

Review

The Management of Facial Fibrous Dysplasia

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REZUMAT

Managementul displaziei fibroase faciale

Displazia fibroasă craniofacială este o afecțiune benignă. Apare în relație cu mutațiile genei GNAS, al căror rezultat interferează în diferențierea și proliferarea celulelor stromale osteoformatoare, ceea ce determină înlocuirea osului și a măduvei cu țesut fibros și os spongios. Poate fi localizată la nivelul unui singur os sau în multiple zone ale scheletului și/sau organe endocrine. Această lucrare prezintă modul de abord multidisciplinar al displaziei fibroase cranio-faciale fiind focusată pe aspectele clinice.

Cuvinte cheie: displazie fibroasă cranio-facială, management multidisciplinar, neuronavigație

ABSTRACT

Craniofacial fibrous dysplasia is a benign disease. It appears in relation with the mutations of the GNAS gene that results interferes with differentiation and proliferation of bone-forming stromal cells and leads to the replacement of normal bone and marrow by fibrous tissue and woven bone. It can appear isolated to a single bone or affect multiple skeletal sites and / or endocrine organs. The paper provides clinically focused multidisciplinary management of facial fibrous dysplasia.

Key words: craniofacial fibrous dysplasia, multidisciplinary management, neuronavigation

BACKGROUND

Fibrous dysplasia is a benign condition consisting in replacement of normal bone with fibrous tissue and unorganized bone woven (1). The malignant change to osteosarcoma can appear in less than 1%

of cases (2). Osteosarcoma is found most often, but other lesions as fibrosarcoma, chondrosarcoma, and malignant fibrohistiocytoma are reported (3,4).

Fibrous dysplasia appears due to somatic activation of mutation in the G protein encoded by the gene GNAS. GNAS gene mutations cause

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McCune-Albright syndrome defined by the triad of PFD, café-au-lait skin macules and endocrinopathies, including among others, precocious puberty (5). It is caused by a random mutation in the GNAS gene that occurs very early in development.

Three quarters of the cases are found under the age of 30 years (6). The disease can affect a single bone (monostotic) or multiple bones (polyostotic).

The most common location of the disease are craniofacial bones, proximal femur, ribs (7). The zygomatic - maxillary complex seems to be the most involved region for the monostotic dysplasia (8). The maxilla and mandible are the most frequent sites to be involved among fibrous dysplasia of the head and neck, followed by the frontal, parietal and occipital bones (9).

Clinical and pathological notes

The disease commonly progress as a slow developing mass. Patients may have no symptoms, family members can detect differences in appearance or diagnosis can be incidental during dental xrays or head and neck computer tomograph (CT).

When patient complain, the most usual symptoms are facial asymmetry/deformity (frontal bone bossing, jaw asymmetries), pain, vertical dystopia (difference in the vertical position of the eyes) proptosis, nasal congestion and/or obstruction, malocclusion and neurological changes (vision changes, paresthesia) (8). The monostotic location gives more deformity than the polyostotic location.

The rapid grows of the lesions occur usually in the patients with growth hormone in excess or young patients at prepubertal age and can cause aneurysmal bone cysts (ABC), mucoceles.

Aggressive expanding fibrous dysplasia lesions complains could include paresthesia, anesthesia of facial pain symptoms. Depending the involvement nasal obstruction, sinus congestion, visual or hearing disturbances, epiphora, pain and malocclusion may encounter. The cause of the symptoms may be: mucocele, malignant transformation, osteomyelitis.

Imagery

To investigate facial fibrous dysplasia there are multiple imaging exams that can be performed: standard craniofacial with no contrast from vertex to thyroid region, cranio-facial CT, dental radiology (Fig. 1, 2).



Figure 1. Fibrous dysplasia of the right maxillary sinus - transverse view

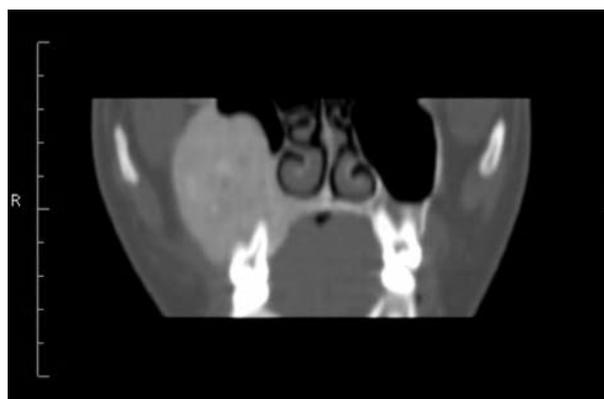


Figure 2. Fibrous dysplasia of the right maxillary sinus - coronal view

Specific imagistic features of the disease include ground glass appearance with thin cortex and without distinctive borders (homogenous appearance) in the early stages, with progression to mixed radio-dense/radio-lucent lesion as the patient ages, which stabilizes in adulthood.

Radiographic findings could be helpful to separate fibrous dysplasia, osteomyelitis and osteogenic sarcoma, but diagnosis cannot rely on radiographic characteristics alone.

