

Case Report

Natural history of cranial fibrous dysplasia revealed during long-term follow-up: Case report and literature review

David L. Penn, Richard J. Tartarini, Carolyn H. Glass¹, Umberto De Girolami², Amir A. Zamani², Ian F. DunnDepartments of Neurological Surgery, ¹Pathology, ²Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USAE-mail: David L. Penn - DLPENN@partners.org; Richard J. Tartarini - rtartarini@gmail.com; Carolyn H. Glass - CGLASS2@partners.org; Umberto De Girolami - UIDEGIROLAMI@partners.org; Amir A. Zamani - AZAMANI@partners.org; *Ian F. Dunn - IDUNN@partners.org
*Corresponding author

Received: 05 January 17 Accepted: 04 May 17 Published: 06 September 17

Abstract

Background: Fibrous dysplasia (FD) is a rare developmental disease characterized by the replacement of bone marrow with proliferating fibro-osseous tissue. There exist three forms of FD—monostotic, polyostotic, and that associated with McCune-Albright syndrome. The disease can present in different locations and with a variety of symptoms. One of the more common locations of FD occurrence is the craniofacial region. Treatment of asymptomatic FD often involves conservative management with serial imaging. Medical management with bisphosphonates is an option, though long-term efficacy data are lacking. Surgical resection is usually reserved for very large or symptomatic lesions.

Case Description: We discuss the most unusual case of a 52-year-old male found to have a left pterional mass while being worked up for sinus headaches. The patient elected to follow this lesion conservatively, and imaging several years later showed obvious growth which accelerated in the last 4 years during an 18-year observational period. He ultimately underwent successful resection of an extradural and intradural FD.

Conclusions: The significant growth potential of these lesions was revealed in this patient, in whom conservative management had been adopted. Despite optimal surgical resection and outcome in this case, the importance of surveillance imaging and perhaps earlier intervention cannot be underestimated when managing cranial FD.

Key Words: Craniofacial, fibrous dysplasia, middle fossa zygomatic approach, polyostotic

Access this article online

Website:www.surgicalneurologyint.com**DOI:**

10.4103/sni.sni_7_17

Quick Response Code:

INTRODUCTION

Fibrous dysplasia (FD) is a rare developmental disease characterized by the replacement of normal bone marrow with proliferating fibro-osseous tissue and thinning of cortical bone that may cause deformities, pain, swelling, loss of coordination, and/or nerve compression.^[2,11] The pathogenesis of the disease is known to involve a postzygotic mutation of the *GNAS1* gene, resulting in

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Penn DL, Tartarini RJ, Glass CH, De Girolami U, Zamani AA, Dunn IF. Natural history of cranial fibrous dysplasia revealed during long-term follow-up: Case report and literature review. *Surg Neurol Int* 2017;8:209.

<http://surgicalneurologyint.com/Natural-history-of-cranial-fibrous-dysplasia-revealed-during-long-term-follow-up:-Case-report-and-literature-review/>

alteration of biochemical pathways ultimately leading to constitutive activation of G proteins and proliferation of undifferentiated mesenchymal cells.^[9,18,28] Mutations occur sporadically and postzygotically resulting in mosaicism and highly variable presentations.^[13,29] The presence of these cells ultimately results in abnormal bone matrix and growth of abnormal tissue. FD can present at any age and as monostotic, polyostotic, or as part of McCune-Albright syndrome.^[2,21] The craniofacial area is commonly affected more often in the polyostotic variant with 50–100% of cases having such involvement, though FD can occur anywhere in the skeleton.^[4,5,21] The frontal bone is the most common site of involvement in the cranial vault.^[4] Importantly, the monostotic variant may arrest or “burn out” after puberty, whereas the polyostotic form may continue through adulthood.^[2,4,5] Symptoms if present may include pain and mass effect upon adjacent structures. Malignant transformation occurs in less than 1% of cases.^[14,22,23]

FD, if asymptomatic, is often managed conservatively. Medical therapy with bisphosphonates is controversial, having been previously shown to result in significant decreases in pain and radiographic lesions; however, a recent randomized, double blind, placebo-controlled trial disputes these effects.^[6,7,20] When the disease progresses either by growth of a lesion or manifestation of new symptoms, surgery is usually considered, although this decision may be complicated should the disease be extensive.

