ÖZGÜN ARAŞTIRMA / ORIGINAL RESEARCH

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Challenges associated with meningiomas with extracranial extension: A clinical study

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Abstract

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Objective: Surgical treatment of extracranial meningiomas is challenging. In this study, we present an illustrated case series to share our experience in the treatment of meningiomas with extracranial extension.
Method: We retrospectively reviewed the data of 11 patients with meningiomas who underwent surgical treatment between 2008 and 2020. The intracranial and extracranial components were radiologically and intraoperatively confirmed for all patients.
Results: The patients included seven men and four women with a mean age of 55.4 years. Most patients presented with facial disfigurement or asymmetrical skull growth. The most common symptom at presentation was headache. The most common location of the meningiomas was the frontal region and those of extracranial growth were the paranasal sinuses and parietal bone invasion. We recognized two distinct modalities of bone destruction: hyperostosis (n=3) and osteolysis (n=8). Pathological investigation revealed atypical features in six patients. Preoperative embolization was attempted in four patients but it proved to be difficult; proper embolization could be achieved only in one patient. The most commonly encountered challenges during surgery were large calvarial and cranial base defects due to bone erosion, dural defects, and managing the superior sagittal sinus with parietal tumors. Excessive blood loss was also of particular concern, which was managed using simple scalp clips, intraoperative transfusion, and other conservative approaches of tumor extensions into paranasal sinuses. No perioperative mortality occurred. Calvarial reconstruction was performed with polymethyl methacrylate cement where needed.
Conclusion: Meningiomas with extracranial extension are surgically challenging but treatable. It contains fine neurosurgical trics in its treatment and follow-up.
Keywords: Meningioma, Extracranial, Skull Base Defect, Cranioplasty, Paranasal Sinus Invasion, Orbital Invasion

Öz

Ekstrakraniyal uzanımı olan menengiomların tedavisinin zorlukları: Klinik çalışma

Amaç: Meningiomlar çoğunlukla intrakraniyal ve intradural yerleşimli benign tümörlerdir ancak nadiren ekstradural ve ekstrakraniyal büyüme gösterebilirler. Ekstrakraniyal meningiomların cerrahi tedavisi özellikli ve zordur. Bu çalışmada, ekstrakraniyal yayılımlı meningiomların tedavisindeki deneyimimizi aktarmak için cerrahi serimizi sunmayı amaçladık.
Yöntem: 2008-2020 yılları arasında cerrahi uygulanan 11 meningiomlu hastayı retrospektif olarak inceledik. Bu hastalarda hem intrakraniyal hem de ekstrakraniyal uzanımı hem radyolojik hem de intraoperatif olarak doğrulandı.
Bulgular: Hastaların ortalama yaşı 55.4 yıl olan 7 erkek ve 4 kadındı. Çoğu, yüz şekil bozukluğu veya kafataslarının asimetrik büyümesi ile kendini gösterdi. Başvuru anında en sık görülen semptom baş ağrısı olarak saptandı. Meningiomların en sık yerleşim yeri frontal bölgeydi ve ekstrakraniyal büyüme paranazal sinüsler ve parietal kemik invazyonuydu. İki farklı kemik yıkımı yöntemi belirledik: hiperostoz (n=3) ve osteoliz (n=8). Patolojik çalışma 6 hastada atipik özellikler ortaya koydu. Preop embolizasyon 4 hastada denendi ve zor olduğu görüldü. Sadece bir hastada uygun embolizasyon sağlandı. En sık karşılaşılan cerrahi zorluklar; kemik erozyonu, dural defektler ve parietal tümörler ile superior sagital sinüs invazyonu, büyük kalvarial ve kraniyal taban defektleriydi. Abondan kanamada cerrahi zorluk oluşturdu ve bu durum hemoklip, intraoperatif transfüzyon ve paranazal sinüslere tümör uzantıları için konservatif yaklaşımla çözümlendi. Perioperatif mortalite olmadı. Skalp altında oluşan postoperatif BOS fistülü yaygın komplikasyondu ancak baskılı bandaj ile konservatif olarak çözülebildi. Gerektiğinde PMMA sementi ile kalvarial rekonstrüksiyon yapıldı.
Sonuç: Ekstrakraniyal yayılımlı meningiomlar cerrahi olarak zor ancak tedavi edilebilir tümörlerdir. Tedavi ve takibinde mikronöroşirürjikal cerrahi püf noktaları içerir.
Anahtar Kelimeler: Menengiom, Ekstrakraniyal, Kafa Tabanı Defekti, Kranioplasti, Paranazal Sinüs İnvazyonu, Orbita İnvazyonu