Biopsy

A bone biopsy is necessary in order to confirm the diagnosis. The histology findings do not predict the behavior of the fibrous dysplasia. The biopsy could not favor the growth of the lesion, but fibrous

dysplasia lesions are likely to be vascular and bioptic intervention could cause bleeding (10,11).

Histologic findings

Pathologically, fibrous dysplasia lesions are characterized by expansion of cortical bone with gradual replacement by fibrous tissue that is firm, rubber-like, and gritty. Cystic lesions can often be filled with an amber fluid and can occasionally be vascular. Microscopically, the lesion is readily identifiable, with an irregular trabeculae of woven bone intermixed with a connective tissue stroma. Lesions will vary in the amount and distribution of bone and in the cellularity and vascularity of the fibrous stroma.

Craniofacial lesions present a dense fibrous bone tissue. The more severe lesions present with immature woven bone which is not replaced by lamellar bone (12). The lack of connectivity and the immature nature of the bone formed results in decreased mechanical properties of the bone, leading to deformations and fractures (13).

In fibrous dysplasia there are abnormalities in formation of osteoprogenitor cells: the number of immature osteoblasts is low, the cells located along the bone surface are distinct from normal cubical mature osteoblasts. The marrow of the bone is filled with immature cells, that outnumber the mature cells, which are low. There is a defective osteoblast differentiation. The dysplastic cells produce collagen fibers that are disorganized. This is proven by abnormal collagen distribution in the immature bone. The collagen fibers are perpendicular instead of parallel to the bone surface and present a comb-like structure (12), (13). Also, some protein synthesis is affected: sialoprotein and osteopontin appear decreased, osteonectin is elevated, these features determining an immature bone matrix. These abnormalities in bone proteins can cause reduced adherence of osteoblasts and cell retraction. In a dysplastic bone also osteocytes are numerous and not well organized, especially in the areas of the fibrous dysplastic bone with lytic areas. The main histological features of fibrous dysplasia are marrow invasion, hyper-resorption, lytic areas, immature bone.

A particular histological pattern that appears at the level of skull base include "cementicles" – bone spicules, loose fibrous background and darkly stained cemented ossicles spread.

Management of facial fibrous dysplasia

A multidisciplinary medical team that include: craniofacial surgeon, neurosurgeon, oral&maxillo-facial surgeon, ENT, ophthalmologist, dentist and audiologist may be needed, depending on the location of the lesions.

In following the patient is important to document the onset of the symptoms, presence of functional impairments, onset of menarche in females, other endocrine abnormalities, growth chart.

The management of facial fibrous dysplasia depends on the age of the patient, pediatric or adult (skeletally mature). The management is dictated by the clinical behavior of the lesion. There are no markers to predict the evolution of the lesions.

Careful monitoring and intermittent craniofacial CT are recommended during the pubertal phase of the young patient. This period of change in CT appearance coincides with case reports of increased activity of the fibrous dysplasia lesions either through rapid growth, worsening facial asymmetry, malignant transformation, or association with other pathologic, radiolucent lesions such as an aneurysmal bone cyst (ABC) and accelerated expansion. If the patient is experiencing new onset of symptoms or rapid enlargement an updated CT is recommended. (14)

The more prudent approach is conservative since the growth after puberty diminished, but in case that the fibrous dysplasia start to develop important deformities or compressing the optic nerve, nasal obstruction or hearing impairment, posterior displacement of the tongue an aggressive surgical resection is needed. A skeletal study is recommended if there are suspicion of polyostotic location, mainly in the patient with immature skeletal development. A orthopedic evaluation has to be done in case of polyostotic location other than the cranio facial lesion.

The lesions of the face can be described as stable, non-aggressive (slow growing) or aggressive (pain, paresthesia, rapid development, pathologic fracture, malignant transformation, association with a second lesion). (15)

For stable fibrous dysplasia lesion when the patient has no complains with the facial deformity the "wait and see" approach is acceptable. The evaluation of the patient have to be done yearly basis.

If the patient complains about the deformity a surgical approach will be considered. In monostotic

lesions a complete resection can be performed usually, but in poliostotic lesions the complete resection is hard to achieve. The resection must be followed by reconstructive step of the surgery. The reconstructive aim is to preserve the function of all nerves and structures and to achieve a good cosmetic outcome. Orthognatic surgery may be need it in order to correct the malocclusion lesions. Bone healing appears to be normal with conventional rigid fixation. Regular follow-up is need it in order to determine a possible recurrence of the disease.

For active, but non-aggressive, lesions it is ideal to wait until the lesion becomes stable and the skeletal maturity is achieved by patient. If the patient complains about the facial deformity a surgical approach can be made with resection of the lesion and reconstruction of the defect. There is a potential regrow of the lesion if there is not a complete resection of the lesion, which sometimes is not possible. Intraoperative navigation tools may be need it to guide the surgeon. The recurrence of the lesion and the stability surgical result can be determined comparing imagistic result. No therapy or imagistic examination can predict the regrowth of the tumor.

Surgical treatment may range from contour to en bloc depending on the histopathological finding.

Osteomyelitis management will be performed using antibiotic therapy, but it is difficult to successfully treat. Sometimes en bloc resection is need it for refractory pain and persistent infection.

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