Caspian Journal of Neurological Sciences
"Caspian J Neurol Sci"

Journal Homepage: http://cjns.gums.ac.ir

Review Paper

Intraosseous Cavernous Hemangioma of the Neurocranium: A Review of the Literature

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Citation Curcio A, Dimitri LMC, Copelli C, Gorgoglione LP, Germanò A, Catapano D. Intraosseous Cavernous Hemangioma of the Neurocranium: A Review of the Literature. Caspian J Neurol Sci. 2023; 9(2):108-119. https://doi.org/10.32598/CJNS.9.33.400.1

Running Title PICH of the Neurocranium

https://doi.org/10.32598/CJNS.9.33.400.1

Article info:
Received: 17 Feb 2022
First Revision: 15 May 2022
Accepted: 29 May 2022
Published: 01 Apr 2023

ABSTRACT

Skull primary intraosseous cavernous hemangiomas (PICHs) are uncommon, benign, and slow-growing tumors. These lesions are not widely known, specifically as regards the pathogenesis. The researchers wanted to describe the clinical presentations and radiological characteristics through a literature review of 140 cranial patients who received surgical treatment and histological diagnosis. Although PICH is uncommon, it should always be considered when a hard, steadily expanding skull lesion is seen. Surgical resection should be the first line of therapy for symptomatic individuals and aesthetic motivation, and their long-term results following complete removal are excellent. Moreover, we describe four patients with PICH to enrich the literature.

Keywords: Hemangioma, Cavernous, Skull, Neoplasms

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Highlights

- Primary intraosseous cavernous hemangiomas of the skull are rare but benign tumors.
- Total surgical excision is required to treat the mass effect and neurological deficit, improve an esthetic deformity, and obtain a definitive diagnosis.

Introduction

Primary intraosseous cavernous hemangioma (PICH) is a rare bone tumor accounting for 0.7% to 1.0% of all bone tumors [1]. PICHs rarely appear in the skull, being 0.2% of cranial bone tumors, considering both splanchnocranium and neurocranium [2]. Toynbee published the first record of this type of tumor in medical literature in 1845 [3]. A review of the literature reveals approximately 140 published cases. Additionally, we describe our patients. Based on the global distribution of skull PICH-related publications and the analysis of their geolocational data, the countries of origin of the publications are mostly concentrated in Europe, North America, and East Asia. PICH is most frequent in middle-aged men [2]. In the neurocranium, the most frequent site is the frontal bone, followed by the parietal bone, occipital bone, and temporal bone in cases with a single PICH. Other neurocranium bones are rarely involved. Sometimes it is possible to find multiple PICHs in the same person.

Case Presentation

Case 1

A 53-year-old woman presented with a swelling on the left side of her forehead. The swelling had rapidly grown for one year. The mass was solid, immobile, and hard in consistency, painless, and adhered to deep planes when palpated beneath normal-looking skin. She denied having a headache, dizziness, or a history of trauma. Other medical history was irrelevant. Routine hematological tests revealed no abnormalities. On the frontal bone, a CT image showed a 20×20×15 mm osteolytic lesion within the diploe (Figure 1). Because of the difficult differential diagnosis, the original radiologist's impression of the mass was not reported. An MRI revealed a bone mass that was hypointense on T1WI but hyperintense on T2WI. There is evidence of outer table lamellar thickening after gadolinium administration (Figure 2). A left frontal craniectomy and total lesion resection with a margin of surrounding normal bones of 0.5 cm were conducted under general anesthesia. It was rich in blood supply by clusters of small vessels, giving a purplish and hemorrhagic aspect to the underlying lesion (Figure 3). The resulting bone defect was repaired with a cylindrical metametacrylate plasty attached to the surrounding bone with titanium miniplates (Figure 4). The specimen's histology revealed an intradiploic cavernous hemangioma (Figure 5). The postoperative period was uneventful, and the patient recovered well. There was no recurrence of the lesion after a one-year follow-up.

