Original article

□ Skull lesions

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SUMMARY: *In this article we will analyze skull lesions, paying particular attention to clinical, radiological and histological characteristics, with therapeutic indications and prognosis. We divided the skull lesions into four groups according to the specific characteristics of each group in order to make this work more schematic and easy to understand. The groups are: 1) primitive lesions, 2) secondary lesions or metastasis, 3) infiltrating contiguous tumours 4) non-tumoral lesions. Primitive lesions: made up of both benign and malignant lesions, that originate from the skull tissues and therefore from a bone component, from the connective or vascular tissue, that together form the various elements of the skull. Osteomas and angiomas, the most frequent lesions, belong to this group. These lesions usually require a radical surgical treatment, for the en-bloc removal of the lesion. Secondary lesions: in this group are the metastasis that effect the bone secondarily, controlling these lesions is more complex and in strict relation with the fundamental neoplastic pathology with its stage of development; even their heterogeneous nature, because of their common characteristics will be discussed together. Contiguous lesions: these are lesions that do not originate from bone tissue, but from neighboring areas such as the cutis and the dura mater. The implication of the bones of the skull in these lesions is generally a secondary phenomenon, nonetheless the skull is included in the removal of these lesions both for a matter of radicality and to improve the prognosis; They are mostly meningiomas and skin tumours as basal-cell carcinomas and squamous cell carcinomas. Non-tumoral lesions: inflammatory pathologies and pathologies whose nature is still uncertain; nonetheless these lesions because of their clinical, radiological and histological characteristics are often part of the differential diagnosis with other lesions mentioned in the article.*

KEY WORDS: *Non tumoral lesions, Skull lesions, Tumors.*

□ Lesioni della teca cranica

RIASSUNTO: *In questo articolo prenderemo in considerazione le lesioni della teca cranica, ponendo particolare attenzione alle caratteristiche clinico-radiologiche ed istopatologiche, con uno sguardo alle indicazioni terapeutiche e alla prognosi. Abbiamo suddiviso le lesioni della teca cranica in quattro gruppi in base alle caratteristiche specifiche di ciascun gruppo al fine di rendere la trattazione più schematica e di facile comprensione. I gruppi indicati sono distinti: 1) lesioni primitive, 2) secondarie o metastasi, 3) lesioni infiltranti per contiguità e 4) lesioni non tumorali. Le lesioni primitive: comprendono lesioni benigne o maligne, che originano propriamente dai tessuti della teca cranica e quindi dalla componente ossea, dal tessuto connettivo o del tessuto vascolare che costituiscono insieme i vari elementi della teca cranica. Di questo gruppo fanno parte gli osteomi e gli angiomi che sono anche le lesioni più frequenti. Queste lesioni prevedono solitamente un trattamento chirurgico con intento di radicalità che implica la rimozione della lesione en-bloc. Le lesioni seconda-*

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rie: comprendono le metastasi che interessano l'osso in modo secondario, la gestione di queste lesioni risulta più complessa, in stretta relazione con la patologia neoplastica di base e con il suo stadio di sviluppo; nonostante la loro natura eterogenea, a causa delle loro caratteristiche comuni verranno trattate insieme. Le lesioni per contiguità: sono delle lesioni che non originano dal tessuto osseo, bensì dai distretti vicini come la cute e la dura madre. Il coinvolgimento delle ossa della teca cranica da parte di queste lesioni, è generalmente un fenomeno secondario, tuttavia nella rimozione di queste lesioni si deve includere la teca cranica sia per motivi di radicalità che per migliorare la prognosi; si tratta prevalentemente di meningiomi e di tumori cutanei come carcinomi basocellulari e squamocellulari. Le lesioni non tumorali: comprendono, sia patologie infiammatorie, sia patologie per cui la diagnosi di natura risulta ancora incerta; tuttavia queste lesioni per le loro caratteristiche cliniche, radiologiche ed istopatologiche rientrano spesso nella diagnosi differenziale con le altre lesioni menzionate nell'articolo.

PAROLE CHIAVE: *Lesioni non tumorali, Lesioni della teca cranica, Tumori.*

□ INTRODUCTION

Pathologies related to the defects of the skull are more and more common in clinical neurosurgery, nonetheless the causes of their increase are not completely known.

The increase in tumours and the progress made in the therapeutic field leading to better prognosis, have determined an increase in the rise of metastasis, highlighting new issues (such as those concerning the treatment of several defects of the skull).

In addition, the number of immunodepressive patients has made more probable the development of infective processes, among these osteomyelitis.

Haematological pathologies, not usually localized in the skull, such as lymphomas, thanks to the improvements in therapies that have led to an increase in the average survival rate, have became more frequent in the skull region.

These factors, connected to an increase in the incidence and survival of neoplastic pathologies have given more importance to the therapeutic approach to these defects also with regard to the reconstructive stage of the skull.

The lesions of the skull can be divided into 3 groups according to their radiological appearance:

1. osteolytic lesions,
2. osteoblastic lesions,
3. mixed lesions; nonetheless we think that for a correct diagnostic and therapeutic framing histopathologic classification is the most useful.

The lesions can be characterized by their primary or secondary localization, if they are neoplastic or non neoplastic and on the base of their degree of malignity (Table 1).

In this article we will describe the details of the nature of these lesions paying attention to the distinctive characteristics of each sub-type.

Skull lesions
1. Primitive tumors of the skull
Benign
• Osteoma • Angioma • Germ cell tumors (*teratomas, epidermoid cysts*) • Giant cell tumor • Aneurysmal bone cyst
Malignant
• Ostesarcoma • Fibrosarcoma • Chondrosarcomi • Ewing's sarcoma
Blood cell proliferative
• Lymphoma • Plasmocytoma
2. Infiltranting tumors by contiguity
• Meningioma • Skin cancers (basal-cell carcinoma, squamous cell carcinomas)
3. Metastasis
4. Non-tumoral lesions
• Eosinophilic granuloma • Paget's disease • Sinus pericranii • Mucocele • Rosai-Dorfman disease • Brown tumor • Fibrous dysplasia • Osteomyelitis • Frontal hyperostosis

Table 1. The main infiltrating lesions of the skull: 1) primitive lesions; 2) secondary lesions or metastasis; 3) infiltrating contiguous tumours; 4) non-tumoral lesions.

□ PRIMITIVE BENIGN LESIONS

❒ Osteoma

Osteomas are benign lesions of mesenchymal origin formed by well differentiated osteoblastic cells that form an osseous lamella tissue similar to that of a normal bone.
In the skull they are frequently localized in the subperiosteal area, unlike other areas where they can have a pure endosteal location. These tumours maintain a normal bone structure that originates mostly in the areas of the outer skull table, mandible and paranasal sinuses, although rare, subdural localization has been reported[1].
Osteomas are neoplasms with a slow growth[26] and represent the most frequent lesions of the skull vault, the most frequent localization is in the frontal sinus (70% of cases).
In the most part they are asymptomatic neoplasms, therefore their real incidence is underestimated and is around 20% of the population.
A patient can be completely asymptomatic, sometimes there can be a swelling in the region interested by the lesion, can report recurrent sinusitis, or, more rarely, neurologic disorders due to the compression of nervous structures; seizures are rare in these lesions. They are more frequent in men with a ratio male:female of 3:1.
Osteomas have usually one localization; multiple localizations are typical of genetic syndromes such as Gardner's Syndrome[26] characterized by gastrointestinal polyposis; soft tissues tumours (such as lipomas, fibromas and sebaceous cysts) and multiple osteomas.
In general because of its paucisymptomatic nature, late diagnosis is frequent and often in patients over the age of 50. Tumours that affect the paranasal sinuses, can become symptomatic for headache and recurring sinusitis.
Osteoid osteoma represents a typical histotype found in long bones, very rarely in the skull, its slow growth and clinical characteristics usually prevent it from having large dimension. Generally, it is a painful lesion, with exacerbation during the night hours and it shows remission when treated with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). This peculiar therapeutic reaction is due to the fact that pain is caused by the release of prostaglandin E, as shown by several studies, therefore NSAIDs interact effectively with this pain pathway blocking its production.
Osteoid osteoma has a high prevalence in males and is typical of the third decade of life.
Osteoblastoma is the most rare histotype, about 30 cases have been reported in literature in almost all of the bone segments, and has a more aggressive behaviour in comparison to other histotypes[46].

■ **Radiology.** These lesions show a homogeneous and well defined shape with respect to the surrounding tissues. At a CT scan and MRI they can have a disomogeneous centre, but without signs of infiltration of the surrounding tissues.
A spiral CT scan is sufficient for the lesion's diagnosis, nonetheless the MRI gives more structural details especially in the intradural and fibrous forms (Figure 1).
A technetium-99 scintigraphy can be used for diagnosis, in which the osteoma appears as a homogeneous hot spot. Pet scans did not prove helpful in the diagnostic phase.
Osteoid osteoma is often surrounded by a reactive bone tissue that in a CT scan results as being hyperdense in comparison to the tumour, forming the so called "nidus" of the tumour, a peculiarity that makes it distinguishable from other lesions of the bone[15].

■ **Histopathology.** Macroscopically, the lesions are round with defined margins, formed by compact bone tissue.
Inside the tumor structure, elements looking like the canals of Havers can be recognized, similar to com-

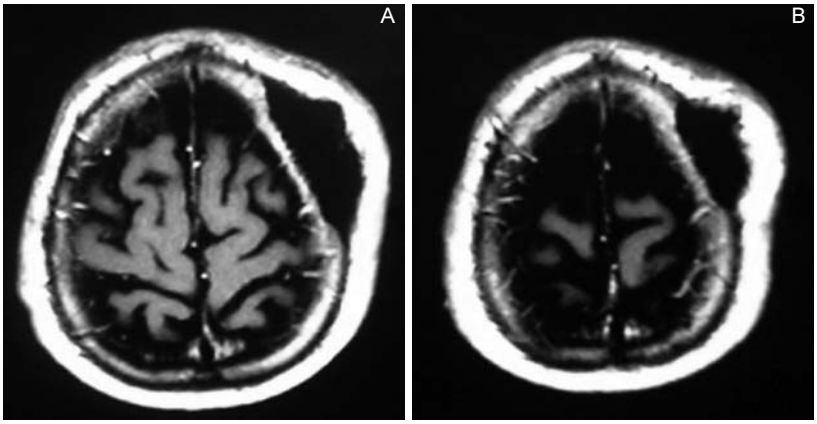

Figure 1. Osteoid osteoma, 75-year-old male with swelling of the front region. Axial T1-weighted gadolinium MRI.

pact bone, often mixed with trabecular bone that can simulate the reactive bone.
Osteomas can be divided into compact and trabecular isoforms.
The first type is made of compact bone tissue and its location is usually in the outer skull table, the second type is made of bone tissue trabecula mixed with adipose tissue and is localized in the diploe or inner skull table.
Osteoid osteoma appears dishomogeneous, of round shape and brown colour, due to hemorrhagic phenomena that can occur.
The lesion is composed mostly of trabecular bone with a woven pattern, interposed by highly vascularized fibrous tissue, covered by osteoblasts.
The lesion can be surrounded by the "nidus", formed by reactive bone, that contains the lesion and has a characteristic radiologic appearance.
■ **Treatment.** Surgery is the treatment of choice for this type of lesion: it is reserved for lesions characterized by a fast growth, that are symptomatic for compression of the parenchyma, the occlusion of a foramen or a pathway.
For some Authors, the removal is indicated for all lesions, when they occupy the nose canals or 50% of the frontal sinus also in asymptomatic patients, because of the risk of sinusitis. For small lateral osteomas the treatment can be conservative and observed during the time. For these patients a two-year radiologic follow-up is sufficient to monitor the lesion and its possible complications[1]. Nonetheless, for aesthetic reasons a surgical treatment of the lesion can be taken into consideration. Generally, osteomas are hard and compact lesions difficult to remove as fragments, therefore it is advisable to proceed with an en-bloc resection.
Nowadays, modern reconstructive techniques have made it possible to repair large bone defects with impressive aesthetic results, the removal of the tumour is therefore suggested with large bone margins, in order to prevent the risk of relapse.
Relapsing is usually a rare event, as are malignant transformations.
Haddad et al.[19] report a 7-year follow up without relapse in patients that underwent a total removal of the lesion.
Osteoid osteoma, 75-year-old male with swelling of the front region. Axial T1-weighted Gadolinium MRI with sequences.

