CASE REPORT

Maffucci's Syndrome and Intracranial Chondrosarcoma

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ABSTRACT—Maffucci's syndrome is a rare, congenital mesenchymal dysplasia characterized by multiple enchondromata and hemangiomata, both of which may undergo malignant degeneration. Intracranial involvement is uncommon. A literature review yielded only six cases of Maffucci's syndrome with intracranial chondrosarcoma and two cases of Ollier's disease (enchondromata alone) with intracranial chondrosarcoma. We report the seventh case of Maffucci's syndrome in a patient with a very large and extensive skull base chondrosarcoma requiring staged operations for removal.

In 1881, Maffucci described the syndrome bearing his name.¹ It is a rare mesodermal disorder consisting of multiple enchondromata and hemangiomata. Nineteen years later, Ollier described enchondromatosis without the hemangiomata, a disease which would later bear his name.² Either one of the lesions may undergo malignant transformation. We report a patient with Maffucci's syndrome and a very extensive intracranial chondrosarcoma. A literature review yielded only six other cases and two cases of Ollier's disease with intracranial chondrosarcoma.³⁻¹⁰

CASE REPORT

A 42-year-old black female presented to our institution with a 2-year history of progressive headaches, hemifacial spasms on the right, and ataxia. Neurologic examination revealed that she was lethargic with evidence of papilledema, multiple cranial nerve palsies, long tract findings, and cerebellar dysfunction. The pre-operative bilateral auditory evoked response (BAER) and audiogram were abnormal, with sensory neural hearing loss on the right with evidence of retrocochlear involvement. A computerized tomographic (CT) scan and magnetic resonance imaging (MRI) scans with contrast revealed a very large tumor in the posterior fossa extending along the petrous ridge, superiorly through

and into the posterior aspect of the cavernous sinus and extending well above the posterior clinoids into the diencephalon (Figs. 1, 2, 3). The tumor measured over 6 cm and was calcified irregularly. The tumor extended into the posterior fossa with deformation of the cerebellum and pons with compression of the neural axis with associated hydrocephalus. The tumor also extended above the tentorium with compression of the midbrain. The patient was treated with high doses of steroids and then underwent the first of her staged operations. The patient underwent a petrosal approach which provided access for both pre- and retrosigmoid routes to the tumor. A very large, extensively calcified tumor with spicules of bone was encountered. The tumor was shown to press against the pons and cerebellum, encircle the ninth and tenth cranial nerves, and completely surround the seventh and eighth nerve complex. The tumor extended from the petrous ridge to the petrous apex, completely surrounding the fifth and sixth cranial nerves and extending superiorly to press against the midbrain and third and fourth cranial nerves. The tumor also extended well above to the posterior clinoids. An arachnoid plane was developed between the tumor and the pons such that the tumor could be removed. With an incision through the tentorium via a presigmoid route, additional tumor was removed also from the midbrain and around the third and fourth cranial nerves. A gross total resection was achieved through this approach with

Figure 1. A. Axial T₂-weighted MR showing the typical high signal of the tumor (large arrow) and the multiple foci of low signal representing the calcifications seen on CT (small arrows). B. Noncontrasted axial CT demonstrating a large low density mass (large arrows) containing many calcific foci (small arrows).

removal of the tumor in the posterior fossa, which resulted in the resolution of her hydrocephalus. The histopathology of the tumor revealed it to be a low-grade chondrosarcoma. Although she had a prolonged postoperative course, she eventually recovered, with resolution of preoperative symptoms and findings including improved sensation to the face, improved facial function, improved swallowing, and improvement of her strength and gait. During her work-up for chondrosarcoma, a bone scan revealed increased activity in her right hand, right femur, and right tibia. Plain radiographs of these areas also demonstrated multiple enchondromas with calcified soft tissue hemangiomas, leading to a diagnosis of Maffucci's syndrome (Fig. 4). Two months later, she was readmitted for the second of her staged tumor resections. She underwent crani-orbital-zygomatic and extended middle fossa approaches with resection of residual tumor superior to the posterior clinoid with access provided into the posterior aspect of the cavernous sinus. Additional tumor that remained in the petrous apex was removed through Kawase's triangle. The tumor also involved the mesial structures of the temporal lobe, which were grossly resected with removal of tumor adjacent to the dien-

cephalon. She recovered slowly but progressively and continues to do well with gradual improvement of all her cranial nerve palsies.