Case 2

A 70-year-old woman diagnosed with non-Hodgkin lymphoma (NHL) presented with a painless occipital swelling. CT scan showed an osteolytic lesion at an inion point of 5 cm diameter, with intact inner and outer bone layers. Magnetic resonance showed a hypointense T1WI and hyperintense T2WI, with heterogenous enhancement after gadolinium administration. Time of flight angiography (TOF) sequences demonstrated no intracranial invasion and no encasement of torcular Herophili. Lymphoma of the bone was considered the most probable diagnosis. Resection was performed and surprisingly revealed an intraosseous cavernous hemangioma. No long-term follow-up was not possible because the patient died of NHL complications.

Case 3

A 42-year-old woman appeared with a painless, slow-growing frontal lesion. She suffered from aesthetic deformity with several psychological implications. Skull X-rays showed an osteolytic lesion 2 cm in diameter. A CT scan revealed a diploe lesion with a honeycomb appearance. Resection was performed, and metametacrylate plasty was used to reconstruct the bone defect, resulting in minimal deformity. Histological evidence supported the diagnosis of cavernous hemangioma.

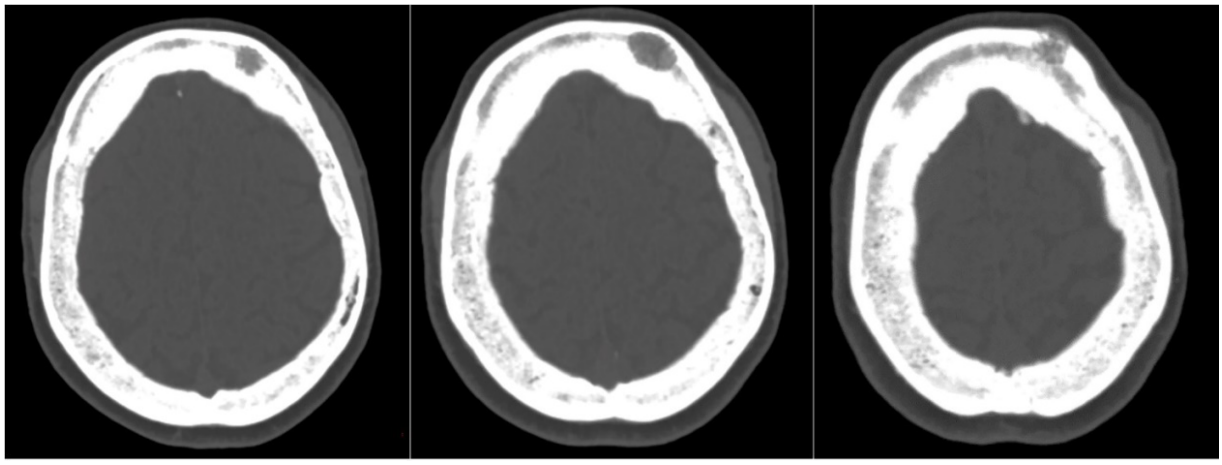

Figure 1. Axial bone CT showing a scalp mass sharply marginated

The inner table is intact, but the outer table is more expanded because of the underlying calvarial hemangioma.