❒ Angiomas

Angiomas are benign lesions formed by malformed vases of neoplastic nature originated in the skull diploe[8].
These lesions can be located, apart from the bone, in any vascularised tissue; in some cases there can be a spontaneous regression with the aging of the patient[12].
Angioma's incidence is estimated at around 10% of all the intrathecal lesions and effects patients in the fourth decade of life, with the prevalence being females[23].
The etiology is unknown, but some authors have put the origin in ectopic mesenchymal tissue, located in the diploe.
Frequently, they are located in the area of the temporal bone, frontal bone, parietal and occipital bone.
The most frequent symptom is headache, caused by the growing of the lesion and by bone erosion, nonetheless the cavernous form, characterized by a slow growth is often asymptomatic.
Neurologic symptoms are rare and can occur in the orbital localization due to compression of intraorbital nervous structures. According to some authors, angiomas can trigger painful syndromes usually in the first two decades of life, due to a fastest growth of the lesion[23].
■ **Radiology.** A correct diagnosis needs a complete radiological study including a direct X- Ray, MRI and CT scan.
Generally, they have a round shape with a "sunburst" or "honeycomb" appearance, with bone trabecular starting from the centre of the lesions going to the periphery.
CT scans show angiomas as osteolytic lesions without sclerotic rim, in an MRI bone trabeculae appear hypointense in T1 weighted gadolinium sequences, assuming homogenously the contrast medium (Figure 2).
■ **Histopathology.** Angiomas are well-defined benign lesions of brownish red colour.
Histologically, these lesions are divided into several sub-types based on the prominence of vascular components; the most frequent forms are: capillary angiomas, venous angiomas and cavernous angiomas.
Cavernous angiomas (Figure 3) are formed by large vascular lacunae with the interposition of fibrous tissue, their vascularization is supported mostly by the middle meningeal artery and by the superficial temporal arteries. The capillary form is characterized by tan-

gled capillaries, while the venous isoform is characterized by dysmorphic veins organized in vascular nidus.
The angioma determines a cortical bone erosion, giving the neoplasm an osteolytic aspect; this phenomenon is also the cause of its painful symptomatology. Osteolysis occurs in the external cortical and only in 3% of cases the erosion can extend towards both sides of the skull[31].

■ **Treatment.** The first to propose a surgical treatment of angiomas was Cushing, in 1923, he indicated the complete removal of the lesion as a fundamental condition to obtain a surgical radicality and reducing the risk of intraoperative bleeding[50]. Indeed, given the difficulty in obtaining a satisfactory hemostasis and given the profuse intraoperative bleeding a lesion debulking is not recommended. Surgery is the treatment of choice, while radiotherapy is reserved for inoperable cases, or when there is a residual after surgery.
In adults, surgery is advisable for symptomatic lesions (headache and neurological deficit), with hemorrhagic phenomena, or with radiologic evidence showing a rapid growth of the lesion or for aesthetic reasons.
According to some authors, an early treatment of the lesions is necessary for pediatric patients, because of the possibility of rapid growth in the first two decades of life[37].

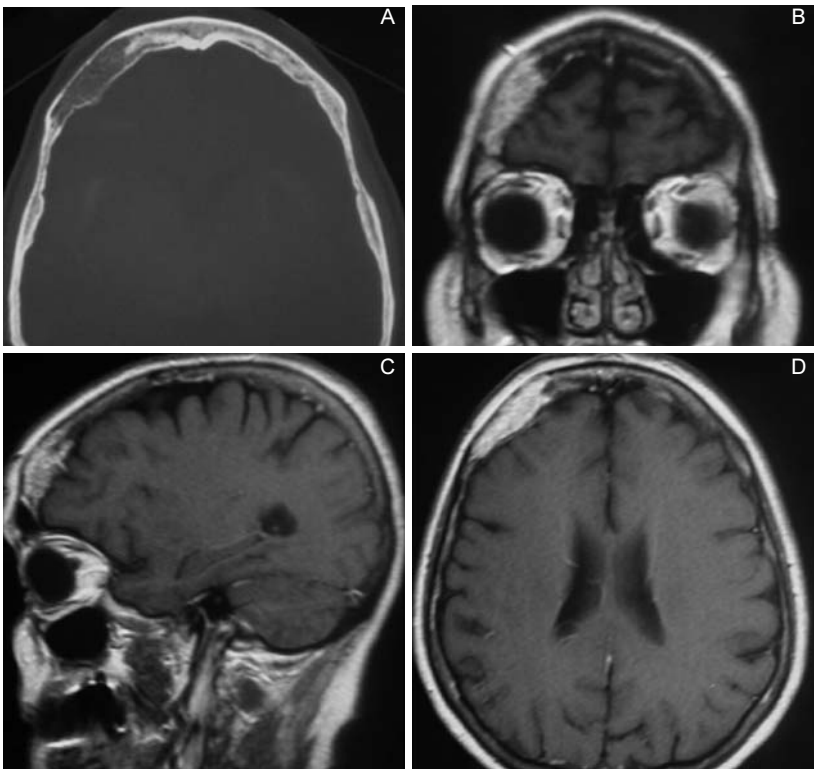

Figure 2. Male, aged 58. Reported headache with pain in the front orbital region, pulsing in clinostatic position. Association of the headache with a swelling located in the skull frontal region: an angioma. Axial cranial CT with bone window (A) and T1 weighted RMI sequences (coronal (B), sagittal (C) and axial (D) sections).

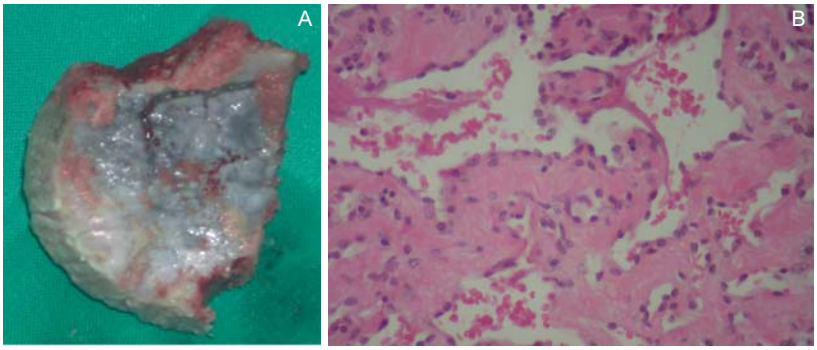

Figure 3. Intraoperative piece (A) and histological section (B) of cavernous angioma.

❒ Neoplasms of the germ layers

❒ **Teratomas.** Teratomas are rare tumours originated by totipotent cells capable of forming tissues deriving from the three germ layers: ectoderm, mesoderm and endoderm. 2.5% of all teratomas are localized in the skull[48].
The term teratoma derives from Greek and means "monster", because of their macroscopically dysmorphic appearance; these lesions are sporadic and do not have familiarity[31].
Many environmental factors have been indicated as being responsible for an increase in the risk of de-

veloping these tumours, nonetheless no direct relationship has been proven; the factors most investigated are: ionizing radiations, folate deficiency, vitamin A excess and exposition to valproic acid[50].
The possibility of developing teratomas has been shown in relation with malformative pathologies, such as the tetralogy of Fallot, and can have various degree of relationship with cerebral tissues.

■ **Radiology.** In MRI it appears extremely heterogeneous varying in relation to the different signal intensity of the tissues contained in the cysts.

■ **Histopathology.** Teratomas are formed by a large variety of tangled tissues in a cystic wall made compact with connective tissue: cartilage, bone tissue, muscles, hair and sometimes also parts of teeth, that form together[31].

❒ **Epidermoid cysts** are lesions that effect mostly females and originate by the inclusion of cells deriving by the ectoderm in the elements of the skull (unlike teratomas that originate by the elements of all the three germ layers)[50].
They have circular shapes, smooth, of white or ivory colour, friable, and, usually come in contact without adhering to the surrounding structures. These tumours can trigger a focal symptomatology for the compression of nervous structures, seizures for irritation of the cortex and only rarely determine a syndrome by intracranial hypertension.

■ **Radiology.** Under a cranial CT scan they present an attenuation similar to the cerebrospinal fluid with a higher density given by their protein content formed mostly by keratins. An MRI allows us to distinguish these lesions from the arachnoid cysts especially in diffusion weighted sequences (Figure 4).

❒ **Dermoid cysts**, unlike epidermoid cysts, are also found in the structure of the dermis, as hair follicles and sebaceous glands, that with their secretions participate to the growing of the lesions[50].

■ **Radiology.** They can easily be distinguished from the epidermoids because they have more consistency and their appearance is more irregular and heterogeneous, furthermore, because of their high lipid content they have a characteristic appearance in MRI, with hyperintense signal on T1 weighted sequence and hypointense signal on T2 weighted sequences (Figure 5).

■ **Histopathology.** Epidermoid cysts are formed by a lamina consisting of epithelial cells that proliferate in the cysts, they desquamate and settle inside the cysts that contain keratin and cholesterol formed by the lysis of the exfoliated cells, together with a lipid content deriving from the secretion of other elements of the cysts.
Dermoid cysts are formed by an epithelial wall surrounded by connective fibrous tissue and enriched by typical elements such as sebaceous glands and complete hair follicles; this is the reason why their content is more heterogeneous, dense and rich in lipid material.

