Case Report

Sylwia Wójcik*, Rafał Koszowski, Bogna Drozdowska, Joanna Śmieszek-Wilczewska, Agnieszka Raczkowska-Siostrzonek

Maxillary fibrous dysplasia associated with McCune-Albright syndrome. A case study.

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Abstract: McCune Albright syndrome (MCA) is a rare complication of genetic origin. The authors present a case study of a patient with MCA diagnosed with multifocal fibrous dysplasia in his limb and craniofacial bones. The symptoms of the disease in the patient’s facial and oral tissue and the treatment administered have been described.

Keywords: McCune-Albright syndrome; Fibrous dysplasia of bone; Multifocal dysplasia; benign bone tumour

1 Introduction

McCune Albright syndrome (MCA) is a rare complication of genetic origin. It was first described by McCune (1936) and Albright (1937) as a triad of the following symptoms: fibrous dysplasia of bone, dysfunction of the endocrine glands combined with precocious puberty as well as “café au lait” coloured macules on the skin [1,2]. The cause of the syndrome is a stimulatory mutation of the GNAS1 gene responsible for the coding of Gs-α subunit of the G protein. The condition leads to increased production of c-AMP, which in turn triggers the proliferation and differentiation of pre-osteoblasts. The mutation affects the somatic cells, hence the disorder is hereditary. It occurs in the early embryonic period. A single mutated cell can be a starting point for daughter cells, which then migrate to cells originating from all three germ layers. This explains the diversity of the complications that occur with MCA [3,4]. The extent and diversity of changes in tissue depends on the developmental stage of the mutation. A characteristic feature of MCA syndrome is its broad spectrum of clinical signs. New signs can develop in the same patient at different ages, while existing ones may progress and worsen [5].

The vast majority of people affected by MCA syndrome are women (90%). Precocious puberty in girls begins before the age of 4 and in boys before the age of 9. The condition is caused by premature activity of the gonads without any preceding increase in the secretion of gonadotropins through the pituitary gland. It is defined as pseudo precocious maturity [6-8].

Fibrous dysplasia of bone as a complication associated with MCA syndrome is a progressive, incurable bone disease. It is characterised by osteolysis and osteogenesis irregularities as well by the replacement of proper bone with the wrong type of fibro-osseous tissue. It is an anomaly of mesenchymal bone-forming tissue, whose maturity was halted at the woven bone stage. Fibrous dysplasia of bone can affect any bone (including long bones, ribs, the pelvis and craniofacial bones) as well as result in significant deformity and even in fracturing. The foci of fibrous dysplasia are formed from a subpopulation of osteoprogenitor cells that resemble fibroblasts. GNAS1 gene mutations are also found in them. Like osteosarcoma cells they also have a high expression of the proto-oncogene c-fos. These conditions incline some authors to suspect that fibrous dysplasia of bone is a neoplastic disease [5,6,9]. In around 4% of cases it can lead to malignant changes [6-8].

Skin lesions in the form of discolorations – café au lait macules of varying size – are usually located on the forehead, neck, upper part of the back, the shoulders, the upper arms, the lumbo-sacral region, and on the but-
toks. They appear during childhood and become increasingly pronounced with age and after exposure to the sun. Hyperpigmentation results from an increase in melanocytes in the dermis, while the number and size of melanocytes does not change [7,8,10].

Other complications associated with MCA syndrome include the following: hyperthyroidism, hyperadrenalism and pituitary adenoma producing growth hormones and prolactin [10, 11].

The objective of the present study is to describe signs of the disease observed in the facial and oral tissue of a patient with McCune-Albright syndrome.

2 Case report

Patient M. K., a white male aged 19, came to the Dental Surgery Clinic at the Academic Dentistry Centre in Bytom on 07.06.2010 for a consultation. In the interview he reported having an elevation in the right cheek area for the past two months, which caused no complications.

Since the age of 13 the patient had been treated for polyostotic bone dysplasia. In 2005, when he was 14 years old, the patient was hospitalised at the Paediatric Nephrology and Endocrinology Clinic of Children’s Clinical Hospital No. 1 in Zabrze with the aim of carrying out diagnostic tests for suspected McCune-Albright syndrome. Tests showed that the patient had suffered recurrent fracturing of both thigh bones. A physical examination at that time showed café au lait macules of irregular shape located on the nape of the neck, the neck, the right arm, on the right side of the back, symmetrically in the sacral region as well as on the outer left thigh. There were post-surgical scars on both thighs. Varus deformity of the thighs was also observed. The development of secondary sexual characters were assessed at P5 G5 Ax3 on the Tanner scale. The results of basic laboratory tests were correct. A calcium-phosphorus homeostasis test showed a raised level of total calcium and phosphates as well as a significant increase in total alkaline phosphatase and its bone fraction. The patient’s daily urine excretion of calcium and phosphates was reduced. The concentration of parathormone was correct. Hormonal tests revealed the presence of euthyresosis, the correct concentration of prolactin, cortisol and ACTH (adrenocorticotropic hormone) with their daily excretion profile maintained as well as the correct concentration of gonadotropins and testosterone. The patient’s bone age was in accordance with his chronological age. X-rays of the wrist showed that lytic remodeling predominated in the area around the finger and metacarpal bones together with distension of the latter and slight deformity in the form of a matt glass appearance. An X-ray of the patient’s skull focusing on the sella turcica showed lesions corresponding to bone dysplasia. Based on performed tests the McCune-Albright syndrome was diagnosed. Owing to recurrent fractures of the thigh bones and pain in the side of the patient’s skeleton, the patient was referred to the Bone Tissue Metabolic Diseases Clinic at the Warsaw University of Medicine so as to be admitted for treatment with bisphosphonates. The patient was admitted for treatment at the Orthopaedics and Traumatology of Locomotor System Clinic at the Medical University of Warsaw, where between 19.10.2005 and 09.10.2009 he was hospitalised nine times. During his stay he was administered Pamidronian.