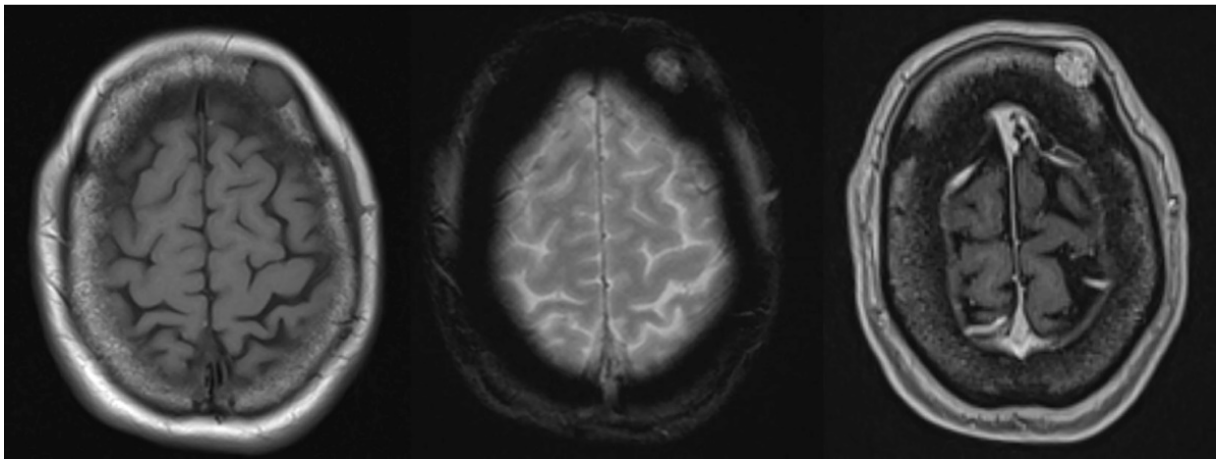

Figure 2. Magnetic resonance image series showing a T1WI hypointense lesion and T2WI and T1WI+c images of hetereogenous hyperintensity, result of vascular enhancement and hypointense trabeculae

Case 4

A 39-year-old woman suffered from frontal headache and sinusitis for months. No analgesic medical therapy was effective. Transnasal endoscopy did not reveal anything pathologic. CT scan demonstrated an intraosseous lytic lesion extended in the posterior wall of the frontal sinus, obliterating inner mucosa-lined airspace. The resection revealed cavernous hemangioma.

Discussion

Toynbee described the first case of cranial cavernous hemangioma in 1845 [3]. Since then, many cases have been described as a single case report. However, some authors collected multiple patients (Table 1). PICHs of the skull are uncommon vascular tumors, accounting for about 0.2% of all skull tumors. They represent 10% of benign tumors of the skull [4]. They are most common in the spine and rarely occur in the skull. Contrary to our four cases, they are more frequent in men. PICH is classified based on the dominant feeding vessel. Therefore, hemangioma is histologically described and classified as cavernous, capillary, or mixed capillary-cavernous. Only papers in which hemangioma is described as cavernous were considered, and capillary and mixed subtypes were excluded. We report our literature review based on PubMed research from 1845 to August 2022, when the last systematic review focused on this argument was published [5]. Described cases have exponentially grown from the first one in 1985 until now. Of 151 cases of cranial PICH reported in the literature (including four cases of our own), 38.4% were located in the frontal bone, 19.9% in

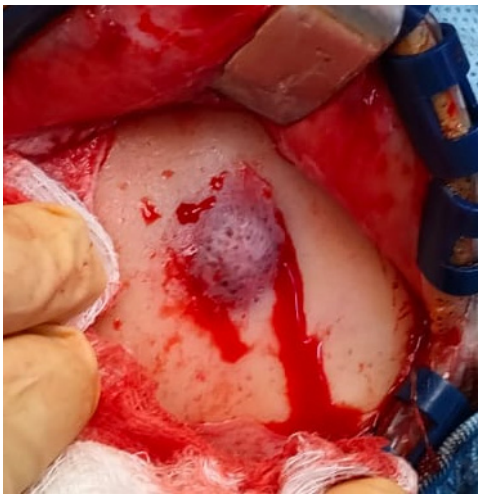

Figure 3. A close-up view of calvarian hemangioma

Note the honey-comb superficial pattern and external diploe lamellar thickening, scalloped, non-sclerotic margin.