■ **Treatment of neoplasms of the germ layers.** When

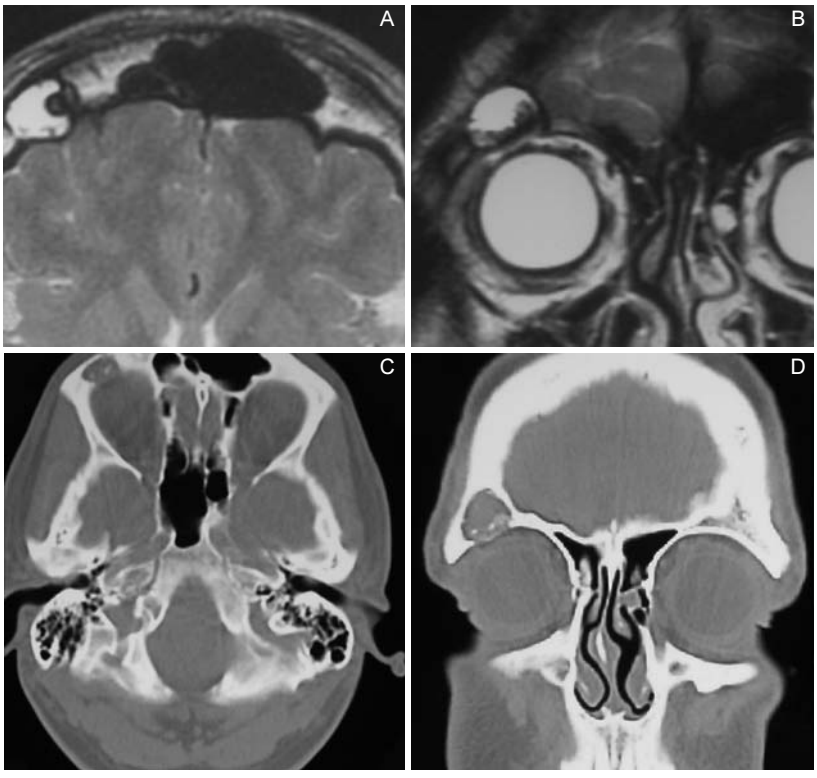

Figure 4. Male, 28 years of age. Reported frontal headache worsened by local digital pressure. RMI gadolinium T2 weighted sequence (2X enlargement): axial (A) and coronal (B) sections; CT cranial scan with bone window, axial (C) and coronal (D) sections. Histological examination confirmed the nature of the lesion: epidermoid cyst.

possible, it is advisable a total en-bloc resection thus determining the complete resolution of the pathology. The surgical removal is always to be taken into consideration as these lesions have the tendency to compress the neighboring structure.

The resection of epidermoid cysts is almost always possible thanks to their friability and scarce adherence to the surrounding structures.

Dermoid cysts are more difficult to remove radically, due to their structure because they can adhere to connective tissues and can often relapse[50].

The treatment of choice is early surgical resection since these lesions grow with time and they also tend to degenerate malignantly[48].

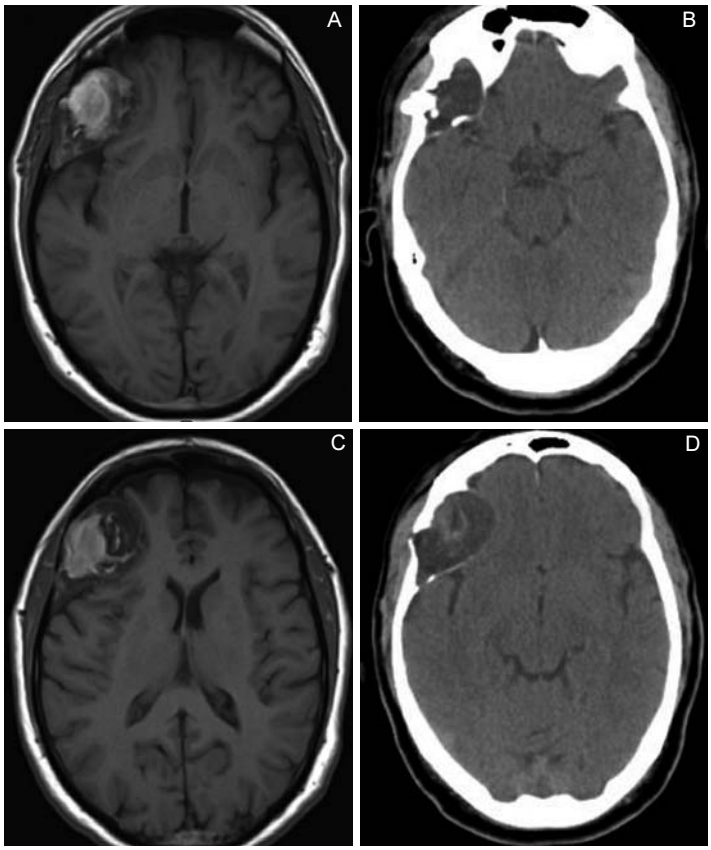

Figure 5. Male, 69 years of age, with visual disorders and drug resistant headache. Dermoid cyst of the sphenoid wing, in T1 weighted RMI sequence, without contrast medium, in axial section (A, C). CT scan of the same lesion in axial section (B,D).

❒ Giant cell tumours

Giant cell tumours or osteoclastomas make up 5% of bone tumours and are usually localised in the long bones and in the mandible. Rarely are they found in the skull. Clinically, they appear as painful growing masses[36].

■ **Radiology.** Under X-rays they appear as osteolytic masses. These tumours do not have specific radiologic characteristics, they can have different density levels in CT scans and different intensity levels in MRI.

Together with these tumours cystic areas are often found and generally captured dishomogeneously by the contrast medium.

■ **Histopathology.** Characterised by a wide structural variety, fibrous and resistant lesions and also gelatinous lesions with a possible cystic presence can be found. Histopathologically, they are formed by poligonal cells, sometimes multi-nucleus, of unknown origin.

These tumours can undergo a malignant degeneration in 10% to 15% of cases.

In cases of a single localisation these lesions are often undistinguishable from granulomas[31].

■ **Treatment.** Total removal of the lesion with ample margins of resection represents the therapeutic gold standard for this pathology, and reduces the risk of recurrence.

Many Authors have underlined the fact that the radicality of the surgery finds its basis in the ample margins of resection of the lesion[31].

To further reduce the possibility of recurrence after surgical removal some authors have proposed the adjuvant treatment of radiotherapy[3].

There are, however, differing opinions on this treatment with some authors saying that radiotherapy is risky in that it could induce a malignant degeneration, also there are many articles describing radio-resistant lesions[50].

❒ Aneurysmal bone cysts

Aneurysmatic bone cysts are benign vascularised lesions, made up of mature ectatic vessels separated by connective and bone tissue[25].

The incidence of these lesions in the cranium theca is around 1%, with no particular prevalence of gender,

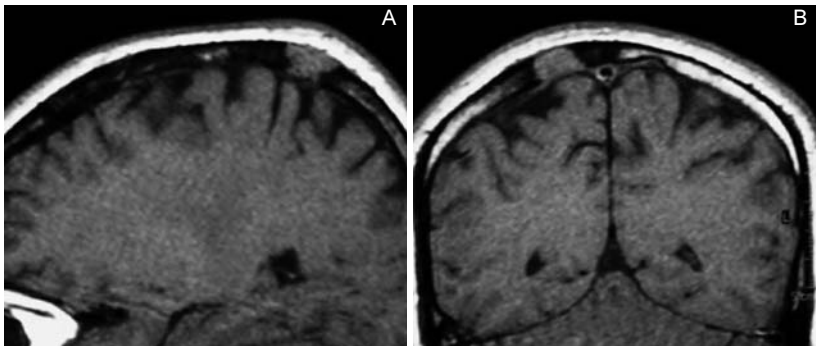

Figure 6. Male aged 22, suffering from headaches for three months. T1 weighted RMI without contrast medium, sagittal (A) and coronal sections (B). Aneurysmal cyst of the parietal bone.

they are usually found in young people under 20 years of age.
The clinical manifestations of these lesions are varied, based on where they are located. The first symptoms can be caused by cerebral bleeding, but more often they behave as lesions occupying space causing: headaches, slowly progressive focal symptomatology and intracranial hypertension.
If they become large enough they can affect the systemic haemodynamics.
■ **Radiology.** Radiological examination of the lesion appears as a multilobular and osteolytic cystic mass similar to "soap balloons" (Figure 6). These lesions have the characteristic of "blowing" the bone tissue without eroding completely the skull tables.
In angiographic sequences they appear as a vascular cluster.
In cranial CT scans the lesion presents hyperdensity, with a signal similar to the blood, divided by trabeculae having the same bone densitometric intensity, that deforms and thins the cortical bone of the skull table.
In MRI they appear as a multilobular cystic lesion with signal intensity as the result of hemoglobin degradation, hyperintensity on T1 weighted sequences with or without gadolinium.
■ **Histopathology.** These are benign lesions made up of dysmorphic vessels with normal endothelium composed of minimal basal membrane.
They form vascular clusters divided by bone septa of normal appearance.
Inside the structure, multinuclear giant cells, small nodules of fibrous or osteoid tissue can be found[31].
■ **Treatment.** Complete surgical en-bloc resection is the treatment for these lesions, thus reducing the risk of intra-operative bleeding[50]. Some Authors advance pre-operation embolization of the vessels as a possible way to reduce the dimension of the lesion and also the risk of intra-operative bleeding[30].
In cases of sub-total resection there is a 50% chance of recurrence, when total removal is not possible radiotherapy has proved to be a valid therapeutic alternative.

□ PRIMITIVE MALIGNANT LESIONS

❐ Osteosarcoma

Osteosarcoma is a malignant mesenchymal neoplasm with tumour elements that produce bone matrix[9].
It is a tumour that typically originates in the metaphyseal region of tubular long bones and is the most frequent istotype of all malignant bone tumours.
Generally, the first sign of their presence is a pathological fracture[19]. Rarely does it affect the skull, the mandible being the area most affected. Osteosarcoma is found mainly in males in two age groups: around 30 years of age and in late adolescence[43].
In the elderly it is usually associated with a pre-existing bone pathology: osteomas, Paget's disease or other benign lesions. Recent studies have linked the malignant transformation in osteosarcoma to mutation of the gene P53.
The most unusual aspect of these tumours is the presence of osteoid in the area of the tumour thus making the tumour appear in part calcified[31].
■ **Radiology.** In standard X-rays these lesions appear as osteolytic areas surrounded by calcification, known as "Codman's triangle", this is a specific radiology indication. This evidence is due to the lesion growth that tends the periosteum and generates lateral calcifications that to radiography appears triangular attenuation areas at the margins of the neoplasm.
The most typical aspect of the lesion is described as "sunburst" where the bone has extended into the surrounding tissues and the cortical has become thin[31].
In most cases intra-cranial lesions can appear as simple osteolytic lesions without any particular characteristics.

■ **Histopathology.** In half of the cases the lesion is painful with associated swelling, firstly extra-cranial and then intra-cranial. These tumours are usually quite large and white or straw coloured due to necrotic-hemorrhagic degeneration with a high proliferation rating and rapid growth.
The aggressive nature of these lesions makes them typically osteolytic with a tendency to completely erode the overlying cortical bone[33].
The cells vary both in shape and size but generally have a hyperchromatic nucleus, with numerous atypical mitoses (often giant cells are present internally).
■ **Treatment.** Treatment consists of the total resection of the lesion followed by chemo and radiotherapy (the chemotherapy consists of several cycles with high doses of methotrexate)[31].
The most favourable factor in surgical en-bloc resection is that 80% of patients remain free of recurrence for 3 years.
Also in the case of sub-total resection a small number of patients have survived up to 10 years.
Another important prognostic factor is how the gene MDR1 which codifies a glycoprotein that induces chemo resistance is expressed[50].