Here, we present a unique case of presumed radiographic FD followed conservatively for 18 years. Its growth rate, symptom onset, and findings of intradural invasion confer important insights into the natural history of FD and may suggest an earlier role for surgery in select cases.

CASE DESCRIPTION

The patient is a 52-year-old right-handed gentleman, who initially presented in 1998 with headaches that were thought to be related to sinus infections. Initial work up consisted of X-ray of the skull, which demonstrated a dense calcified lesion in the left frontotemporal region [Figure 1]. This study was followed by a magnetic resonance imaging (MRI), which demonstrated a densely calcified lesion in the frontotemporal region abutting the sylvian fissure. After neurosurgical consultation, conservative management was adopted. The lesion was deemed stable according to the patient, however, images and reports are not available for long periods of this interval.

The patient presented again in 2014 with similar headaches, again thought to be caused by sinus infection. At this time, an otolaryngologist ordered a computed tomography (CT) scan, which demonstrated growth of the mass [Figure 1]. This was verified by MRI,

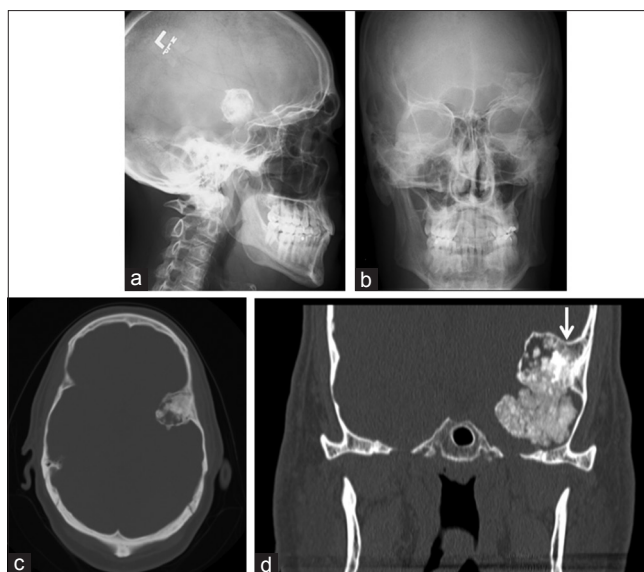


Figure 1: (a and b) (Lateral and AP views of skull) and (c and d) (axial and coronal CT) show a heavily calcified lesion in the left frontotemporal region with its origin from the temporal bone immediately behind the pterion. The mass is non-homogeneous with sharply defined margins. The arrow indicates where the lesion may have become intradural

which also showed an increase in surrounding edema with transtentorial herniation and mass effect on the midbrain [Figure 2]. With the exception of headache, the patient remained otherwise asymptomatic. While surgery was advised, continued surveillance was adopted showing progressive enlargement, with the onset of very subtle circuitous speech. Surgery was strongly recommended, to which he ultimately consented.

CT angiography (CTA) was obtained demonstrating close proximity of the mass to the left cavernous and ophthalmic internal carotid artery, as well as M2 branches of the middle cerebral artery (MAC), without obvious stenosis, involvement, or entrapment of these vessels. While his hearing was intact and face symmetric, there was an unclear relationship of the mass to the geniculate ganglion and cochlea on immediate preoperative imaging studies [Figure 3].

In 2016, approximately 18 years after the discovery of this mass, the patient underwent surgery for resection of this lesion through a frontotemporal craniotomy and craniectomy, and zygomatic osteotomy to maximize our access to the middle fossa floor. We sectioned the zygoma and reflected the temporalis inferiorly after subfascial dissection to gain adequate access to the floor of the middle fossa. We used neuronavigation to identify the mass emanating from the inner table, placing burr holes immediately around this region and connecting these. This allowed us to separate the mass from the larger frontotemporal craniotomy flap, which we then elevated. We used a high-speed drill to remove the extradural portion of the mass which at the superficial depth of the

sylvian fissure became intradural. The MCA branches were easily dissected from the lesion and the middle fossa dura found to be intact. After a complete resection we replaced the frontotemporal flap, reconstructing the central portion with titanium mesh. Postoperative imaging showed a complete resection [Figure 4] and he was discharged in excellent condition on the second postoperative day. Despite analysis of the frozen section