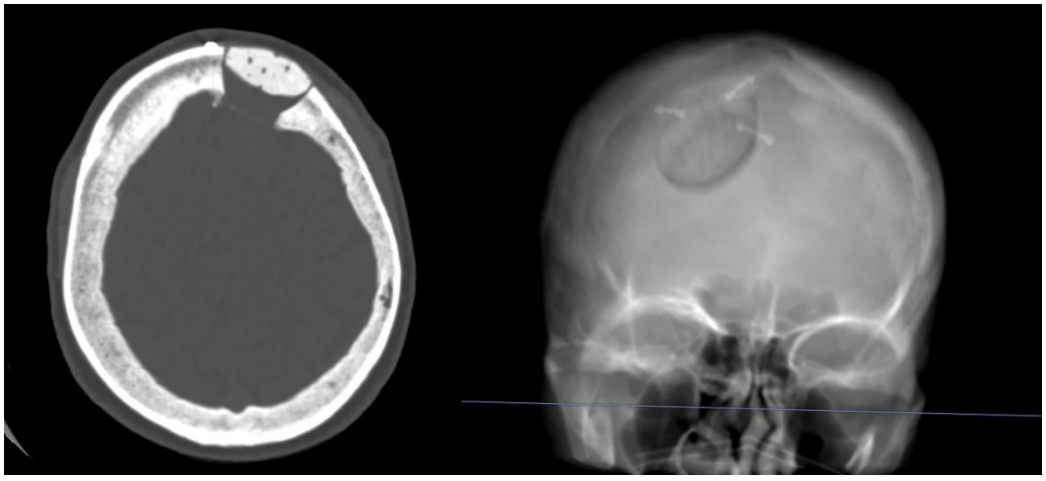

Figure 4. Postoperative CT scan (axial and 3D) showing circular safe margin resection of the primary intraosseous cavernous hemangioma and bone-smooth tailored reconstruction

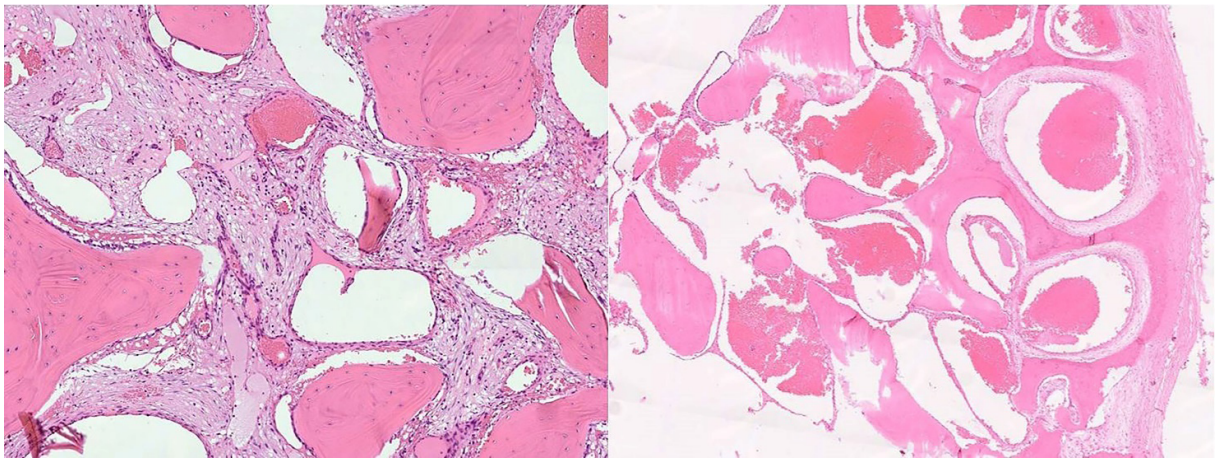

Figure 5. Microscopic findings with H&E stain: Cavernous hemangioma showing thin-walled vessels lined by a single layer of endothelial cells (×40)

Table 1. Report of PICHs: 58 frontal (38.4%); 30 parietal (19.9%); 20 occipital (13.3%); 14 temporal (9%) 20 other (13.3%) 9 diffuse (6.9%). (n=151)