❒ Fibrosarcoma

Fibrosarcoma is a rare form of tumour that originates in connective tissue present in bone marrow, in overlying muscle and periosteum the involvement of the bone is therefore secondary in most cases[35].
They can be secondary to other bone pathologies such as fibrous dysplasia, benign tumour lesions that transform, Paget's disease when undergoing radio treatment.
■ **Radiology.** In x-rays the lesion appears as an osteolytic area of homogeneous density, without great calcification and with no particular characteristics, scarcely capturing the contrast medium both in CT scans and MRI.
■ **Histopathology.** At a macroscopic level these tumours appear as a white mass of soft infiltrating non capsulated tissue, characterized by cells that split and merge into a "fish bone" pattern with necrosis hemorrhagic areas, mitosis and an unorganized cytoarchitecture. Neoplastic cells produce a matrix of collagen around themselves, this occurs also with osteosarcoma and fibrous dysplasia making diagnosis very complex[31].
■ **Treatment.** Radical resection with wide margins is the principal surgical treatment, the main prognostic factor is the absence of infiltration at the margins after the resection. The treatment is usually accompanied by radiotherapy[46,50].

❒ Chondrosarcoma

Chondrosarcoma is a neoplasia formed by cells that produce cartilage[46]. These lesions are rare (0.9% of all lesions) and occur mainly in the fourth decade, the incidence rate among males is twice that of females[6].
The reason for its rarity is in the membrane calcification of the bones of the skull, which doesn't allow for the formation of cartilage during the growth process.
The bones of the skull do not contain cartilage, therefore chondrosarcoma do not form, if not in rare cases as a secondary development to pre-existing bone pathologies, such as Maffucci syndrome[7].
These lesions most often develop in the soft tissue surrounding the skull and begin to grow inwardly eroding firstly the outer and then the inner skull table.
They are mainly found at the base of the skull.
The growth of these tumours is slow and they rarely metastasize, only in the advanced stage.
Local pain or the growth of a lump along with pathological fractures are the primary clinical manifestations of these tumours. Compression of nerves by the tumour may also indicate its presence.
■ **Radiology.** In x-rays these lesions have an osteolytic appearance, surrounded by sclerotic rim, lesions of higher degree contain calcifications and grow rapidly so as to appear nodular in x-rays.
In CT scans the lesion appears hypodense like fat, with multiple internal calcifications that give a starry sky appearance. Using MRI the lesions appear not homogeneous in structure and intensity.
■ **Histopathology.** The lesion appears as a greyish-white mass, lobulated and of hard-elastic consistency.
The larger lesions may have areas of cystic degeneration, signs of necrotic-hemorrhagic degeneration and small calcified areas.
Chondrosarcoma are divided into three grades of malignancy based on their histopathological characteristics and prognosis.
Grade 1 lesions are formed by cells of regular size and shape, with nuclear atypias together with multinucleate elements. The lesions are rich with calcifications and cartilage matrix.

In *grade 2* lesions cells present more atypias and multinuclear cells, giant cells are also present, and it is possible to recognise areas of necrosis in the pericellular matrix and cystic degeneration are frequent.
In *grade 3* lesions cells have irregular dimension and form, their number increases so that the extracellular matrix is almost absent, there are areas of necrosis, several mitosis, and multinuclear cells.
These tumours are also classified based on the base of their histocellular characteristics in clear cell chondrosarcoma, dedifferentiated chondrosarcoma and mesenchymal chondrosarcoma.
Clear cell chondrosarcoma appears hypochromic to histologic colours, because of an abundance of intracellular Golgi apparatus, contains cells with eosinophil cytoplasm and multinuclear giant cells[31].
The dedifferentiated form is the most malignant, associating classic chondrosarcoma areas with areas of highly undifferentiated sarcoma with atypical cells. This form is the result of the halt in the maturing of staminal elements contained in the parenchyma.
The mesenchymal form of chondrosarcoma is characterized by: small, round cells, with little stroma and appear as highly vascularized lesions.
■ **Treatment.** The treatment for these tumours is wide resection right up to apparently healthy tissue.
Recurrence is frequent due to the difficulty in totally removing the lesion.
Chemotherapy is ineffective and not indicated, radiotherapy (proton beam) however has given good results and is indicated as an adjuvant treatment of these lesions[50].

❒ Ewing's sarcoma

Ewing's sarcoma is a malignant tumour of mesenchymal origin found mainly in children and young adults[278]. These lesions rarely affect the skull (only 4% of Ewing'sarcoma are localized in skull bones) and are found mainly in males[28].
■ **Radiology.** With neuroimaging these lesions are often described as "onion skin" or "sunburst" in appearance, they can appear as an osteolytic area capturing dishomogeneously the contrast medium thus simulating a sarcoma[28].
■ **Histopathology.** The tumour consists of an osteolytic mass accompanied by an intense periosteal reaction with the formation of reactive bone tissue.
The cells have scarce cytoplasm, a small, dense, hyperchromatic nucleus, and tend to form pseudo roses.
■ **Treatment.** The treatment of choice is surgery associated with chemotherapy (with cyclophosphamide and doxorubicin) and radiotherapy.
In general, the prognosis is better in the primitive forms of the cranium with respect to other localizations[50].

□ BLOOD CELL PROLIFERATE TUMORS

❒ Lymphoma

Lymphomas are tumours formed by neoplastic cells of the lymphoid variety.
Lymphomas are divided into Hodgkin and non-Hodgkin varieties[34] (Figure 7 and 8). Hodgkin's lymphomas are mostly benign and are localized most often in lymph nodes, they usually do not cause endocranial lesions[34]. Non Hodgkin lymphomas can be found in all tissues and therefore also in skull bones. Non Hodgkin lymphomas are classified into four groups (Revised European-American Lymphoma: REAL classification): T-cell precursor; B-cell precursor; peripheral T-cell; peripheral B-cell[27].
Skull lymphomas are quite rare and are found in 25% of non-Hodgkin tumours, as secondary localizations[50].
They present clinically in various ways depending on growth rate and early diagnosis. Endocranial hypertension, focal deficit, drug-resistant headache, weakness and recurring infection are possible symptoms[31]. Other symptoms can depend on the systemic distribution of the disease depending on the tissue and organs affected.
■ **Radiology.** For a correct diagnosis radiological exams are fundamental: in CT scans they result as hyperdense osteolytic lesions capturing the contrast medium, in MRI they are hyperintense in T2, capture homogeneously the contrast medium and signs of invasion of the dura mater may be seen.
■ **Treatment.** Resection is not generally indicated for lymphoma with chemotherapy or radiotherapy the preferred treatment, only in the case of a singular localization can resection be an option.

❒ Plasmacytoma

Plasmacytomas are neoplastic lesions of plasma cells present in the diploe and are usually found as single lesions[4].

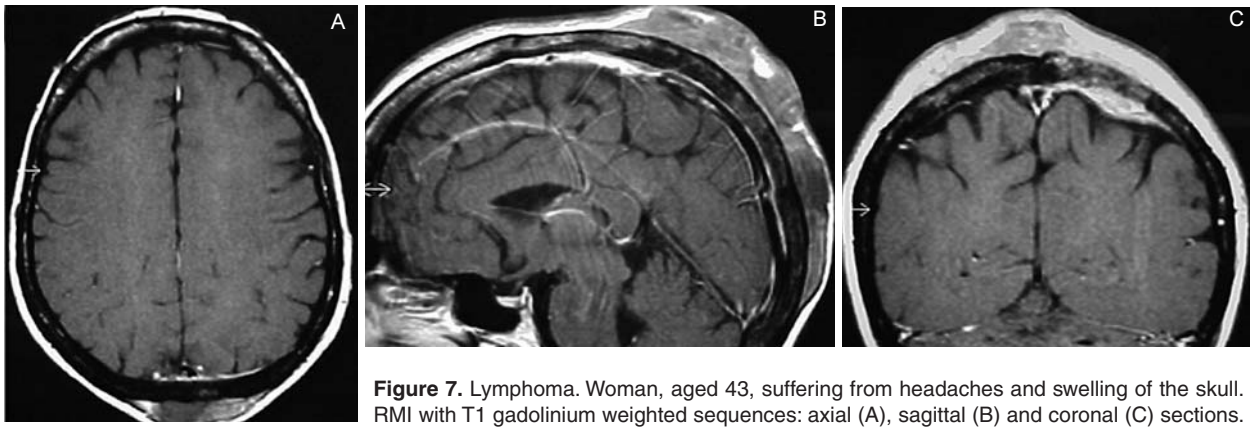

Figure 7. Lymphoma. Woman, aged 43, suffering from headaches and swelling of the skull. RMI with T1 gadolinium weighted sequences: axial (A), sagittal (B) and coronal (C) sections.

They make up 3% of multiple myeloma (where lesions can be found throughout the skeleton)[10].
Bone localizations of plasmacytoma can be similar to those of multiple myeloma (vertebrae, skull, pelvis and femur) and in most cases these lesions lead to multiple myeloma.
Plasmocytoma rarely occurs in skull bones and is found mainly in elderly patients with no prevalence between the sexes.
Symptoms are often due to other disease and infiltrate and destroy bone tissue producing high levels of immunoglobulin and reducing humoral immunity.
The most important symptoms are: hypercalcemia, pathologic fractures, renal failure, recurring infections, amyloidosis, bone pain and ischemias[4].

■ **Radiology.** In radiology exams plasmacytoma can show as a single osteolytic lesion or as multiple myeloma. Generally these lesions have well marked margins easily distinguished from the surrounding structure, possibly surrounded by a reactive sclerotic rim.

■ **Histopathology.** The plasmocytal cells form an osteolytic mass that erodes the bone cortical causing pathologic fractures and periosteum tension, this last factor is responsible for strong local pain.
In histological exams plasmacytoma has an elevated plasma cell count infiltrating bone marrow or substituting it with cellular cordons.
The cells have an eccentric nucleus surrounded by a clear halo that represents a very well developed Golgi apparatus.
The cell population is made up of an abnormally high number of mature cells, along with these cells various other neoplastic cells develop such as: plasmablast, with a clear and prominent nucleus; multinuclear cells; flame cells, exhibiting red cytosol; Mott cells, including several fibrillars (fibrils, Russel bodies)[31].

■ **Treatment.** Treatment is generally based on the treatment of the underlying pathology, usually radiotherapy or chemotherapy, surgery is indicated only when the plasmacytoma is localized in a single location[50].

