Review Article

Craniofacial Fibrous Dysplasia: An Update

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Fibrous dysplasia was first described by Lichtenstein in 1938 as a disorder characterized by progressive replacement of normal bone elements by fibrous tissue. It is a bone tumor that, although benign, has the potential to cause significant cosmetic and functional disturbance, particularly in the craniofacial skeleton. Its management poses significant challenges to the surgeon. Its compression of the optic nerve with resulting visual impairment is especially alarming. Over the years, we have gained a better understanding of its etiology, clinical behavior, and both surgical and non-surgical treatments. Its characteristics, under various imaging modalities, have been thoroughly described in recent years. These developments have taken place with the goal of optimizing treatment of those who suffer from this disease. However, the role of prophylactic optic nerve decompression in cases of optic canal involvement has recently been challenged: the results of a few recent studies have raised questions regarding its role. Further studies would be required to assess its value. *(Chang Gung Med J 2006;29: 543-9)*

Key words: craniofacial fibrous dysplasia, optic nerve, optic canal, decompression, bisphosphonate, pamidronate.

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Fibrous dysplasia (FD) is a benign disease of bone that was originally described by Lichtenstein more than sixty years ago.[1,2] Although its actual incidence is not known, it accounts for between 2.5 and 10 percent of all bone tumors, thus a relatively common disease. FD is a developmental dysplastic disorder of bone in which the normal bone matrix is replaced by fibroblastic proliferation. Lesions contain irregular trabeculae of partially calcified osteoid. Some believe that the immature woven bone is formed directly from abnormal fibrous connective tissue that is unable to form mature lamellar bone, hence the term dysplasia. Others believe that there is underlying abnormal fibroblast proliferation that results in the replacement of normal cancellous bone with an immature fibrous tissue that is poorly mineralized.[3] Its etiology has been linked with a mutation in the Gsα gene that is located at chromosome 20q13.2-13.3.[4,5] The mutation was first identified in patients with McCune-Albright syndrome but was later demonstrated in the lesions of patients suffering from either monostotic or polyostotic FD. All cells that arise from the mutated cells manifest the dysplastic features. Severe disease may be associated with an earlier mutational event that leads to a larger number or a more widespread distribution of mutant

cells.[6] The clinical pattern of the disease also varies in distribution and appearance. Whether the disease is generalized or localized depends on (i) the size of the cell mass at the point the mutation takes place during embryogenesis and (ii) the site in the cell mass where the mutation occurs.[6]

Clinical features

Craniofacial FD typically presents at around 10 years of age and then progresses throughout adolescence.[7] The disease was initially thought to become inactive after childhood but subsequent reports have proved this to be untrue.[8] The clinical presentation depends on the site, duration, extent and nature of the lesion. It ranges from a mild local swelling with little or no pain to a gross deformity with complications such as proptosis, visual disturbance and sensorineural hearing loss.[9]

The ocular effects of craniofacial FD are of particular concern. It may cause globe displacement due to the involvement of the sphenoid and/or ethmoid bones. Loss of vision may occur secondary to involvement of the sphenoid bone that compresses the optic nerve. Hence, in cases of optic canal involvement, a complete ophthalmological assessment, including testing for visual acuity, visual field, color perception and visual evoked potential, is necessary. The part of the optic nerve affected in such situations is almost always that which is fixed within the surrounding bony canal. The narrowest part of the optic canal, the optic ring, is particularly important surgically as it should be included in any prophylactic decompression of the optic nerve.[10]

Cystic mass lesions may develop in areas affected by FD; these include cystic degeneration and other cystic lesions such as aneurysmal bone cysts. There are various reports of cystic degeneration of FD in the craniofacial region.[11-13] Although relatively uncommon here, an area of bone affected by FD undergoes rapid enlargement by cystic degeneration. This enlargement can lead to disastrous complications, such as optic nerve compression. Such patients often present with sudden deterioration in vision.[14] Due to its rapidly progressing nature, cystic degeneration is often confused with malignant transformation.[13] The management of cystic changes in FD is well established; total excision of the lesion is more appropriate than simple curettage,[15] as simple curettage of bone cysts is associated with a 21% recur-

rence rate.[16] Hence, total excision of FD with cystic degeneration in areas of the craniofacial skeleton, such as the mandible, may necessitate relatively more complex reconstructive procedures such as microvascular free flap (e.g. free fibula flap) reconstruction.