IMAGING CHARACTERISTICS OF CHONDROSARCOMA

Chondrosarcoma (CS) can originate from embryonal rests in the skull base which derive embryologically from cartilaginous matrix. More often, CS begins in the petro-occipital fissure than in the petrous apex. Chordomas are usually midline and retrosellar, whereas CSs are parasellar or in the cerebellopontine angle.¹¹⁻¹³ Calcification is common in CS (Figs. 1B, 3B) and can be seen in chordomas.¹⁴⁻¹⁶ Both of these tumors enhance mildly to moderately on CT. On MR images, both usually show hypointense signal on T₁-weighted sequences (Fig. 3A) and hyperintense on T₂-weighted sequences (Fig. 1A).^{13,14,16} Enhancement on MR can show a high signal containing a variegated pattern of focal null signals representing calcium within the tumor (Figs. 2A, 2B). The differential diagnosis of CS located at the skull base includes chondroma, meningioma,

Figure 2. A. Axial T₁-weighted postcontrast (Gadoteridol) MR sequence displaying high signal enhancement by the chondrosarcoma (large arrow) somewhat similar in degree to the signal seen on the T₂-weighted series. Numerous small foci of low signal represent the calcifications (small arrows), which can also be seen on CT (Fig. 1B). B. Axial T₁-weighted postcontrast coronal image of the tumor demonstrating the typical location for this tumor (large arrow). Multiple calcifications are seen as small low-signal foci (small arrows).

Figure 3. A. T₁-weighted sagittal noncontrast sequence demonstrating the low signal of the chondrosarcoma (large arrow), making it difficult to appreciate the numerous small calcific foci of lower signal. B. Three-dimensional sagittal reconstruction from axial CT data utilizing a dedicated computer workstation (General Electric). An operator-controlled cursor is not needed to generate this image, which is accomplished by software technique. Note the multiple small calcific foci (small arrows) which appear to be suspended intracranially using this technique.

Table 1. Enchondromata With Intracranial Chondrosarcoma

	Age/Sex	Presenting Symptoms	Radiographic Data	Procedure
Boinet 1904	37 M	Not given	None	Autopsy
Strang 1950	47 F	L eye pain, L CN VI palsy—5 days Presented acutely with SAH	None	Autopsy
Cook 1977	29 F	L face numbness/tingling; diplopia on L gaze—5 years Hoarseness, sudden transient blindness—1 year	CT: Destruction of L skull base from anterior clinoids to L side of dorsum sellae thru sphenoid body, petrous apex to L jugular foramen. Angio: Avascular mass, extra-axial	Not given
Armstrong 1981	27 F	L sided blindness—acute onset	CT: Calcified mass arising in L basisphenoid ridge with deformed sella	L frontotemporal craniotomy
Matsumoto 1986	52 F	Temporal HA, R orbital pain —6 years Diplopia, R ptosis, R visual impairment—6 months R sided blindness, L hemiparesis —acute onset	CT: Calcified mass in R parasellar region	1. R pterional craniotomy 2. R pterional craniotomy with VP shunt
Bushe 1990	33 M	R sided hearing loss—18 months Ataxia, dizziness—acute onset	CT: R CPA mass distorting pons and R middle cerebellar peduncle. Destruction of both petrous apices. MRI: Increased T2 signal to mass Angio: Avascular	R suboccipital craniotomy
Reuter 1981	18 F	R sided HA—2 years R ptosis—9 months R face paresthesias—6 months	Plain films: Calcification of sellar cavity and suprasellar region AP tomos: erosion of R posterior clinoid and dorsum sella	R frontal craniotomy
Clifton 1991	36 F	Diplopia on R gaze —10 months	CT: Large mass eroding R side of clivus, sella turcica and greater wing of sphenoid Angio: Avascular	R pterional craniotomy

M-male, F-female, L-left, R-right, CN-cranial nerve, SAH-subarachnoid hemorrhage, HA-headache, VP-ventriculoperitoneal, CPA-cerebellopontine angle

chordoma, plasmacytoma, carcinoma of the sphenoid sinus, and metastasis. CS causes bone destruction rather than bone sclerosis or hyperostosis like meningiomas. The MR images of these tumors may be similar enough to preclude any precise diagnosis.¹³ However, when a tumor having the above characteristics is found in a patient with a skeletal dysplasia such as Maffucci's syndrome (Figs. 4A, 4B), the diagnosis can become more certain. MR is more accurate than CT for soft tissue resolution, while CT is complimentary because it depicts the calcification and bone destruction better than MR.¹³