□ INFILTRATING CONTIGUOUS LESIONS

❒ Meningiomas

Meningiomas are the most frequent lesions to infiltrate skull bones, arising from the arachnoid cap cells of the Pacchioni granulations in the meninges[18,42].
They are benign, solid, hard elastic lesions that grow throughout the dura mater, occasionally they can be found inside ventricles and rarely in bone tissue[13].
Meningiomas generally cause hyperostosis in skull bones, this can be due to the infiltration of bone tis-

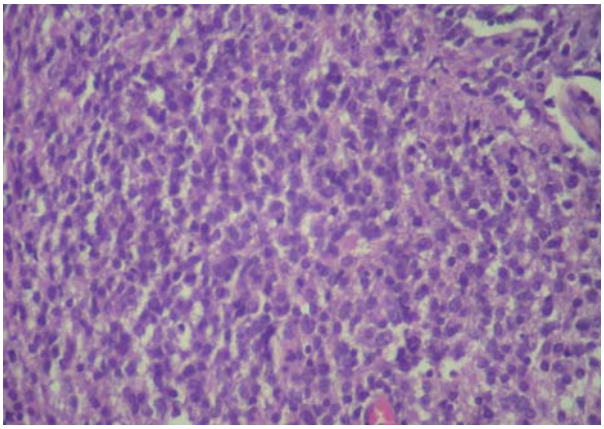

Figure 8. Histological section of a B-cell non Hodgkin lymphoma.

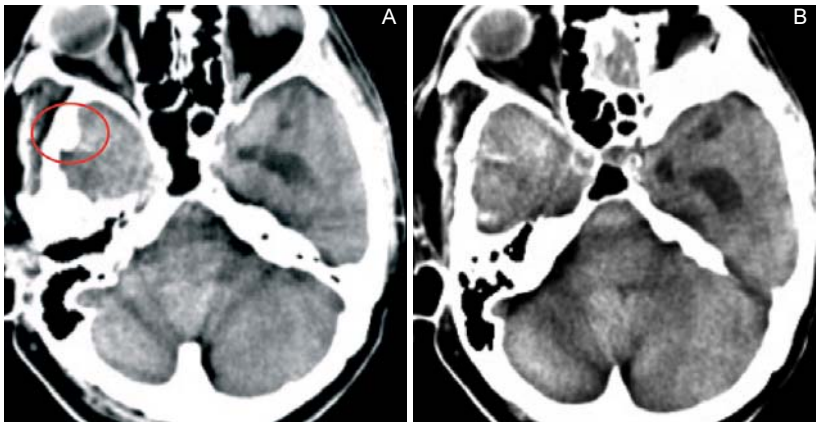

Figure 9. Particulars of an axial section of a 67 year old female patient with meningioma in the sphenoid bone (the circle indicates the reactive hyperstosis zone).

sue by neoplasm or the reaction of normal bone. In cases in which the meningioma infiltrates the bone, in histological exams it is possible to find meningioma cells in the context of bone tissue, tumour cells may also be found in surface cells.

In reactive hyperostosis there is no pathological infiltration of bone tissue, the bones do however take on a disorganized aspect, typical of an inflammation.

In more rare cases meningioma can erode bone tissue even to the point of breaking their continuity and proliferating in surface tissue.

■ **Radiology.** In cranial CT scans they appear isodense, with the possible presence of edema, of internal calcifications and signs of reactive hyperostosis (Figure 9). The skull bones may appear thicker, eroded or discontinuous.

MRI represents is the most specific form of radiology, in MRI with contrast meningioma appears as an iso-hyperintense area (Figure 10 and 11) with internal calcifications and possible evidence of "dural tail"; they are generally seen as lesions that compress and dislocate without infiltrating the cerebral parenchyma.

Meningiomas capture homogeneously the contrast medium and, above all, if of a large dimension they can be surrounded by perilesional edema.

■ **Histopathology.** Meningiomas grow as rounded lesions with an obvious dural attachment that compresses rather than infiltrates the cerebral parenchyma.

Meningiomas usually grow in the direction of the cerebral parenchyma but have also been known to grow externally infiltrating the skull causing reactive hyperostosis.

Another form of growth of meningioma is the so called "*en claque*", where the lesion

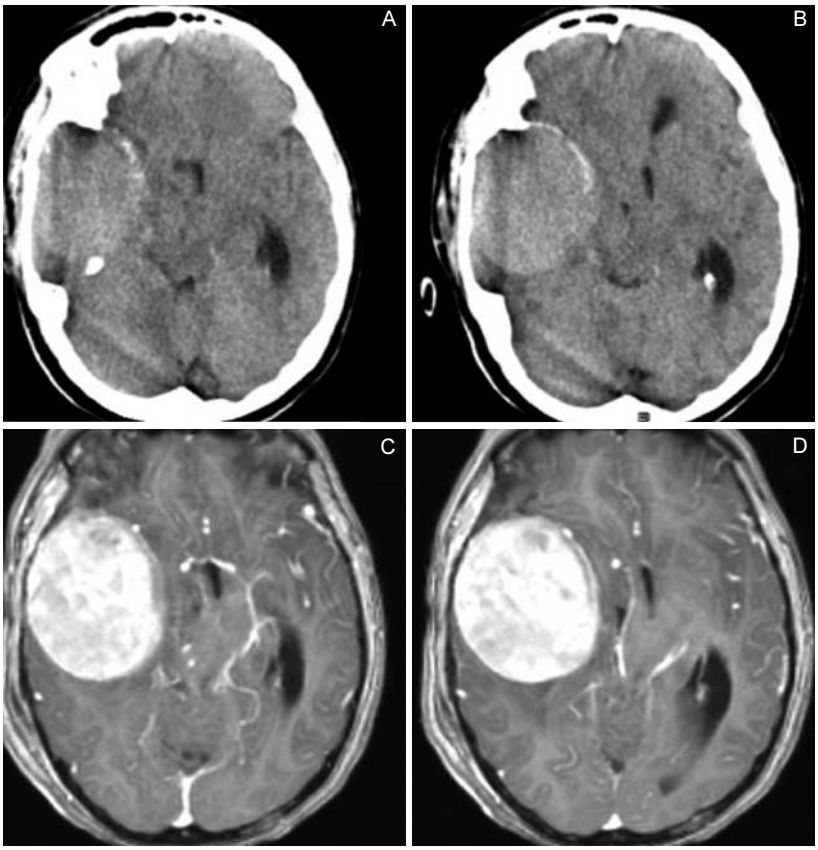

Figure 10. 67 year old female with meningomia lesion in emergency room for epilepsy. Section of CT scan of the skull, without contrast, and axial sequence of MRI in T1 with gadolinium.

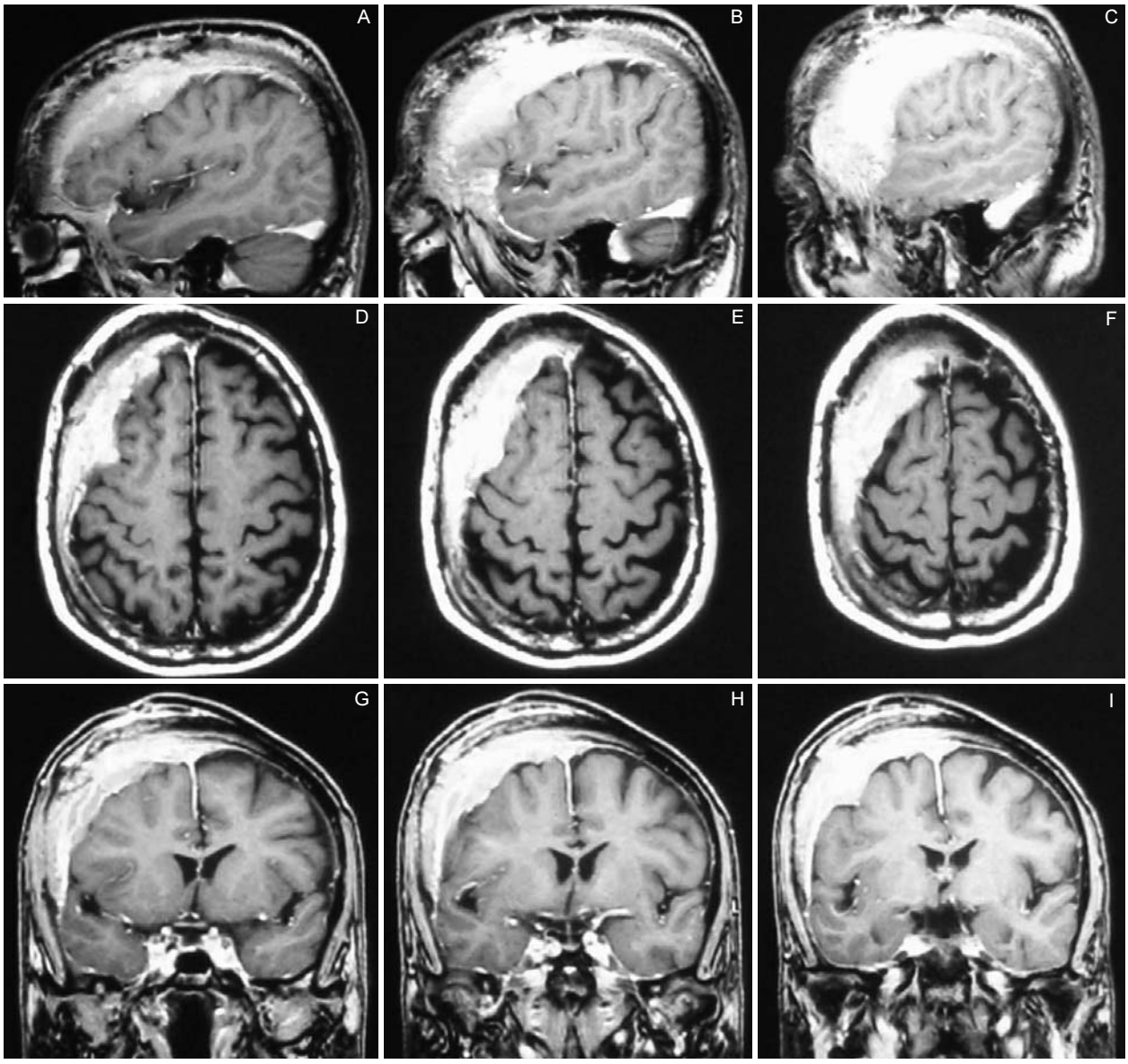

Figure 11. Male, 68 years of age, complains of excessive frontal headaches on a daily basis. Associated with the headaches is swelling of the pericranial soft tissues and tonic-clonic seizures. Coronal (A, B, C), sagittal (D, E, F), and axial (G, H, I), section MRI in T1 with gadolinium. Right fronto-parietal meningioma.

tends to form a laminate and grows in a transversal sense.

The consistency of the lesion is hard elastic of a pinkish-grey colour, calcification is possible as is, in rare cases, necrotic hemorrhagic phenomena.

Meningiomas are distinguishable in various histotype each with different prognosis and therapy.

BENIGN MENINGIOMA (grade I classification World Health Organization: WHO: low risk of recurrence and aggressive growth) includes histological variant other than clear-cell, chordoid, papillary, or rhabdoid, and lacks criteria of atypical and anaplastic meningioma.

The *meningothelial* (also called syncytial or endothelial) *form* is the most common, its cells are uniform and tend to form whorls (Figure 12); the *fibroblastic* (*fibrous*) *form* has fused elements that produce collagen, and the *transitional* (*mixed*) *form* is an intermediate form of the previous two.