Diagnosis/Evaluation

Aside from McCune-Albright syndrome, it is usually difficult to diagnose FD on clinical, radiographic or histological criteria alone; one must consider all three factors.[7] The plain radiological features of FD are non-specific and vary widely.[17] The typical appearance is that of radiolucent lytic lesions with a homogenous ground-glass appearance and ill-defined borders. Occasionally, the radiograph may reveal predominantly sclerotic lesions with or without accompanying lytic lesions.[7] Naturally, its non-specific radiological appearance makes it difficult to differentiate from other conditions such as ossifying fibroma and Paget's disease.[7,18]

Computed tomography (CT) is a better radiological tool, especially for assessing the extent of the tumor in cases of suspected optic canal involvement.[19] While it is invaluable in pre-operative planning, it is also a superior diagnostic tool, although CT alone is insufficient to make a diagnosis of FD.[20] FD has characteristic appearances on CT and consists of three varieties: ground-glass pattern (56%), homogeneously dense pattern (23%) and cystic variety (21%).[21] Various studies have suggested the use of magnetic resonance imaging (MRI) as a diagnostic tool for FD.[22,23] Lesions have been characterized by a decreased signal as well as sharply demarcated borders on both T1- and T2-weighted images. Some authors, however, have highlighted the potential for misdiagnosis with MRI.[24] The MRI characteristics of FD do not share the distinctive features seen on radiography or CT, and often resemble that of tumors. This is particularly so when the lesion shows intermediate signal intensities on T1-weighted images and high signal intensities on T2-weighted images, and enhances brilliantly after the injection of contrast material. The likelihood of correctly diagnosing FD by MRI is high only when the signal intensities on both T1- and T2-weighted images are low in spite of the injection of contrast material.[25] Radionuclide scans, such as bone scintigraphy, have some role in the diagnosis/evaluation of FD.[26]

Radionuclide scan has high sensitivity but low specificity. Single photon emission computed tomography (SPECT) has been reported to be more sensitive in detecting the areas involved in cases of FD.[27]

Although the histology of FD is well-established, cytological descriptions are rare. One group reported on fine needle aspiration cytomorphology of FD; the smears contained blood, occasional osteoclastic multinucleated giant cells, and frequent C-shaped fibrillary structures with dark central areas and lighter peripheries representing woven bone.[28] The role of fine needle aspiration cytology remains limited.

There is some role for biochemical markers in the management of FD. Serum alkaline phosphatase and urinary hydroxyproline are examples of useful markers, and are used to monitor response in the nonsurgical treatment of the disease rather than for diagnosis. The role of growth hormone as a predictor of the severity of the disease has also been recently reported, although the results are yet to be published.

Treatment

Surgical treatment of FD consists of either conservative shaving/contouring or radical excision with immediate reconstruction. The choice of surgical option depends on several factors: site of involvement, rate of growth, aesthetic disturbance, functional disruption, patient preference, general health of the patient, surgeon's experience and the availability of a multi-disciplinary team (neurosurgeon, ophthalmologist, otolaryngologist, orthodontist).[7] In the surgical management of craniofacial FD, the craniofacial skeleton has been classified into 4 major zones.[29] This classification was based on the experience of treating 28 craniomaxillofacial FD patients at the Craniofacial Center of Chang Gung Memorial Hospital. Zone 1 includes the fronto-orbital, zygomatic and upper maxillary regions; zone 2 represents the hair-bearing cranium; zone 3 is the central cranial base; and zone 4 includes the teeth-bearing regions of the maxillary alveolus and mandible. For lesions in zone 1, total excision of the dysplastic bone is recommended. For lesions in zones 2, 3 and 4, conservative excision or shaving has been proposed.

Decompression of the optic nerve in cases of optic canal involvement can be classified as therapeutic or prophylactic. Optic nerve decompression has generally been advised, especially in those patients with decreasing visual acuity.[30,31] The value of therapeutic decompression has been questioned, especially in delayed cases. Studies have demonstrated that vision is less likely to return if the decompression is done more than one week after established blindness.[32-34] Decompression has been shown to have no value in cases of blindness of more than one month duration.[29,35,36] Prophylactic decompression is based on the belief that visual loss is directly related to optic canal stenosis and there have been encouraging reports on its value.[30,37] The procedure is generally safe, although it is associated with a steep learning curve and results are dependent on the experience of the surgeon performing the procedure. There seems to be a recent shift in understanding of optic canal stenosis in FD and its relationship to visual loss. There have been reports of patients with encasement and narrowing of the canal yet without resultant visual loss.[38] Thus the relationship of canal stenosis to visual loss is not completely clear. In fact, visual loss has been proposed to be due to a primary or secondary mass lesion rather than optic canal stenosis.[14] In light of these new findings, further studies are needed to define the value of prophylactic optic nerve decompression.