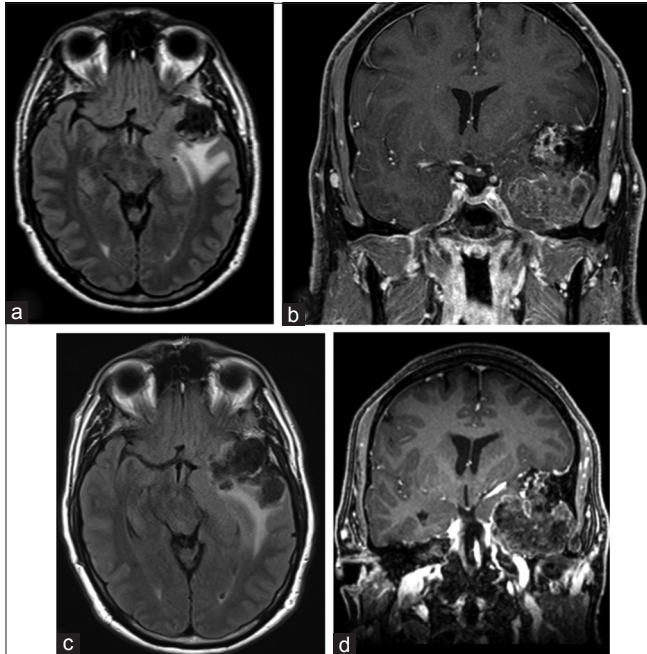


Figure 2: MR images (a and b) are from 2014; (c and d) are from 2016, just prior to surgical resection. These demonstrate growth of this lesion over a two-year period. Axial FLAIR images (a and c) demonstrate adjacent vasogenic edema extending in the left temporal lobe and optic radiation. These images reveal the extensive nature of this mass, occupying a large part of the left middle cranial fossa with resultant shift of the uncus medially deforming the suprasellar cistern and shifting the midbrain. On coronal images upward displacement of left MCA is seen

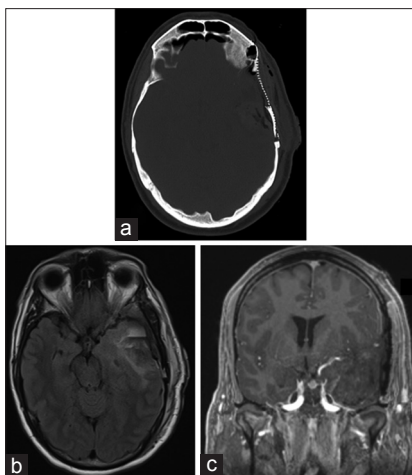


Figure 4: Postoperative CT (a) and MR (b and c) obtained on postoperative day one, demonstrate complete resection of the large calcified lesion with stable residual vasogenic edema and uncus shift

raising a concern for meningioma, permanent analysis showed FD [Figure 5].

DISCUSSION

The natural history of FD, as well as the manifestation of symptoms, is not well understood, making it difficult for clinicians to develop standardized treatment plans.^[2] Not all cases of FD manifest with new, aggressive symptoms, although ones that do typically involve progressive growth of the lesion. Careful review of the literature reveals that many cranial cases of FD begin asymptomatic with more aggressive symptoms manifesting as the lesion grows.^[19,30] Symptoms of aggressive lesions include worsening headaches, severe edema, mass effect, compromised vision, compromised hearing, and altered

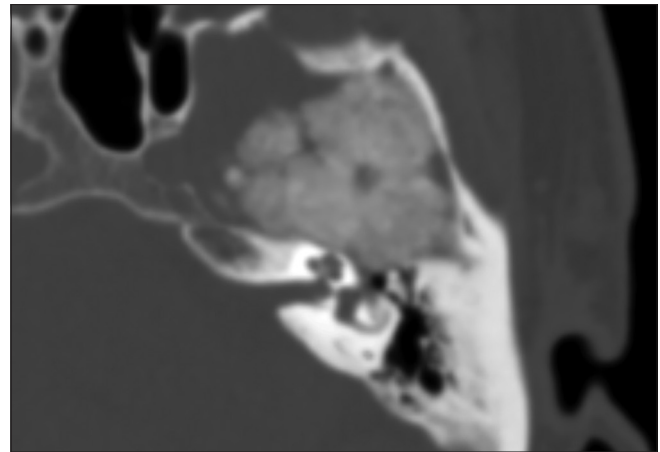


Figure 3: CT through middle cranial fossa shows the mass and its relations with the left petrous bone. Note close relations of the mass to the left cochlea and geniculate ganglion