In December 2005 the patient suffered a pathological fracture of his left thigh bone together with displacement of the bone. The patient was admitted to the Chorzow Paediatrics and Oncology Centre, where as part of his treatment he underwent axial correction of the lower limb and its immobilisation. In June 2006 the patient underwent surgery, which involved filling the cystic focus in the proximal end of the right femur with bone grafts as well as the fixation of the pathological fracture.

Since 01.04.2010 the patient has been receiving treatment at the Independent Public Regional Hospital of Trauma Surgery in Piekar Śląskie, where he was initially admitted for a pathological fracture of the shaft of the left humerus and the shaft of the right femur. The patient suffered these fractures when he fell on the way to school. The patient underwent surgery, which consisted in the repositioning and plate stabilisation of the fractured bone fragments.

When he registered at the Dental Surgery Clinic the patient had an extraoral examination, which confirmed the presence of facial asymmetry caused by the elevation of soft tissue and bone in the infra-orbital, zygomatic and nasal regions on the right-hand side (Fig. 1). The skin above the elevation was of the correct colour. The elevation had a hard consistency, was painless and attached to the bone. The lymph nodes were not palpable and the exits of the peripheral branches of the trigeminal nerve produced no pain when tested with palpation. The nasal passages were unobstructed. Irregularly shaped café au lait macules were visible on the skin on the nape and the neck (Fig. 2).

The patient experienced no problems with mouth opening. The oral mucosa was smooth, pink and shiny. Elevation was confirmed and was deemed to be caused by distension of the bone in the hard palate area as well as in the alveolar process of the maxilla on the right hand.
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The OPG showed an osteolytic defect in the angle of the mandible area that was oval shaped and resembled a cyst-like lesion neighbouring tooth 37. An osteolytic defect was also observed in the region of the root of tooth 12 in the maxillary alveolar ridge. It was a cyst-like defect which had diverted the root of tooth 13 in a distal direction. Teeth 13 and 37 had vital pulp that reacted appropriately to thermal stimuli and a faradic current.

Due to disparities between the patient’s clinical state and radiological image the patient was referred for a CT scan. CT scans showed distension of the maxilla and the zygomatic bone on the right-hand side with its proper structure completely obliterated owing to irregular osteoporotic and osteolytic foci. Similar lesions were observed in the maxilla and zygomatic bone on the left hand side, although without any increase in their dimensions and with the correct shape of the outer contour of these bones being maintained. On the other hand, on the left side of the angle of mandible an osteolytic focus was present in the form of a cyst-like lesion. It was located in the cancellous bone without any discontinuity of the inner and outer compact lamella (Fig. 4a, 4b).

To verify the character of the lesion in the patient’s alveolar process it was decided to collect material from the patient for histopathological examination. Infiltration and block anaesthesia of a 3% solution of lidocaine hydrochloride with norepinephrine hydrogen tartrate (Xylonor) to the infraorbital foramen was used, then a muco-periosteal flap was elevated from an angular incision on the vestibular surface of the maxillary alveolar process in the area of teeth 12-15. Protrusion of the maxillary alveolar process was observed in the area of teeth 12–14. The tissue at the site of the elevation differed macroscopically from the surrounding bone. It had a paler colour, was uneven and had a rough surface. It turned out to be flaky when touched with surgical instruments and could easily be separated from the surrounding area(Fig. 5a., 5b.). The tissue, which had a fatty consistency, was cut away, after which a fragment of bone with a soft consistency was collected with a trephine. Healing occurred with no complications.

Microscope findings led to a diagnosis of fibrous dysplasia. The lesion took the form of fibrous connective tissue that had replaced the regular bone tissue. Typically, we observed small, irregular-shaped bone trabeculae and a stroma between them built by fibrous connective tissue. The trabeculae are often likened to Chinese script (Fig. 6.).
Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors’ institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from individual included in this study.