DISCUSSION

Intracranial cartilaginous tumors are rare. In Cushing's report of 2023 tumors, only 3 were cartilaginous in

origin.¹⁷ The sphenoid bone is the most common site of enchondroma of the skull and, more especially, the parasellar region.⁹ Maffucci's syndrome is described as the association of multiple enchondromata and hemangiomas. Maffucci's original report featured: (1) an onset in either childhood or adolescence; (2) the lack of a family history; (3) numerous enchondromata leading to the shortening and deformity of the affected bones; (4) a malignant degeneration of the lesions; and (5) multiple hemangiomas.¹³ Intelligence is unaffected, and there is no predilection for race or sex. The hemangiomas are of a cavernous or capillary type and are usually subcutaneous.¹⁸ The syndrome is congenital but not hereditary. Patients can be severely affected with dwarfing and gross deformities of the extremities. The skeletal deformity, usually affecting the long bones, arrests when growth ceases, and the main complication thereafter is the transformation to malignancy. In the largest review,

Table 1. Enchondromata With Intracranial Chondrosarcoma, continued

<i>Operative Findings</i>	<i>Location</i>	<i>Pathologic Diagnosis</i>	<i>Disease Process</i>
6-cm mass in body of left sphenoid 8 × 5 cm nodular mass in L basisphenoid. Pituitary stalk stalk and optic chiasm were stretched over the mass.	Body of sphenoid Basisphenoid	Malignant chondroma Well-differentiated, low-grade chondrosarcoma	Maffucci's syndrome Maffucci's syndrome
Large cystic mass beneath L temporal lobe attached to basisphenoid	Basisphenoid	Chondrosarcoma	Maffucci's syndrome
Encapsulated mass protruding from sphenoid wing. No intradural component. Optic nerve compression on both sides.	Basisphenoid	Low-grade chondrosarcoma	Maffucci's syndrome
Mainly extradural mass along R sphenopetrosal synchondrosis. Intratumoral hemorrhage extending to hypothalamus and brainstem	Parasellar region	Malignant enchondroma	Maffucci's syndrome
Soft, extradural mass with extension to CNS V, VII, VIII	CPA	Low-grade chondrosarcoma	Maffucci's syndrome
Cartilaginous tumor in R parasellar region	Parasellar region	Chondrosarcoma	Ollier's disease
Not given	Parasellar region	Low-grade chondrosarcoma	Ollier's disease

the overall incidence of malignancy was 23%, and lesions of the skull occurred in only 8% of cases.¹⁸

Ollier's disease is a rare, congenital condition in which cartilaginous masses are found in bone without the presence of hemangiomas. Chondrosarcoma can result from malignant degeneration of these masses in up to 30% of these lesions.¹⁹ While there is no difference between the dyschondroplasia of Ollier's disease and Maffucci's syndrome, it was previously considered diagnostically important to make the distinction between the two because of the supposed higher potential for malignant change in Maffucci's syndrome not seen in Ollier's disease. In 1988, Mellon et al showed that sarcomatous degeneration, as well as other mesenchymal malignancies, occur in Ollier's disease. They also suggested that hemangiomas may be subtle or subclinical, and therefore they proposed that there is a con-

tinuum between Ollier's disease and Maffucci's syndrome.²⁰

There have been approximately 170 reported cases of Maffucci's syndrome, but a literature review found only 6 cases of sarcomatous degeneration of a skull base enchondroma, and only 2 cases of intracranial chondrosarcoma with Ollier's disease.³⁻¹⁰ Table 1 gives the characteristics of these patients. The average age at the time of surgery for these patients, including our patient, was 35.6 years. We found a female to male ratio of 7 to 2, which had not previously been noted. There was no predilection for side: four tumors were on the left side, four were on the right side, and one tumor was bilateral. As has been previously noted, the sphenoid bone and especially the basisphenoid was most commonly involved with four cases, the parasellar region was involved in three cases, and the cerebellopontine angle in one case.⁹

Figure 4. A. Roentgenogram of the patient's hand demonstrating the multiple enchondromas (short arrows) distending the metacarpal bones. A soft tissue mass is due to a hemangioma, which contains multiple phleboliths (long arrow). This is a typical appearance in Maffucci's syndrome. B. Roentgenogram of the forearm demonstrating negative variance (shortening) of the ulna (short arrow) causing wrist deformity. There is an abnormal curvature to the ulna and radius (long arrow). These are typical findings seen in Maffucci's syndrome.

Our patient had tumor centered at the right cerebello-pontine angle with extension to the petrous apex and pons, thereby not readily fitting in any of these categories. All patients had chondrosarcoma and, of those differentiated, all were of low grade in keeping with previously published results.³

Karyotyping yielded a normal pattern in 10 of 10 cases reviewed by Lewis and Ketcham.¹⁸ Recently, however, others have shown aberrations of chromosome one. In 1986, Matsumoto et al reported a case of Maffucci's syndrome with an inversion of chromosome one.⁸ In 1994, Nakayama et al demonstrated heterochromatin in chromosome one in a patient with Maffucci's syndrome.²¹ We were unable to find any gross abnormalities of chromosome one in our patient, and it remains uncertain if Maffucci's syndrome is associated with any chromosomal aberrations.