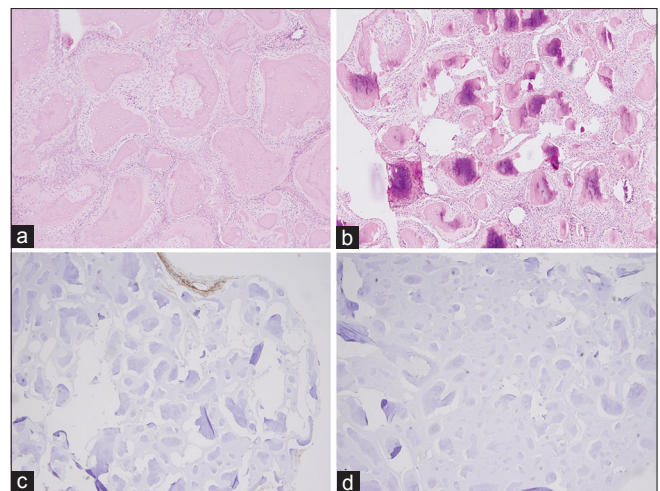


Figure 5: Permanent pathology obtained after surgical resection of the lesion. Panel (a and b) represent H&E stained sections demonstrating curvilinear trabeculae of woven bone surrounded by moderately cellular fibrous stroma. Negative epithelial membrane antigen stain and negative somatostatin receptor 2 staining are represented in Panel (c and d), respectively

cosmetic appearance.^[2,12,16,18,25] Our case offers 18 years of insight into the natural history of cranial FD with worsening mass effect and headaches manifesting from a growing lesion in the frontotemporal area.

In general, surgical treatment is not necessary in asymptomatic cases of FD; however, surgery is a consideration when lesions become symptomatic, grow, or exert mass effect. Many authors view radical surgical resection as the most successful and definitive treatment over more conservative procedures.^[15,17,27] Chen and Noordhoff suggested an anatomical classification to guide treatment: zone 1 includes the fronto-orbital, zygomatic, and upper maxillary regions; zone 2 includes the hair-bearing cranium; zone 3 is the cranial base including petrous and mastoid portions of the temporal bone, as well as the pterygoid region; and zone 4 includes teethbearing bones, such as the maxilla and the mandible.^[8] They recommended aggressive surgical resection for lesions in zone 1 and to be considered in zone 2, while conservative management should be favored in zones 3 and 4. Zone 3 should only be surgically treated if symptoms or growth occurs.^[1,8] Taken together, the surgeon should thoroughly consider the location of the lesion and clinical presentation when surgical treatment is indicated.

Amit *et al.* performed a case series of 241 patients with cranial FD and optic nerve involvement (386 optic nerves investigated) to assess the outcomes of surgical treatment versus conservative management.^[3] This study consisted of patients with cranial FD adjacent to the optic nerve with 30% presenting monostotic, 21% presenting polyostotic, and 49% presenting with McCune-Albright syndrome. All symptomatic patients with vision impairment underwent optic nerve decompression and radical resection. Of the 282 clinically intact optic nerves, 15% underwent optic nerve decompression prophylactically, and 85% were managed conservatively. Of symptomatic patients, 67.4% experienced improved vision after surgery. Of the asymptomatic patients who underwent prophylactic optic nerve decompression, 75.6% had stable vision postoperatively, compared to 95.1% of the conservatively managed patients, whose vision remained stable. This study demonstrated that surgery in asymptomatic patients was associated with visual compromise (RR: 4.89; CI: 2.26–10.59). Though many reported cases of asymptomatic cranial FD did have success in optic nerve decompression, those managed conservatively had better overall outcomes in vision preservation. Other case series in the literature have reported similar data and conclusions.^[10,24] These data support the recommendation that patients with cranial FD need to be managed on clinical presentation and not solely, radiographically. Furthermore, thorough discussions must be had with patients regarding expectations and risks of aggressive surgical management in the setting of a still poorly understood disease process.