Frontal		Temporal	Occipital	Parietal	Other Sites	Diffuse
Pilcher, 1894 [12]	Cheng et al. 2006 [13]	Sargent et al. 1965 [14]	Cervoni et al. 1995 [15]	Toynbee, 1845 [3]	Dickins, 1978 [16]	Peterson et al. 1992 [2]
Wyke, 1949 [17]	Buhl et al. 2007 [18]	Mangham et al. 1981 [19] x3	Corr, 2000 [20]	Kumar et al. 1993 [21]	Jackson et al. 1980 [22]	Reis et al. 2008 [23]
Gupta et al. 1975 [24]	Nasser et al. 2007 [25]	Glasscock et al. 1984 [26]	Garcia-Marin et al. 2001 [27]	Yoshida et al. 1999 [9]	Inoue et al.1982 [28]	Sasagawa et al. 2009 [29]
McIntyre et al. 1977 [30]	Naama et al. 2008 [31] x2	Mazzoni et al. 1988 [32]	Khanam et al. 2001 [33]	Heckl et al. 2002 [8] x2	Suss et al. 1984 [34]	Xu et al. 2013 [35]
Gross & Roth, 1978 [36]	Carrasco et al. 2009 [37]	Buchanan et al. 1992 [38]	Heckl et al. 2002 [8] parietally x2	Ajja et al. 2005 [39]	Glasscock et al. 1984 [26]	Gupta et al. 2013 [40]
Fouad et al. 1979 [41] x2	Nasrallah et al. 2009 [42]	Friedman et al. 2002 [43]	Muzumdar et al. 2002 [44] x2	Paradowski et al. 2007 [45]	Mazzoni et al. 1988 [32]	Hsiao et al. 2015 [46]
Inoue et al. 1979 [28]	Haeren et al. 2012 [47]	Sade et al. 2009 [48]	Buhl et al. 2007 [18]	Naama et al. 2008 [31]	Tashiro et al.1991 [49]	Liu et al. 2019 [50]
Shinno et al. 1986 [51]	Patnaik et al. 2012 [52]	Silva et al. 2013 [53]	Gibson et al. 2007 [54] x2	Cosar et al. 2008 [55]	Bottrill et al. 1995 [56]	Jha et al. 2021 [57]
Hook et al. 1987 [58]	Park et al. 2013 [1]	Fierek et al. 2014 [59]	Baltzar et al. 2008 [23]	Vural et al.2009 [60]	Slaba et al. 1999 [61]	Bantan et al. 2021 [62]
Zucker et al. 1989 [11]	Gupta et al. 2013 [40]	Yetiser et al. 2014 [63]	Nair et al. 2011 [64]	Martinez et al. 2010 [65]	Moore et al. 2001 [66]	
Hoffmann et al. 1990 [67]	Murrone et al. 2014 [68]	Verma et al. [69]2015	Mahore et al. 2014 [70]	Tyagi et al. 2011 [71]	Khanam et al. 2001 [33]	
Sinnreich 1990 [72]	Chun et al. 2015 [73]	Turii et al. 2021 [74]	Mohindra et al. 2016 [75]	Philpott et al. 2011 [76]	Liu et al. 2003 [77]	
Aurora et al. 1991 [78]	Sharma et al. 2016 [79]		Srinivasan et al. 2016 [80]	Yucel et al. 2011 [81]	Yamashita et al. 2006 [82]	
Faerber & Hiatt 1991 [83]	Uemura et al. 2016 [84]		Wang et al. 2020 [85] x3	Rumana et al. 2013 [4]	Salunke et al. 2010 [86]	
Relf et al. 1991 [87] x2	Yang et al. 2016 [88]		Nagamine et al. 2021 [89]	Atci et al. 2013 [90]	Moravan et al. 2012 [91]	
Cervoni et al. 1995 [15] x2	Saenz et al. 2018 [10]		Curcio et al.2022 [Current paper]	Lee et al. 2014 [92]	Gologorsky et al. 2013 [93]	
Voelker et al. 1998 [94]	Bravo et al. 2019 [95]			Hsiao et al. 2015 [46]	Yu et al. 2014 [6]	
Pastore et al. 1999 [96]	Akhter et al. 2019 [97]			Kilani et al. 2015 [98]	Serrano et al. 2015 [99]	
Sharma et al. 1999 [100]	Bentivegna et al. 2020 [101]			Davern et al. 2015 [102] x2	Singh et al. 2019 [103]	
Suzuki et al. 2001 [7]	Wang et al. 2020 [85] x7			Sarmast et al. 2016 [104]	Wang et al. 2020 [85]	
Heckl et al. 2002 [8]	Ren et al. 2021 [105]			Brichacek et al. 2018 [106]		
Pottelbergh et al. 2004 [107]	Curcio et al. 2022 x3			Prasad et al. 2018 [108]		
Politi et al.2005 [109]				Prasanna et al. 2019 [110]		
Dogan et al. 2005 [111]				Wang et al. 2020 [85] x5		

x1: 1 Case; X2: 2 Cases, X3: 3 Cases, V4: 4 Cases, X5: 5 Cases, X6: 6 Cases, X7: 7 Cases