Reconstruction after excision is important in the management of craniofacial FD. This is particularly true in cases of zone 1 involvement. The use of autologous tissues, namely grafts of calvarial bone and rib, is preferable. Split calvarial grafts are usually obtained from the frontal, temporal or parietal regions. As these bones have diploe between the inner and outer cortices they are easily split. The inner cortex is used as the graft while the outer cortex is placed back to its original position. Rigid fixation is achieved with mini or microplates.[7] Rib grafts are also frequently used in a split fashion. One reconstructive technique is the "chainlink fence" technique, useful for the reconstruction of large defects especially in the fronto-orbital region, particularly when calvarial bone graft is not available.[39] Full-thickness rib grafts are useful for the reconstruction of the superior orbital rim as they are effective in re-establishing rim contour.[7] Microvascular free flap reconstruction has a role, especially for lesions involving the mandible where segmental excision is necessary.[40] Orthognathic surgery may be necessary in some patients with zone 4 lesions, as these patients have been found to have higher rates of mal-

occlusion:[41] orthognathic surgery helps to restore stable occlusion and good facial aesthetics. Results after orthognathic surgery have been maintained long-term, without cases of recurrence after surgery. This demonstrates that fibrodysplastic bone is capable of healing adequately using standard methods of fixation.[42] Routine dental therapies, including orthodontic treatment, have been found not to exacerbate the disease.[41]

Medical treatment has a role in the management of craniofacial FD. Some authors have reported their experience with the use of steroids, mainly in the treatment of visual symptoms from optic nerve compression. One group reported one case of reversal of visual loss,[43] while others reported control of visual deterioration with the use of steroids.[44-46] Another line of medical treatment is the bisphosphonates, for example pamidronate. This group of drugs inhibits osteoclastic activity. Most experiences have been in patients with polyostotic FD or McCune-Albright Syndrome; there is limited data on patients with craniofacial FD and these experiences were mainly in children.[47] Bisphosphonates are generally safe and well-tolerated, although one reported side-effect is atypical fever.[47]

Unfortunately there are no objective methods to assess or predict the outcome of treatment, especially medical treatment. Subjective criteria have been suggested, such as a decrease in inflammatory symptoms like pain and swelling.[47] Serum alkaline phosphatase, a marker for bone turnover, is consistently reduced in patients treated with pamidronate, making it a good monitor of response to medical treatment.[48-50] The use of urinary hydroxyproline as a marker has also been suggested, although experience with it is more limited. Serial radiographs have been used to assess response but results are not consistent. One study demonstrated response to treatment by the filling of osteolytic lesions and/or cortical thickening,[49] while another showed no radiological response.[50] Local bone mineral density has been found be more consistent than serial X-rays in the monitoring of response to treatment.[47]

Conclusion

FD is a benign disease that has the potential to cause significant cosmetic and functional disturbance, especially visual impairment. With proper understanding, diagnosis and management, however, good outcomes can often be achieved. Much progress has been made over the past decade, for example the identification of the genetic mutation linked to the etiology of the disease. This area still needs further exploration in order to establish the role of genetic manipulation in the management of the disease. In light of recent findings that suggest an inconsistent relationship between optic canal stenosis and visual loss, more research is required to determine the role of prophylactic optic canal decompression in cases of FD with optic canal involvement.

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顱顏骨纖維異生症

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　　纖維異生症的特徵是纖維組織漸漸取代正常的骨骼，可視爲一種良性腫瘤。在顱顏骨的纖維異生症可導致眼球突出、移位，視力不良，咬合不正及臉部扭曲變形等。治療顱顏骨纖維異生症主要是用外科手術做部分或徹底切除病變部位，切除後的顏面骨的缺損，以自體骨移植並加以固定，目的是改善顏面的外觀，咬合及解除神經的壓迫。近幾年來，學界對纖維異生症的病因，臨床表現，內科及外科治療的結果及各種影像學的研究，讓我們能發展出有效的治療原則，尤其是近年來視神經管的纖維異生症的預防性減壓術備受矚目，有些甚至質疑視神經減壓術的必要性，故長期的追蹤研究顱顏骨纖維異生症的治療成果是必要的。(長庚醫誌 2006;29:543-9)

關鍵字：顱顏骨纖維異生症，視神經，視神經管，雙磷酸鹽。