Another critical consideration is the timing of surgical intervention. Growth of lesions can serve as an indicator for future symptoms. In addition to our patient, several cases reported in the literature have involved monthly growth with worsening symptoms appearing closer to surgical intervention.^[12,16,18,25] One interesting aspect of this particular case is the aggressive and invasive nature of the lesion observed intraoperatively, in conjunction with growth of the lesion over 18 years. Over years, the patient elected to monitor the lesion radiographically. Although the increasing size of the lesion added a more challenging component to the surgical procedure, it is unknown whether earlier surgical resection would have found a less invasive or aggressive lesion, and consequently a less challenging surgery. Despite all these characteristics, it is important to note, in this particular case, deferring surgery did not adversely affect our ability to achieve gross total resection of the lesion and an optimal clinical outcome.

Radiographically, FD typically has an asymmetric ground-glass appearance on CT scan. FD blends with normal bone and results in thinning of the cortical bone.^[26] The lesion in the present study exerted significantly more mass effect outside of the bone than commonly seen with FD and the typical ground glass appearance is not present. Early imaging demonstrates a cauliflower-like appearance that can be more consistent with osteochondroma. Lastly, the significant vasogenic edema in the brain parenchyma surrounding the lesion is an indication that this lesion invaded the meninges. These unusual radiographic findings suggest a more invasive and aggressive lesion than typical FD and could serve to influence surgical timing. Based on the insight our case provides into the natural history of this disease, a surgical treatment plan and timing should be carefully considered among specialists when growth of the lesion occurs, symptoms progress, or radiographic studies suggest a more aggressive phenotype of the disease.

CONCLUSIONS

FD is a developmental disease characterized by the replacement of normal bone marrow with proliferating fibro-osseous tissue, presenting in multiple forms and with a variety of symptoms. One of the most common places for FD to occur is the craniofacial region, in particular the frontal bone, presenting with symptoms including headaches or cranial nerve deficits. The present study follows an initially asymptomatic patient with a growing, atypical left frontotemporal FD lesion clinically and radiographically over 18 years, providing some insight into the natural history of cranial FD. Although treatment strategies are controversial, complete surgical resection of large cranial FD lesions remains a viable plan for successful management of this disease. In this