Table 2. Differential diagnostic considerations between intraosseous lesions

Lesion	Clinical Features	Imaging	Treatment
Dermoid and epidermoid cyst	Mass effect from continued growth. Painless	X-ray: Well-defined and sclerotic margins CT: Hypodense and non-enhancing MRI: Hypointense on T1, hyperintense on T2 and hyperintense on DWI	Surgical excision avoids rupture and cellular leakage. Bone margins are curetted
Metastases	Generally asymptomatic, usually, a primitive tumor is known.	CT: Usually osteolytic lesion, rarely lesion osteo-thickened. Sometimes infiltrates adjacent tissue. Enhancing lesion. MRI: Unspecific pattern onT1 and T2, ring enhancement with gadolinium.	Surgical excision is possible. For inaccessible lesions, radiotherapy and chemotherapy are useful.
Low-grade hemangioendothelioma	Bone pain rapidly worsening	X-ray: Bubble-like osteolytic lesion with sclerotic margins. CT: Hyperdense lesion, not visible on the bone window. MRI: Hypointense on T1 and hyperintense on T2. Heterogeneous marked enhancement after contrast administration.	Surgical resection, eventually with radiation. Only radiation therapy when surgery is not feasible.
Osteoporosis circumscripta	Very rare. Usually associated with systemic osteoporosis	X-Ray: Circumscribed lytic lesion CT: Hypodense with cortical thickening. MRI: Hypointense on T1 and T2, coarse trabeculation	Medical therapy for osteoporosis. Surgery is useful only for complications (fractures)
Cephalocele	Occur in newborn	Bony defect with tissue herniation	Surgical treatment required
Intradiploic arachnoid cyst	Nontraumatic are rare and rarely are symptomatic. Posttraumatic are more common but asymptomatic, only diagnosed with emergency post-trauma CT-scan.	X-ray: Ill-defined osteolytic cavity in a bone CT: Isodense as CSF MRI: CSF isointensity on both T1WI and T2WI	Nontraumatic intradiploic arachnoid cysts are indicated for surgery when giant, causing brain structure displacement or aesthetic malformations.
Intradiploic meningioma	Headache and cranium occupation, progressively enlarging	X-ray and CT: Both hyperostosis and osteolysis in the CT bone window MRI: Isointense to grey matter on T1, iso-hyperintense to grey matter on T2, homogeneously enhances after contrast administration	Total surgical excision. Adjuvant radiation therapy can be used for incomplete excision.
Leptomeningeal cyst	Enlarging mass with a headache, sometimes with a focal neurological deficit	X-ray: Round lucency with smooth margins CT: Appears as a "growing fracture" near posttraumatic encephalomalacia MRI: CSF isointensity near posttraumatic brain damage	Repairing defects with surgical treatment
Malignant mesenchymal tumor (Chondrosarcoma, chordoma, giant cell tumor, and solitary fibrous tumor/ hemangiopericytoma)	Rare, symptoms and signs related to subtype and location. Usually rapidly growing	CT: Hypodense round lesion with septa. MRI: Variable presentation. High enhancing after contrast administration.	Surgical excision, adjuvant chemotherapy, and radiotherapy
Lymphoma	Primary skull lymphoma is painless progressive swelling. Or a history of systemic lymphoma	X-ray: Moth-eaten lytic lesion CT: Hyperdense enhancing lesion MRI: Hypointense on T1 and hyperintense on T2. Areas of enhancement within the lesion after gadolinium administration.	Surgical excision and medical therapy