The *psammomatous form* is composed of cells containing psammoma bodies formed by calcium deposits

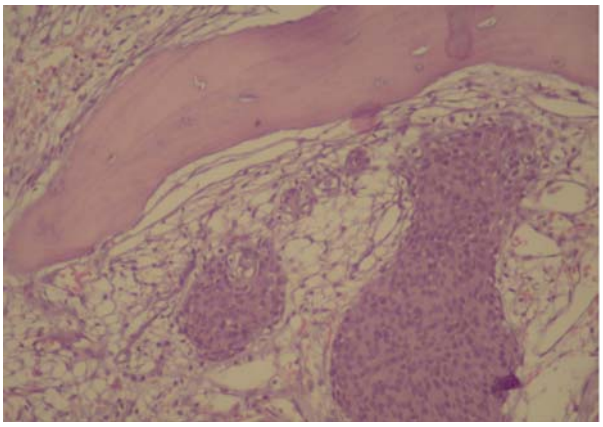

Figure 12. Histological section of meningothelial meningioma.

of "onion skin" appearance. The *secretory form* is composed of cells that secrete a PAS (Periodic Acid-Schiff) positive substance that is deposited in cell vacuoles, whilst in the microcystic form the neoplastic tissue has a cystic structure.
Other forms of meningioma that are much rarer are: the *lymphoplasmacyte-rich meningioma* rich in plasmocytes with inflammatory infiltrations; the *metaplastic form* with an unclear level of malignancy and the infiltration of the mesenchymal tissue (from which bone and cartilage components originate and are found in meningioma); the *chordoid meningioma* with histological resemblance to chordoma (grade II WHO: meningiomas with greater likelihood of recurrence and/or aggressive behaviour); and finally the *clear cellular form* (grade II WHO) with polygonal shaped cells with clear cytoplasm but rich in glycoprotein[34].
Atypical meningioma constitutes another malignant variety (grade II WHO) and is characterized by a higher MIB-1, with cells having a very prominent nucleus[34].
Papillary maningioma is also considered malignant, grade III WHO, associated to a high rate of local relapsing (55%) and a worse prognosis in comparison to other forms developing systemic metastasis (20%)[34]. The papillary form is constituted of metaplastic cells with polymorphic nuclei formed around a fibrovascular axis, in 75% of cases the underlying parenchyma is infiltrated.
Malignant forms of meningioma exist, characterized by the presence of mitosis and necrosis in the context of the neoplasm[31]. The two principal malignant hystotypes are: the *rhabdoid* and the *anaplastic*, both are considered to be grade III WHO[34].
The *rhabdoid form* is characterized by the presence of rhabdoid cells with eccentric nuclei and eosinophil cytoplasm, by the infiltration of the underlying parenchyma with areas of mitosis and necrosis.
The *anaplastic form* is characterized by atypical and dishomogeneous cells with a high level of mitosis. In malignant hystotypes the prognosis is generally poor, around 2 years[34].

■ **Treatment.** Treatment for these lesions involves complete surgical removal including resection of the associated dura[50] (Figura 13). Where complete removal is not possible an acceptable level of radicality can be achieved by removing the lesion and coagulating the base of the dural attachment.
Residual tumours require adjuvant radiotherapy or radiosurgery especially for small lesions or in the proximity of functional areas[38].
Where infiltration of the overlying bone tissue has occurred the surgery must be more radical and also include the removal of the infiltrated bone at least to where the bone appears healthy[38].

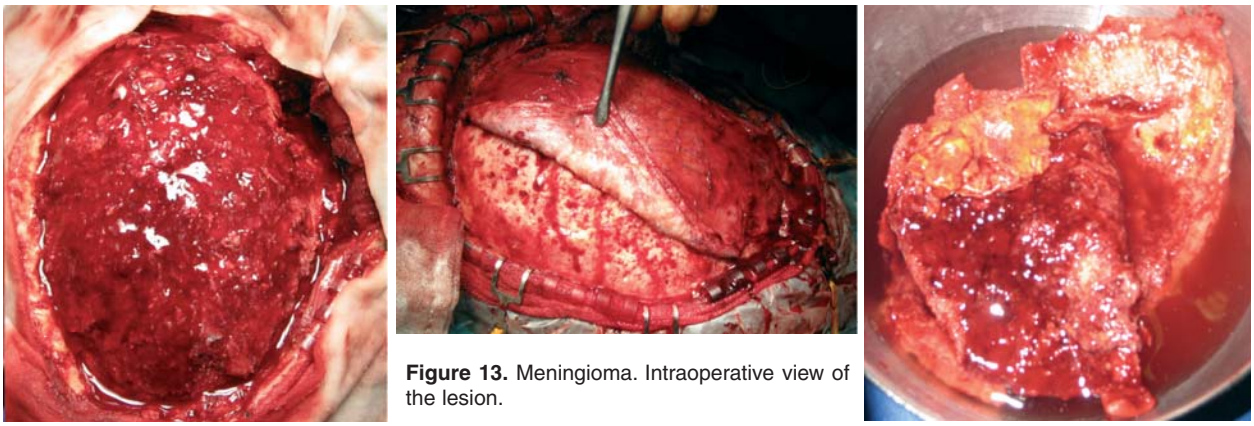

Figure 13. Meningioma. Intraoperative view of the lesion.

Where there is infiltration of superficial tissue this must also be removed, thus reducing the chance of recurrence.

❒ Cutaneous tumours

The head is a region where skin tumours are frequently located because of its exposure to UltraViolet (UV) rays for long periods of time[2].
Malignant cutaneous lesions are epidermic tumors, that can infiltrate the underlying bone[2].

❒ **Squamous cell carcinoma.** The squamous cell carcinoma is the most frequent cutaneous tumour of the scalp, affecting mostly elderly males.
The main factors favoring these neoplasms are: exposure to UV rays, baldness (facilitates scalp skin exposure to the sun rays), exposure to derivatives of arsenic or tar, or previous scarring[47].
Some genetic diseases such as the xeroderma pigmentosum have been associated to an increase of the risk of incidence of these tumours[31].
The most important random factor for this neoplasm is the exposure to UV rays as they induce DNA alterations causing the formation of abnormal Thymine dimers[47].
These alterations are responsible for the mistakes of transcription and translation of the genetic code causing mutations responsible for the loss of cell proliferation control.
■ **Histopathology.** Macroscopically, these lesions are red and flat during the phase of carcinoma in situ then become nodular and keratinised in the most advanced phases of malignant degeneration.
The tumor cells have atypical nuclei, show mitosis and occupy all the epidermis layers.
The lesions in the most advanced invasive phases change their cell patterns due to the appearance of cylindrical cellular elements aggregated in cell groups that produce keratin and highly anaplastic round cells mixed with necrotic areas.
In the more malignant tumor, given the absence of cell elements of differentiation, immunohistochemical analysis can be essential to find desmosomes and keratin, expressed by the precursors of the tumour cells.

❒ **Basal cell carcinoma.** Basal cell carcinomas are common slow growing skin lesions, that affect mainly people of fair skinned complexion[40]. These tumours can have an exophytic form, similar to a red underskin papule that with keratin can simulate a nevus (Figure 14), or they can appear as cutaneous ulcers that frequently invade the skull bone tissue (ulcus rodens phenomenon)[31].

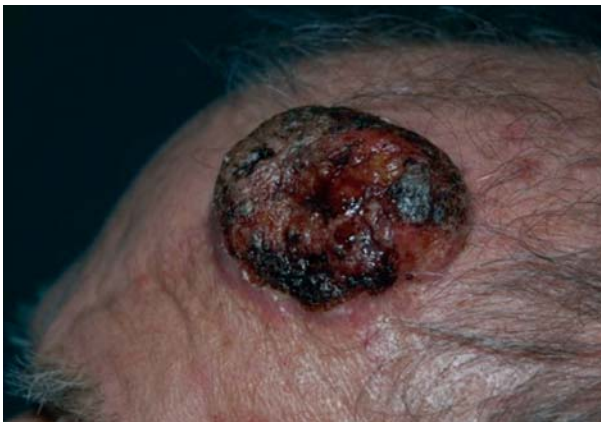

Figure 14. Male aged 78: reported frontal skin swelling. Basalioma.

■ **Histopathology.** Basal cell carcinomas have two growth patterns: multifocal, with multiple lesions that are flat and superficial; and nodular, where the growth extends quickly to the deeper layers of the skin.
The lesion is formed by polygonal cells with hyperchromatic nuclei organized as nidus or cords.
A myxoid stroma is found around the cells surrounded by fibroblasts and inflammatory cells[31].
The cells are organized in palisades, that during the fixation procedures, because of the retraction of the mixoid matrix, form clefts, these phenomena are useful for the diagnosis even if of artefactual nature[31].

■ **Treatment.** Treatment depends on primary tumor location and extension. Surgery and radiotherapy appear to be the most effective treatments. Squamous cell carcinoma tends to be more aggressive than basal cell carcinoma, and as such needs a promptly and complete extirpation with the best possible cosmetic result.

□ SECONDARY LESIONS

❒ Metastasis

Metastases are the most frequent malignant lesions in skull bones, 60% of skull lesions come from lung or

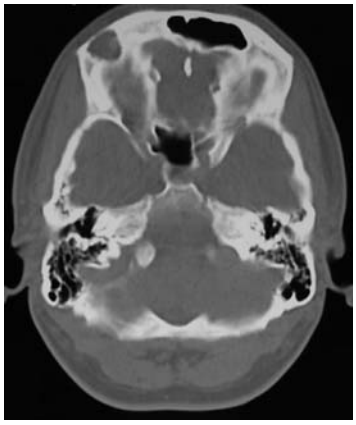

Figure 15. Male, 23 years of age, with orbital headache that is drug-resistant. Projections of skull CT with sequences reconstructed in axial view. Eosinophilic granuloma.

breast neoplasms caused by selective tropism via bone tissue[50].

Other tumours such as carcinoma of the prostate, of the uterus, of the thyroid and hepatocellular carcinoma tend to metastasize toward the skull, they are however quite infrequent and therefore have little effect on the skull[50].

Metastatic lesions can be divided into: osteolytic, osteoblastic or mixed and have a tendency to grow towards both the bone corticals.

Symptoms frequently include persistent, drug resistant headaches, focal impairment caused by compression, endocranic hypertension, and seizures. These symptoms are found together with the symptoms of the original pathology.

In radiologic exams these lesions appear as osteolytic areas or osteoblastic lesions[22].

Osteolytic lesions are more common, whilst osteoblastic lesions in metastasis from carcinoma of the prostate and the breast[29].

Metastasis of the skull are often lesions capturing contrast medium in MRI, these exams are vitally important as they allow us evaluate relationship with the meninges and surrounding tissue as well as the exact extension of the lesion.

The treatment of the metastasis is subordinate to the treatment of the original diseases, and depends on the number (usually not more than three), the localization and the general condition of the patient (Karnofsky Perfomance Status: KPS), lesions present in other locations, neurological status and histotype of the lesion).

KPS and the stage of the disease are the prognostic factors for patients, excluding cases of acute deterioration, an oncological evaluation and the stage must be taken into account before deciding on a treatment.