3 Discussion

Initially, McCune-Albright syndrome was regarded as a rather mild disease with a good prognosis. However, later observations have changed this view [1, 2]. The first symptoms of the disease are usually pigmented skin lesions and precocious puberty. They usually appear in the first months or years of life. In girls the mammary glands increase in size and a high level of estrogens are excreted by ovarian cysts. Bleeding can also occur from the genital tract. Precocious puberty occurs more rarely in boys. Most commonly it takes the form of enlarged testicles. In the case described in the present study, skin lesions were...
located on the skin of the nape of the neck, the neck, the right arm, the right side of the back, in the sacral region, and on the left thigh. However, the patient had not experienced precocious puberty [7,8].

The next most common symptom of MCA syndrome is fibrous dysplasia of bone. It occurs in an estimated 40% - 98% of all MCA cases. The probability of bone lesions occurring in children in the first 8 years of life is around 50%. Fibrous dysplasia can affect one bone in its monoosteotic form, or it can be present in many bones in polyosteotic form. The polyosteotic variant is the most common form in MCA syndrome. It is severe in nature and is characterised by a large number of fractures. Lesions are most commonly located in the thigh bone, followed by the facial skeleton and the spine, which is often the cause of scoliosis [10,12]. The first sign of the disease in the present case was a pathological fracture of the right femur that the patient suffered at the age of 13 when returning from school. The fractures recurred in later periods and affected both femurs as well as the left humerus bone. Fixation of the fractures was achieved through stable plate osteosynthesis. The fixation of humerus fractures was achieved through intramedullary nailing. In each case post-osteosynthesis healing was complicated and further operations were required. Dysplastic lesions also appeared in the sella turcica and the metacarpal bones.

In the facial skeleton dysplastic lesions were mainly monoosteotic in character. However, there is a tendency for the disease to spread contiguously to neighbouring bones. Most commonly, the focus of dysplasia is located in the alveolar process of the maxilla, which causes progressive and usually painless distension of the bone, which can then pass to the zygomatic bone, thereby causing facial deformity. In the present case the focus of dysplasia in the patient’s facial skeleton appeared as the final one. Two months earlier the patient began to suffer from facial asymmetry in the form of elevated tissue in the right cheek area. Initially, the patient went to a dentist with the aim of ruling out any odontogenic cause of his symptoms. Following clinical and radiological tests in a number of dental offices and after ruling out an odontogenic cause the patient was referred to the oral surgery clinic.

There is still no consensus on the procedure for treating fibrous dysplasia. Some authors adopt a wait-and-see attitude based on observations of patients. This approach is especially justifiable after puberty, when the progress of the disease is observed more rarely. Others propose a surgical procedure, but usually for cases of monofocal dysplasia, or when there is a danger of a loss of eyesight or hearing [12,13]. Another method involves the use of bisphosphonates, which can be administered orally or parenterally. Initially, these were only recommended for adults, but in the last few years children have also undergone such treatment. Treatment with disodium pamidronate reduces pain and improves motor skills. Some authors have observed a decline in the frequency of fractures and an increase in bone density. The administering of disodium pamidronate does not, however, lead to a subsidence in bone lesions, although there are individual cases of improvements observed in radiological imaging [14-16]. The patient described in the present study was treated with disodium pamidronate when aged between 14 and 18. The medication was administered parenterally in a dose of 90 mg every 3 months. On one occasion the dose was not administered due to increased bone metabolism. However, the treatment ended as it proved insufficiently effective.

Fibrous dysplasia of the bone can on rare occasions lead to neoplastic transformation toward osteosarcoma. This occurs in around 4% of MCA syndrome cases. It was previously thought that sarcomas that developed on the basis of a bone dysplasia focus were a result of radiotherapy. However, even after irradiation was no longer used for the treatment of dysplasia foci, cases of neoplastic transformation still occurred. The current consensus is that malignant changes are of genetic origin. Moreover, apart from sarcoma, dysplasia can lead to fibrosarcoma or chondrosarcoma. There may be gap of several years or even decades between a first diagnosis of dysplasia and the appearance of a sarcoma. Sarcomas usually appear in the facial-cranial and femur bones. Usually the first symptom is a sudden increase in the size of a bone lesion, accompanied by pain and a rise in alkaline phosphatase in the blood serum. Sarcomas that develop on the basis of fibrous dysplasia are very malignant and have a poor prognosis. In view of this fact patients with fibrous dysplasia should be subject to thorough and systemic testing and observation [6,17].

Material from a progressive dysplastic lesion in the patient’s maxillary alveolar process was collected for histopathological examination. Oncological vigilance in the case of a primary health condition such as MCA was justified in this case. The patient remains under constant supervision. Since the time the material was taken from the maxillary alveolar process for histopathological examination, the existing lesions have not expanded and no new fibrous dysplasia foci have appeared.

Conflict of interest statement: Authors state no conflict of interest.
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