Lesion	Clinical Features	Imaging	Treatment
Hyperparathyroidism	Systemic signs and symptoms of hyperparathyroidism. Multiple endocrine neoplasias (MEN) syndrome	X-ray and CT: "salt and pepper" skull bone MRI: not useful	Treat primary disease
Myeloma	Bone pain is the most frequent symptom, sometimes evolving into a bone fracture.	X-Ray and CT: osteolytic destruction with a "moth-eaten" appearance. MRI: Hypointense on T1 but enhancing lesion and Hyperintense on T2. High signal on high b-value DWI.	Chemotherapy or grafting of hematopoietic cells. The aim of surgical intervention is eventually to alleviate pain or decompress.
Osteomyelitis	Posttraumatic or associated with systemic co-morbid conditions	X-ray and CT: Osteolytic lesion near intracranial/subgaleal air bubbles MRI: Hypo- or iso-intensity on T1 images, T2 hyperintensity, and heterogeneous enhancement on T1-weighted fat-saturated contrast-enhanced sequences.	Pathogen-specific antibiotic therapy. Surgical debridement of necrotic bone and soft tissue may be necessary.
Osteoma	The most common primary bone tumor. Slow growth occurs most commonly in the cranial vault. Generally asymptomatic. Gardner's syndrome: multiple cranial osteomas, colonic polyposis, and soft-tissue tumors.	X-ray and CT: well-demarcated, round, and homogeneous dense lesion MRI: homogeneous hypointense on T1 and variable presentation on T2	Surgical excision for cosmetic reasons or big lesions causing symptoms. If osteoma arises from the outer table, the inner table must be left intact.
Aneurismal bone cyst	Rare in children. Pain with or without pathological fracture	X-ray: Sharply defined osteolytic lesions with thin sclerotic margins. CT: Like X-ray but shows fluid level inside and extensions in soft tissues. MRI: Sometimes hyperintense on T1 and T2 with different intensities of its capsule.	Surgical curettage or percutaneous instillation of fibrous agents
Langerhans histiocytosis (eosinophilic granuloma or histiocytosis X)	Invade cranial bones from craniofacial bones or meninges. Variable symptoms and signs in depending on originating bone.	X-ray: circular non-sclerotic lesion with sharply defined margins. It may contain intact bone sequestrum. CT: Hypodense tissue mass within the area of bony destruction. Hyperdense bone sequestrum. MRI: Hyperintense both on T1 and T2, highly enhancement.	Conservative treatment for a small and single lesion. For diffuse or aggressive forms: surgical excision and or radiotherapy and or chemotherapy.

the parietal bone, 13.3% in the occipital bone, 6.9% in the temporal bone, and 13.3% in other neurocranium bones. About 5.3% of cases have more than one PICH, or giant PICH growing in more than one anatomical bone. They arise from the vessels of the diploic space, fed by branches of the external carotid artery. They are made of capillaries widely dilated and separated by fibrous tissue. The pathogenesis is still unknown, but a history of trauma seems to be related in some case reports [6]. No hereditary cases were still described, contrary to intraparenchymal cavernous hereditary disease. Like our four cases, the typical presentation is a slow-growing palpable mass in a certain period of a patient's life without any significant symptoms or signs. When hemangioma is big enough or quickly increases its size, it could be associated with headache [6]. Radiologic evaluation includes plain skull X-rays, CT scans, and magnetic resonance imaging (MRI). Cranial X-ray is sometimes the first radiographic evaluation, showing a circular lucency with a trabecular or honeycomb pattern. Above all, the gold standard is represented by cranial CT with a bone window since it is more sensitive than simple radiography. MRI is not helpful but can help differential diagnosis from other kind of skull bone lesions. Although the appearance in the CT be different depending on the characteristics of the PICH. Usually CT image consists of a circular osteolytic lesion (hypodense), expansive, and well delimited, with sclerotic spaced trabeculations, giving sometimes an appearance of honeycombing in the axial cuts [7]. It frequently expands the external table respecting the periosteum, and rarely invades it. Because it is a slowing benign lesion reactive hyperostosis, it is never identified at its margins (8 parietally (two cases). MRI

images consist of hypo- to iso-intense lesions on T1WI, sometimes with hyperintensity depending on fatty content, and hyperintense on T2WI. Trabecula and spicula should modify the intensity on MRI images, as a highly vascularized lesion enhances diffusely and heterogeneously after gadolinium administration. Sometimes could be hemorrhagic [9]. In some cases, angiography of these lesions can help diagnose, for example, the largest PICH. Angiography demonstrates a hypervascular lesion in the latest arterial phase, without drainage or venous phase. As it is a vascular lesion, and there is a risk of bleeding during surgical removal, preoperative embolization may be useful in some cases [10].