In general, if this is the first manifestation of neoplasm the treatment will depend on the type of lesion. Some authors advise the treatment firstly of the original lesion and only after the treatment of the metastasis; our view is that while correct from a prognostic point of view this line of intervention is not always possible, and depends on the state of the disease as well as on the neurological progression and the histotype of the lesion. A case by case evaluation with oncologists and radiologists is a must.

When possible and indicated, surgical treatment consists of complete resection en-bloc with wide margins, verifying the margins with intraoperative samples.

Collegial evaluation seems to be the optimal strategy for patients especially in cases where the lesion cannot be completely removed.

□ NON-TUMORAL LESIONS

❐ Eosinophilic Granuloma

Langerhans cell histiocytosis is a term used to indicate three types of pathologies that express a disorder involving the proliferation of the histiocytic cells. They include eosinophilic granuloma, Hand-Christian pathology and Letter-Siwe syndrome[49].

The Letter illness is the most widespread form of the pathology. It is highly malign and behaves in a fulminating manner. Christian syndrome features diencephalic disturbances with diabetes insipidus, diffuse granulomas and exophthalmia[31].

The eosinophilic granuloma, on the other hand, is a benign, focal lesion involving the bones of the cranium, featuring proliferating histiocytes that infiltrate the surrounding tissues.

X-rays show the lesion as an expansive mass that erodes the surrounding bone tissue.

The granuloma can be found in any bone tissue, though it mainly affects the cranium (the most frequently-affected site), ribs and pelvis[31].

This illness affects young people, Caucasians under the age of 30, and chiefly involves the frontal and parietal bones.

There is also the multi-focal form known as Langerhans cell histiocytosis, a benign disease which spreads to the bone and skin tissue as well as organs, involving the ears and respiratory tracts[31].

The most widespread form is common in children and presents itself with pains throughout the body, temperature and recurring otitis.

■ **Radiology.** In standard X-rays the lesion appears as an osteolytic mass with a sclerotic rim.
Under a CT scan, it appears as an isodense mass in relation to the cerebral parenchyma which can extend towards both the bone plates, or only towards the outside plate (resembling a champagne cork) (Figure 15).
■ **Histopathology.** These lesions are mainly made up of dendritic cells whose surfaces possess the antigens of immune cells. They possess abundant cytoplasm, with vacuoles and so-called HX bodies characterised by tubular rods whose ends are dilated (resembling a tennis racket)[31].
■ **Treatment.** Treatment can include the total resection of the lesion (Figure 16) or radiotherapy, some protocols include radiotherapy in low doses after surgery to prevent local relapses from occurring.
The relapse rate is 30% 12 years after resection, and is higher in young people, where radiotherapy is indicated to help prevent systemic dissemination of the lesion. Some centres have proposed chemotherapy for individuals of paediatric age[50].

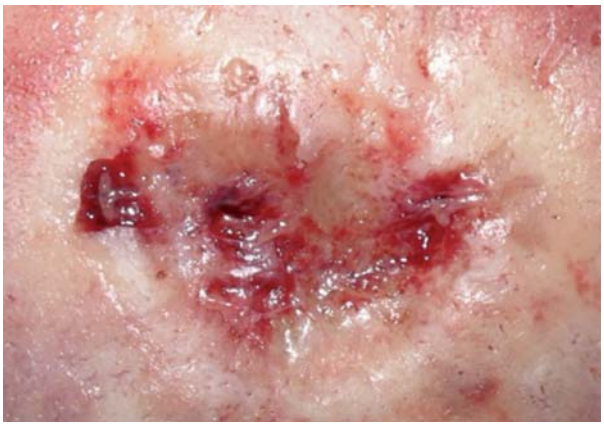

Figure 16. Intra-operative part of the lesion: eosinophilic granuloma.

❒ Paget's disease

Paget's disease involves an alteration of bone metabolism, with a high turnover, and abundant cells organised in a chaotic manner.
The development of this disease involves two pathogenetic phases: the bone loss phase, and the bone-producing phase, which alternate with one another, and in the end generate a sclerotic, over-abundant bone[17]. The process is not unitary, and there can be areas of the same bone at different production stages.
Paget's disease mainly affects the elderly (3% of the population) without any one sex being prevalent. It affects the skull in 65% of cases.
The dysmorphic bone is painful as well as being more fragile, and can provoke pathological fractures, compression of the cranial nerves, flattening of the base of the skull and basal impression in 33% of patients[11].
It is often linked to malign forms of degeneration, with the formation of chondrosarcomas, fibrosarcomas and osteosarcomas.
The possibility of a malign degeneration occurs in 0.9%, in rare cases they can also give rise to osteoclastomas in the same site as that of the Paget's disease, particularly in the case of the elderly[31].
■ **Radiology.** X-rays show the disease as having three main appearances: sclerotic, osteolytic radiolucency and mixed form. The sclerotic form is made up of thick cortical bone and trabeculae not transparent to X-rays. The osteolytic form presents itself as a circumscribed area of bone loss. In Paget's disease, the radiolucent areas are foci of bone loss.
The CT scan with bone windows reveals a thickened, irregular cortex with various areas of bone loss.
The MR images reveal bone that is thicker than normal, misshapen and with an intensity that is different to nearby bone segments, compressing the parenchyma.
■ **Treatment.** Treatment for these patients is generally of a medical nature, with bisphophonates and calcitonin; surgery should only be taken into consideration in selected cases as the bone is highly vascularised and therefore at a high risk of serious blood loss.
Paget's disease is a systemic disease of the bone, and as such tends to recur[17].
Surgery is also reserved for cases with malign degeneration of the pathological bone. This is highlighted by the presence of a faster growing osteolytic mass with or without a sclerotic rim[50].

❒ Sinus pericranii

Sinus pericranii is a lesion featuring a series of abnormal communications between the cranial venous sinuses and the pericranial and subcutaneous veins[5].
In general they are lesions that develop along the median line, along the superior sagittal sinus, and can cause headaches, discomfort and bradypnea.
The cause of the lesion is not known. There are many theories; some Authors view it as an extended venous

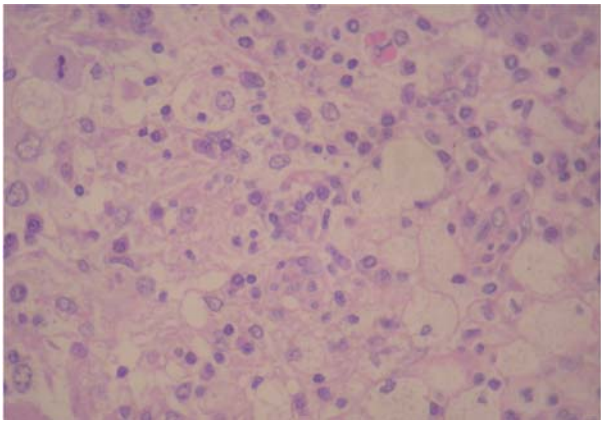

Figure 17. Histological section of a Rosai-Dorfman lesion.

angioma, and therefore as a congenital malformation lesion; others consider it the outcome of a post-traumatic lesion on the site of a previous fracture; other Authors propose a mixed aetiology, both traumatic and malformative, where a nest of small anomalous emissary veins becomes hypertrophied owing to the presence of post-traumatic endocranial hypertension, or is induced by a cough reflex[39].

The mass comprises a median vascular nest which tends to increase with Valsalva manoeuvres and with changes in posture, is of a soft consistency, and is easy to reduce with direct compression.

■ **Radiology.** It appears as an osteolytic mass in X-ray images. In angiographics it is shown as a cluster of veins which is particularly clear in the venous phases, with clear communications between the cortical and superficial veins. Only rarely does it involve intra-dural circulation.

■ **Treatment.** Treatment is suggested chiefly for aesthetic reasons, or to avoid copious local bleeding. Treatment involves complete resectioning of the bone involved and cranioplastic reconstruction, or the resection of the mass alone, with coagulation of the vascular peduncles[50].

❒ Mucocele

A mucocele is a benign cystic lesion which sees slow growth and the development of mucus-filled material produced by the cells of the wall[50].

The aetiology of the lesion is not known, but it can cause sinusitis by obstructing the cavity linking the sinus with the nasal cavities[14,21].

The mucocele can also extend to pericranial tissues, eroding the external cortex completely, and in most cases is entirely asymptomatic.

■ **Radiology.** In CT sequences, the radiological appearance is iso-hyperintense in relation to the cerebral parenchyma, with deformation of the bone containing it, which appears as though "blown-up" by the lesion. MR images tend to be varied in appearance owing to signal intensity. This variability depends on the presence or otherwise of infections, and the hydro-lipid content of the cyst secretions (most of these lesions appear hypointense in T1 sequences).

■ **Treatment.** Treatment for these lesions involves surgical removal with an end to removing the mass effect, removing the wall that is responsible for relapses and restoring communication with the nasal cavities if this has been interrupted[50].

❒ Rosai Dorfman disease

This disease sees the proliferation of the lymph nodes, and mainly affects young individuals, with incidence peaking around 20 years of age[41].

Patients may present a lymphadenopathy in the neck and local pain associated with leucocytosis, anaemia and hypergammaglobulinemia.

Around one third of cases also affect other areas, such as the eye, the respiratory system, the meninges and the skull.

Its aetiology is not known. However, there are many pathogenetic hypotheses regarding the origin of these lesions: viruses, tumours and that of immune pattern alterations.

The differential diagnosis should be compared with other disorders affecting the histiocytes[27].

The main histological characteristics (Figure 17) are: infiltration of plasma cells, infiltration of histiocytes and the phenomenon known as emperipolesis (namely the passage of immune cells to the area of eucariote cells). This element is vital for diagnosing this disease, although not exclusive.

The involvement of the skull by these lesions triggers epileptic fits and intracranial hypertension without specific symptoms. Figures in literature describe rare cases of malign evolutions. Generally speaking the adenopathies remain asymptomatic and can also follow an intermittent course.

In addition, treatment with chemotherapy and radiotherapy do not seem to have an effect on the course of the illness. Cases in which the disease resolves itself spontaneously have been recorded[50].

❒ Brown tumour

Brown tumours are lesions that involve an excessive proliferation of osteoclasts stimulated by over-secretion of parathormone[24].

Hyperparathyroidism is an endocrinological disorder involving anomalous secretion of parathormone, and can be divided into various types, according to the tissue responsible for the anomaly.

Primitive hyperparathyroidism is caused by the hyperplasia or tumoral degeneration (generally the formation of an adenoma) of the parathyroids; secondary hyperparathyroidism is caused by chronic hypocalcaemia (of renal, dietary or genetic origins) with subsequent compensation of the parathyroid, and hypertrophy and hyperplasia of the glands.

Brown tumours are the chronic manifestation of hyperparathyroidism featuring the thinning of the bone cortex until "erosion cones" are formed along the length of the structure.

The pathology is mainly located in the trabecular bone where the osteoclasts, stimulated by the osteoblasts activated by parathormone, are located mainly in the middle of the trabecular bone. The process of reabsorption of the bone matrix gets underway, dividing the trabecular elements in half and giving rise to the "osteochondritis dissecans" phenomenon[31].

The brown tumour forms when the destruction of the cortex (Figure 18) triggers micro-fractures that attract macrophages and inflammation cells to the site. These cells cause the formation of fibrous tissue, and a brownish mass which replaces the area where bone was lost.