case, deferring surgical resection did not adversely affect surgical resection and outcome, but many characteristics of the lesion should be accounted for when creating a treatment plan.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Adada B, Al-Mefty O. Fibrous dysplasia of the clivus. *Neurosurgery* 2003;52:318-22; discussion 323.
- Adetayo OA, Salcedo SE, Borad V, Richards SS, Workman AD, Ray AO. Fibrous dysplasia: An overview of disease process, indications for surgical management, and a case report. *Eplasty* 2015;15:e6.
- Amit M, Collins MT, FitzGibbon EJ, Butman JA, Fliss DM, Gil Z. Surgery versus watchful waiting in patients with craniofacial fibrous dysplasia--a meta-analysis. *PLoS One* 2011;6:e25179.
- Amit M, Fliss DM, Gil Z. Fibrous dysplasia of the sphenoid and skull base. *Otolaryngol Clin North Am* 2011;44:891-902, vii-viii.
- Benhamou J, Gensburger D, Messiaen C, Chapurlat R. Prognostic Factors from an Epidemiologic Evaluation of Fibrous Dysplasia of Bone in a Modern Cohort. The Francelys Study. *J Bone Miner Res* 2016;31:2167-72.
- Boyce AM, Kelly MH, Brillante BA, Kushner H, Wientroub S, Riminucci M, et al. A randomized, double blind, placebo-controlled trial of alendronate treatment for fibrous dysplasia of bone. *J Clin Endocrinol Metab* 2014;99:4133-40.
- Chapurlat RD, Huguency P, Delmas PD, Meunier PJ. Treatment of fibrous dysplasia of bone with intravenous pamidronate: Long-term effectiveness and evaluation of predictors of response to treatment. *Bone* 2004;35:235-42.
- Chen YR, Noordhoff MS. Treatment of craniofacial fibrous dysplasia: How early and how extensive? *Plast Reconstr Surg* 1990;86:835-42; discussion 843-834.
- Cohen MM, Jr., Howell RE. Etiology of fibrous dysplasia and McCune-Albright syndrome. *Int J Oral Maxillofac Surg* 1999;28:366-71.
- Cutler CM, Lee JS, Butman JA, FitzGibbon EJ, Kelly MH, Brillante BA, et al. Long-term outcome of optic nerve encasement and optic nerve decompression in patients with fibrous dysplasia: Risk factors for blindness and safety of observation. *Neurosurgery* 2006;59:1011-7; discussion 1017-8.
- DiCaprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, evaluation, and treatment. *J Bone Joint Surg Am* 2005;87:1848-64.
- Gupta A, Mehta VS, Sarkar C. Large cystic fibrous dysplasia of the temporal bone: Case report and review of literature. *J Clin Neurosci* 2003;10:364-7.
- Happle R. The McCune-Albright syndrome: A lethal gene surviving by mosaicism. *Clin Genet* 1986;29:321-4.
- Lee JS, FitzGibbon EJ, Chen YR, Kim HJ, Lustig LR, Akintoye SO, et al. Clinical guidelines for the management of craniofacial fibrous dysplasia. *Orphanet J Rare Dis* 2012;7(Suppl 1):S2.
- Munro IR, Chen YR. Radical treatment for fronto-orbital fibrous dysplasia: The chain-link fence. *Plast Reconstr Surg* 1981;67:719-30.
- Muthusamy S, Subhawong T, Conway SA, Temple HT. Locally aggressive fibrous dysplasia mimicking malignancy: A report of four cases and review of the literature. *Clin Orthop Relat Res* 2015;473:742-50.
- Ozek C, Gundogan H, Bilkay U, Tokat C, Gurler T, Songur E. Craniofacial fibrous dysplasia. *J Craniofac Surg* 2002;13:382-9.
- Pardo-Maza A, Lassaletta L, Ruiz-Bravo E, Perez-Mora R, Penarrocha J, Gavilan J. Fibrous dysplasia of the temporal bone secondary to ear surgery: A case report. *J Med Case Rep* 2015;9:129.
- Park B, Abode-Iyamah K, Lee SL, Kirby P, El-Khoury G, Wilson S. Fibro-osseous lesion of the cranium in an adolescent patient. *Surg Neurol Int* 2015;6:12.
- Plotkin H, Rauch F, Zeitlin L, Munns C, Travers R, Glorieux FH. Effect of pamidronate treatment in children with polyostotic fibrous dysplasia of bone. *J Clin Endocrinol Metab* 2003;88:4569-75.
- Ricalde P, Horswell BB. Craniofacial fibrous dysplasia of the fronto-orbital region: A case series and literature review. *J Oral Maxillofac Surg* 2001;59:157-67; discussion 167-58.
- Ruggieri P, Sim FH, Bond JR, Unni KK. Malignancies in fibrous dysplasia. *Cancer* 1994;73:1411-24.
- Sadeghi SM, Hosseini SN. Spontaneous conversion of fibrous dysplasia into osteosarcoma. *J Craniofac Surg* 2011;22:959-61.
- Tan YC, Yu CC, Chang CN, Ma L, Chen YR. Optic nerve compression in craniofacial fibrous dysplasia: The role and indications for decompression. *Plast Reconstr Surg* 2007;120:1957-62.
- Turner OA. Fibrous dysplasia of bone; neurosurgical considerations in two cases. *Yale J Biol Med* 1951;23:501-4.
- Unal Erzurumlu Z, Celenk P, Bulut E, Baris YS. CT Imaging of Craniofacial Fibrous Dysplasia. *Case Rep Dent* 2015;2015:134123.
- Valentini V, Cassoni A, Marianetti TM, Terenzi V, Fadda MT, Iannetti G. Craniofacial fibrous dysplasia: Conservative treatment or radical surgery? A retrospective study on 68 patients. *Plast Reconstr Surg* 2009;123:653-60.
- Weinstein LS, Chen M, Liu J. Gs (alpha) mutations and imprinting defects in human disease. *Ann N Y Acad Sci* 2002;968:173-97.
- Weinstein LS, Shenker A, Gejman PV, Merino MJ, Friedman E, Spiegel AM. Activating mutations of the stimulatory G protein in the McCune-Albright syndrome. *N Engl J Med* 1991;325:1688-95.
- Yuceer N, Kutluhan A, Bekerecioglu M, Arslan H, Akman E. Polyostotic fibrous dysplasia with craniofacial localization presenting with frontal lobe compression in a 14-year-old girl. *Acta Neurochir (Wien)* 1999;141:203-7.