The differential diagnosis includes other slow-growing, expanding bone lesions, both benign or malignant, such as dermoid and epidermoid cysts, metastases, low-grade hemangioendothelioma, osteoporosis circumscripta, cephalocele, intradiploic arachnoid cyst, intradiploic meningioma, leptomeningeal cyst, malignant mesenchymal tumor (chondrosarcoma, chordoma, giant cell tumor, and solitary fibrous tumor/hemangiopericytoma), lymphoma, hyperparathyroidism, myeloma, osteomyelitis, osteoma, aneurismal bone cyst, Langerhans histiocytosis (eosinophilic granuloma or histiocytosis X). The radiological and clinical characteristics that help the differential diagnosis are presented in Table 2. Surgical treatment is recommended for accessible lesions, which may be cured by en-bloc excision, including a circumferential margin of the healthy bone [6, 11]. Curettage is not recommended because an incomplete resection can cause relapse; however, the possibility of recurrence is avoided by including a margin of safety [6]. Total surgical excision is the treatment of choice and the prognosis after complete excision is excellent and recurrence is usually rare. Their surgical treatment must be considered because intraosseous cavernous hemangiomas grow progressively without spontaneous involution. This condition permits avoiding the painful clinical and cosmetic implications and, depending on their first symptoms and anatomical location, avoiding complications such as hemorrhages or nerve damage cranial, although with low frequency [8]. Most authors recommend total surgical excision to treat the mass effect and neurological compromise, improve an esthetic deformity, and obtain a definitive diagnosis [11]. The surgical approach becomes more difficult for those with an extension to the base of the skull. For the lesions considered non-accessible or unresectable, radiation therapy may be considered. Furthermore, radiotherapy should be reserved in the case of recurrent tumors too. However, this therapeutic modality does not reduce or heal the tumor but only stops lesion growth reducing vascularization.

Conclusion

Cranial cavernous hemangiomas are benign vascular lesions usually surgically treated when another type of bone neoplasm is suspected. The most common clinical feature is a solid tumor in the skull, which can be painful or not. Histopathologic examinations continue to be the gold standard for diagnostic purposes. The preferred treatment is a craniectomy with total resection to safe margins in healthy bone. A good prognosis is associated with complete resection. If the surgery is successful, relapse is uncommon. Case studies are mostly from the Western world and China. Data from emerging nations, such as South America and Africa, are needed to assess the precise statistical prevalence of PICH. The authors believe that PICH is not a rare tumor, but it has become more common in recent decades.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were in compliance with the ethical guidelines of the Declaration of Helsinki 2013.

Funding

This research received no financial support for preparing or publishing this paper.

Authors contributions

Conceptualization: Domenico Catapano; Methodology, writing, review, and editing: Antonello Curcio; Investigation: Antonello Curcio, Domenico Catapano, and Lucia Maria Cecilia Dimitri; Writing the original draft: Antonello Curcio, Domenico Catapano, Lucia Maria Cecilia Dimitri, and Chiara Copelli; Supervision: Leonardo Pio Gorgoglione, Antonino Germano; Reading and approval of the published version of the manuscript: All authors.

Conflict of interest

The authors declared no competing interests.

Acknowledgements

I am grateful to all of those with whom I have had the pleasure to work during my fellowship in Division of Neurosurgery of Hospital Casa Sollievo Della Sofferenza: Gorgoglione Leonardo, Carotenuto Vincenzo, Impusino Antonio; De Bonis Costanzo; Paiano Luigi Maria, Fazzari Elena, Icolaro Nadia, Savarese Luciano and Bonfitto Antonio.

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