorders, and abnormal gas exchange due to ventilation problems. Lung tissue compliance was normal. The treatment involved etidronate at a dose of 6 mg/kg body weight/day fol-
Several months before admission to the Clinic, the patient complained about epigastric pain; magnetic resonance imaging (MRI) demonstrated an uterine tumour (probably myoma).

A family history did not reveal previous cases of FOP, and the patient’s brother was diagnosed with empty sella syndrome.

On the day of admission, physical examination demonstrated postsurgical scars on the left thigh, left hip joint and over metatarsophalangeal joints. Skin of the face and forearms was excessively smooth and tense, the mandible was posteriorly placed, skin of the face and anterior surface of the chest displayed acne lesions. The patient ambulated with a walker, contractures were observed in elbow, hip and knee joints. The left hip joint was immobile, the spine was immobilised in all sections, slight scoliosis was seen in the thoracolumbar section, mobility in shoulder and wrist joints was restricted and thumbs and big toes were shortened. Neither soft tissues oedema nor other signs of local inflammation were observed. Lung auscultation revealed normal symmetrical vesicular sound and single bilateral wheezes. The abdomen was soft, with tender hypogastric area.

Results of laboratory tests were normal except mildly elevated serum alkaline phosphatase (144 IU/l with normal values, 57-111).

In radiological studies numerous ectopic ossifications could be seen. Chest X-ray revealed massive ossification along the inferior margin of the right scapula, the left side had similar however less intense changes with additional ossification of cartilaginous parts of 9–12 pairs of ribs and exostoses on the lower costal margins (fig. 2). Pelvic X-ray demonstrated a massive ossification connecting the ala of ilium with the femur on the left and one ossification around the pubis and ischium on the right (fig. 3). Radiograms of knee joints displayed deformations of tibial and femoral epiphyses, on the right narrowed articular space in the medial compartment, spine X-ray demonstrated cervical vertebral fusions (fig. 4) and multiple paraspinous ossifications in the thoracic and lumbar sections.

Gynaecological examination and consultation, and abdominal MRI confirmed an uterine myoma, 12 cm in diameter, with foci of single calcifications. No absolute indications to surgery were identified, therefore further observation was recommended with consideration of hormonal therapy if the tumour enlarges.

During hospitalisation in the clinic, no new ossification foci were detected. Kinesitherapy was used (breathing exercises, active strengthening of back muscles, maintenance of the range of joint motion) and previous pharmacotherapy was continued. In case of necessary surgery, the patient was instructed to take etidronate at a daily dose of 20 mg/kg body weight for one month before and 3 months after the surgery.
The first case of FOP was reported by Gay Patin (1692), who presented a case of young patient that “became hard as wood”[7]. Then in 1867, Munchmeyer coined a term *myositis ossificans progressiva* for a set of clinical signs typical for this disease. However, it turned out inappropriate, because the primary changes affect the connective tissue, as seen in histological examinations, with secondary degeneration and atrophy of muscle fibres. Aetiology of this disease is unknown. It has been suggested that FOP can be caused by overproduction of bone morphogenetic protein 4 (BMP4) [8].

A course of bouts was followed by FOP, and new ossification foci appeared regardless of extrinsic factors. There is, however, evidence that microtraumas and surgical procedures attribute to the initiation of the disease.

In the presented patient, the disease appeared in typical bouts, and appearance of new ossification foci was usually independent of extrinsic factors. Effect of the surgery as a triggering factor was, however, confirmed. After surgery involving removal of osseous masses around the left hip joint and left thigh, massive ossification at this site followed that resulted in stiffened hip joint with consequent difficulties in ambulation. The patient displayed a full-blown course of FOP with typical congenital defects and disease bouts that manifest as a painful swelling of soft tissues, with subsequent ossification from 10 to 18 years of age. The disease led to a significant dysfunction of the locomotor system; further complications included upper respiratory tract infections and hearing loss, which is a typical symptom of FOP [9]. Epilepsy diagnosed in this patient does not typically accompany FOP; coexistence of these two disease has not been reported so far.

Treatment of FOP is ineffective; effectiveness of ACTH, glyocorticosteroids and calcium-binding agents has not been proven so far. Effects of sodium etidronate are controversial, however it can be helpful in the prevention of ectopic bone formation after surgical procedures [10,11]. Kinesitherapy and physiotherapy are also used in these patients; treatment of recurrent pneumonias is also necessary. There are studies under way aimed at evaluating the usefulness of thalidomide, interferon alpha, angiostatin and endostatin in the therapy of FOP.
In the case described here, pharmacotherapy with prednisone, etidronate and nonsteroidal anti-inflammatory drugs hardly had any effect on the disease. In contrast, use of motor rehabilitation was beneficial and advisable, because despite massive ossifications and significantly restricted joint mobility, the patient was able to move aided by orthopaedic devices and was partially able to perform some basic self-care activities.

REFERENCES