The lesion is typically brownish in colour owing to the intense vascularisation and the haemorrhages which occur inside.

Brown tumours have a considerable tendency towards cystic degeneration.

Surgery is essential for removing and treating the lesion, but cannot be carried out without definitively curing the cause of the hyperparathyroidism[31].

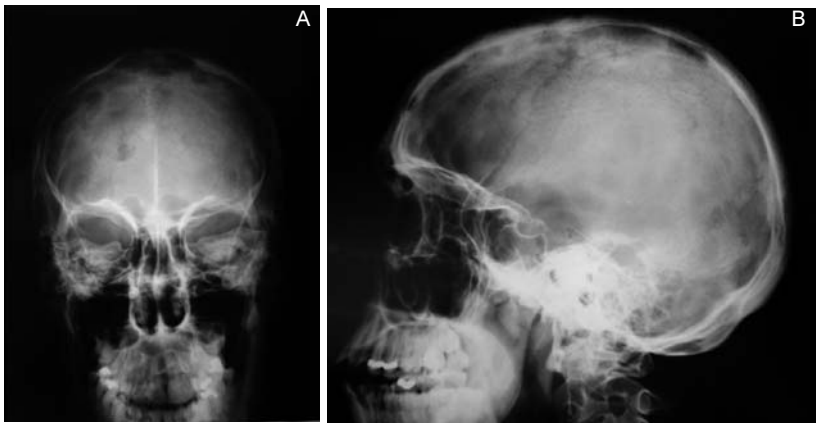

Figure 18. Female aged 25 suffering from a brown parietal tumour. X-rays with anterior-posterior (A) and latero-lateral (B) views.

❒ Fibrous dysplasia

Fibrous dysplasia is an illness affecting the mesenchyme, and sees the stoppage of the bone maturation process without sufficient mineralisation of the tissue[16].

The aetiology is currently unknown. It mainly affects young people, with no particularly prevalence of gender.

The illness tends to increase in the development age and to stop at an adult age.

Literature reveals there are malignant degenerations in 1% of cases, with the possible formation of fibrosarcomas and osteosarcomas[16].

In most cases it is an illness that affects a single bone. The forms affecting multiple bones tend to develop in young people, or patients suffering from genetic syndromes such as Albright syndrome (manifesting milky-coffee marks and endocrine dysfunctions such as early onset of puberty, hyperthyroidism, acromegalia and Cushing syndrome, with gynaecomastia in males).

■ **Radiology.** In X-rays they appear very similar to Paget's syndrome with the alteration of the bone structure, irregular calcifications and areas of bone reabsorption.

In CT scans the lesions have an appearance described as "frosted glass" (Figure 19), and can present calcified sclerotic areas and cystic areas.

The sclerotic areas can obstruct the connecting cavities, leading to sinusitis and trapped nerve syndromes.

Under MR the lesion appears hyperintense in T2-weighted sequences, whilst

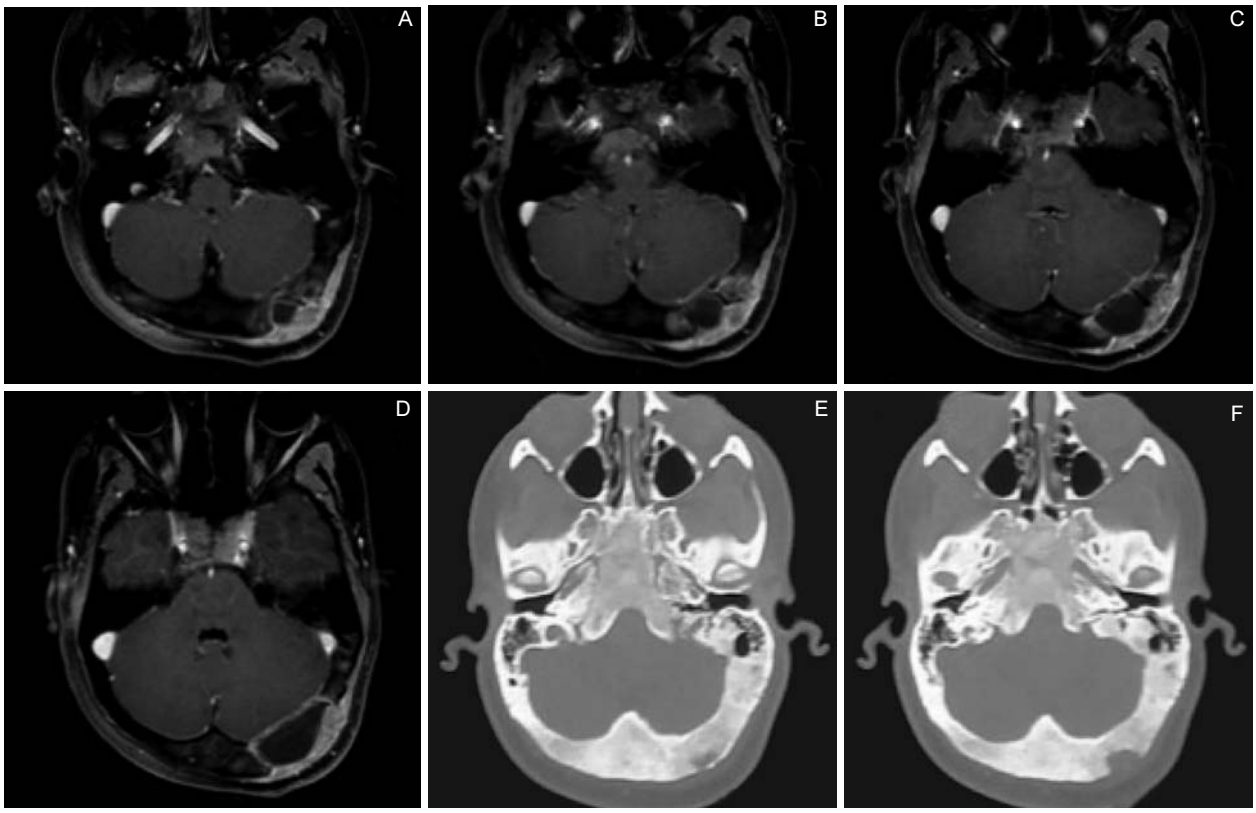

Figure 19. Female aged 21 with swelling in left occipital region and headaches. Fibrous dysplasia: axial sequences of MR (A, B, C, D) with T1-weighting using gadolinium, showing the structure of the lesion and the voluminous cyst. Same patient in axial CT (E, F) sequences with bone window. Detail showing the "frosted glass" appearance of the skull.

in sequences using gadolinium a moderate enhancement can be seen on the rim of the lesion.

■ **Histopathology.** The histological structure of this disease recalls a primitive bone tissue with cell elements immersed in a matrix of fibrous tissue.

Inside the lesion it is possible to distinguish areas forming cartilage, calcifications and actual bone trabeculae, although without the normal calcification or the morphological and structural organisation[31]. There may be cystic areas inside the lesion.

■ **Treatment.** The treatment usually chosen for these lesions is surgery, and resectioning must be ample, reaching as far as the healthy margins. Literature does not detail significant data on the effectiveness of chemotherapy and radiotherapy for treating these lesions[50].

❒ Osteomyelitis

Osteomyelitis refers to an infection of the bone tissue. The pathology is mainly caused by certain bacterial and mycobacterial strains that show a specific tropism for this tissue, although in fact all pathogens have the potential to cause osteomyelitis.

There is a primitive form that affects the bone as the only site of infection, as well as a secondary form which sees the metastatic colonisation of the bone (prevalently by hematogenic means, or by being directly adjacent) by a pathogen from another infection focus[32].

As with other infective illnesses, osteomyelitis has in recent years increased in incidence. It has been promoted by migrations and the increased survival rate of individuals with a depressed immune system, as well as those with tumoral diseases.

The pathogenic bacteria that most frequently cause osteomyelitis are Staphylococci, Enterococci, Pseudomonas and Klebsielle, which generally affect the bone following infections of the oral cavity, the urinary tracts or in drug addicts (endovenous injection of pathogens).

Salmonella types generally affect individuals suffer-

ing from sickle-cell anaemia, whilst Haemophiles and Streptococci frequently affect newborns[31].

■ **Radiology.** In standard X-rays this appears as an osteolytic lesion with surrounding sclerosis.

The cranial CT scan shows the lesion as being like an abscess, isointense compared with the parenchyma in the central region, with slight hyperdensity of the wall, calcifications on the inside, and uniform enhancement of the capsule. The MR shows a typical hypointense signal for the wall in T1-weighted images, with a clear enhancement after administering gadolinium, in the T2 sequences it shows a hyperintense centre with a hypointense wall and perilesional edema. The DWI sequences show a hyperintense lesion in the central region, and the spectroscopy shows a peak of amino-acids.

■ **Histopathology.** The structure of the bone affected is altered owing to the presence of inflammation cells, pathogen agents and necrosis of the tissue.

The abscess that collect spreads lengthwise along the canals of Havers, and by destroying the cortex can surface towards the periosteum.

This phenomenon generates a "subperiosteal abscess", which spreads very quickly and leads to pain and the formation of reactive bone apposition.

This acute phase of the infection often involves the "sequestration" phenomenon, whereby healthy bone is included in the necrotic abscess.

The potential breakage of the periosteum creates an itchy fistula which extends infection to the soft surrounding tissues.

If the infection affects the metaphysis of the long bones, it can generate a septic arthritis, which can lead to the destruction of joint tissues, resulting in a permanent disability[31].

In the chronic forms, on the other hand, alongside the destructive phase there is also a form of reactive bone production which creates progressive bone coverings around the necrotic bone, known as an "involucrum".

■ **Treatment.** Antibiotic therapy is the main means of treatment. Generally speaking a wide-spectrum treatment is used first, before continuing, after cultures and antibiograms, with treatment aimed specifically at the pathogen.

Surgical removal of the abscess is vital for restoring the infected areas completely. Moreover, it also improves the outcome of the treatment, thanks both to removal of the collected abscess puss and to the sampling of material for cultures and an antibiogram[31].

❒ Frontal hyperostosis

Internal frontal hyperostosis is an illness which involves the irregular thickening of the internal bone surface, and is almost exclusively located on frontal bones.

The aetiology of this illness is unknown, and involves bone tissue forming on the inside surface, in some cases accompanied by the formation of diploe below the thickening that has formed[20].

The pathology mainly affects the female sex and is linked to other diseases such as obesity, mental retardation, depression and mellitus diabetes.

Development of the pathology is slow and constant. The signs and symptoms linked to this pathology include headaches, endocranial hypertension syndrome, epileptic fits and focal deficits, but generally speaking it is an asymptomatic malformation diagnosed as an occasional finding.

■ **Radiology.** In CT scans it shows an irregular thickening of the skull with a reduction in the subdural spaces and compressive phenomena on the cerebral parenchyma.

The MR shows the frontal bone has an isointense appearance in T1 and hyperintense in T2 and is of increased thickness in all its parts[50].

■ **Treatment.** Treatment is reserved for the most serious cases, with removal of the bone in excess. Prognosis in acute onset cases is unfavourable[50].

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