CONCLUSION

We report the case of a patient with a very large and extensive skull base chondrosarcoma and Maffucci's syndrome. This syndrome is rare and characterized by enchondromatosis and hemangiomas, both of which may undergo malignant change. A literature review yielded only six previously reported cases of Maffucci's syndrome with intracranial chondrosarcoma and two cases of Ollier's disease with the same. Ollier's disease is also a rare disorder consisting of enchondromatosis without the hemangiomas, and it has been suggested that these two processes are a continuum and not distinct entities. Our review revealed a previously unreported predilection of malignancy towards women. Although this series is small, we suggest women with

Maffucci's syndrome and enchondroma of the skull be given extra consideration and close observation for malignant change.

REFERENCES

1. Maffucci A: Di un caso di enchondroma ed angioma multiplo. *Mov Med Chir Nap* 3:399-412, 1881
2. Ollier L: De la dyschondroplasie. *Bull Soc Chir Lyon* 93:23-24, 1900
3. Armstrong EA, McLennan JE, Benton C, Chambers AA, Perlman AW, Connors JW: Maffucci's syndrome complicated by an intracranial chondrosarcoma and a carotid body tumor. *J Neurosurg* 55:479-483, 1981
4. Boinet ME: Enchondrose Rachitiforme. *Arch Gen de Med* 194:2689-2717, 1904
5. Bushe KA, Naumann M, Warmuth-Metz M, Meixensberger J, Muller J: Maffucci's syndrome with bilateral cartilaginous tumors of the cerebellopontine angle. *Neurosurgery* 27:625-628, 1990
6. Clifton AG, Kendall BE, Crockard HA, Hughes T: Intracranial chondrosarcoma in a patient with Ollier's disease. *Br J Radiol* 64:633-636, 1991
7. Cook PL, Evans PG: Chondrosarcoma of the skull in Maffucci's syndrome. *Br J Radiol* 50:833-836, 1977
8. Matsumoto N, Fukushima T, Tomonaga M, Imamura M: Maffucci's syndrome with intracranial manifestation and chromosome abnormalities: A case report. *No Shinkei Geka* 14:403-410, 1986
9. Reuter K, Weber AL: Parasellar chondrosarcoma in a patient with Ollier's disease. *Neuroradiology* 22:151-154, 1981
10. Strang C, Rannie I: Dyschondroplasia with haemangiomata (Maffucci's syndrome). *J Bone Joint Surg* 32-B:376-383, 1950
11. Bahr AL, Gayler BW: Cranial chondrosarcoma. *Radiology* 124:151-156, 1977
12. Heffelfinger MJ, Dahlin DC, MacCarty CS, Beabout JW: Chordomas and cartilaginous tumors of the skull base. *Cancer* 32:410-420, 1973
13. Som PM, Curtin HD: *Head and Neck Imaging*. 3d Edition. St. Louis: Mosby-Year Book, 1996
14. Atlas SW: *Magnetic Resonance Imaging of the Brain and Spine*. 2d Edition. Philadelphia: Lippincott-Raven, 1996
15. Grossman RJ, Davis KR: Cranial computed tomographic appearance of chondrosarcoma of the base of the skull. *Radiology* 141:403-408, 1981
16. Oot RF, Melville GE, New PFJ, et al: The role of MR and CT in evaluating clival chordomas and chondrosarcomas. *AJNR* 9:715-723, 1988
17. Cushing H: Notes on a series of two thousand verified cases with surgical-mortality percentages pertaining thereto. In: H Cushing, ed. *Intracranial Tumours*. Springfield, IL: Thomas, 1932, p 133
18. Lewis RJ, Ketcham AS: Maffucci's syndrome: Functional and neoplastic significance. Case report and review of the literature. *J Bone Joint Surg* 55:1465-1479, 1973
19. Liu J, Hudkins PG, Sweet RG, Unni KK: Bone sarcomas associated with Ollier's disease. *Cancer* 59:1376-1385, 1987
20. Mellon CD, Carter JE, Owen DB: Ollier's disease and Maffucci's syndrome: distinct entities or a continuum? *J Neurol* 235:376-378, 1988
21. Nakayama Y, Takeno Y, Tsugu H, Tomonaga M: Maffucci's syndrome associated with intracranial chordoma: Case report. *Neurosurgery* 34:907-909, 1994