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INTRODUCTION

Meningiomas are mostly benign and constitute 20% of all primary brain tumors (1). Approximately 90% of all meningiomas occur intracranially and are confined to the intradural space (2). However, rare atypical behavior and malignant histological subtypes are well known (1). Extradural and extracranial manifestations occur in up to 20% of meningioma cases, where in the paranasal sinuses, the oral cavity, the ear or temporal bone, and the orbital space are taken into account (3–6). Pure extradural manifestation may occur in 1%–2% of all meningioma cases (1).

Extracranial extension is mostly associated with malignant and atypical meningiomas (3, 6). Extracranial growth may be the primary presentation or maybe concealed as the tumor silently grows into the paranasal sinuses through the cranial base. Extracalvarial growth may result in facial disfiguration or distortionin the shape of the skull and present with esthetic concerns for the patient long before neurological symptoms develop (4-6).

Surgical treatment of such tumors may be challenging as it requires creativity and improvisations by the neurosurgeon during the procedure (4, 6). Studies on meningiomas with extracranial extension are scarce and mostly are presented as case reports (4, 6, 7); thus, the radiological and clinical images in these studies are not sufficient. In this study, It was presented an illustrated case series of cranial meningiomas with extracranial extensions and describe the clinical presentation, the surgical techniques used, and the challenges encountered during surgery.

METHOD

The present study was performed according to the principles of the Declaration of Helsinki. The approval of the local ethics board was obtained (01/22 Date: 14/01/2020). Informed consent was obtained from patients attending the Neurosurgery Clinic for the use of their radiological and clinical data.

It was determined that a total of 2346 patients with intracranial tumor were operated in the clinics where the study was conducted in 12 years. 497 of them were diagnosed as meningioma, 405 of them had radiological examinations available, and only 11 patients were eligible for the study, of which extracranial invasion could not be confirmed or patient had no consent.

Statistical Analysis

Basic complementary statistical methods were applied using Microsoft Office Excel 2010 for statistical analysis. Results were expressed as means for average or percentage for frequency.

RESULTS

It was retrospectively reviewed the data of all patients with meningioma who underwent surgery between 2008 and 2020. A total of 11 patients (seven men and four women) were included in the study according to the inclusion criterion of the intracranial and extracranial components being radiologically and intraoperatively confirmed (Fig 1). The mean age of the patients was 55.4 years, and all patients were diagnosed with meningiomas with extracranial extension and invasion through the entire layers of the dural sheath and calvarial bones.

Tumor volume was determined using post gadolinium MRI and calculated by measuring the radius of the lesion on MRI scans in three planes (r1–r3) and using the following formula: V = 4p/3 9 r1 9 r2 9 r3. The same formula has been used for calculating the volume of irregularly shaped tumors (8). The average tumor volume was 92.09 mm3.

All except two cases were radiologically determined to have extracranial extensions before surgery. In one case, the meningioma was only observed to grow outside the skull during surgery (Fig 2A). Another case showed frontal hyperostosis but of the tumor was intraoperatively outcropped (Fig 2B) as confirmed by pathology testing. The extracranial portion of the tumor had a larger volume than the intracranial portion in all patients with meningiomas of parietal origin (Fig2C-D). Six patients presented with facial disfigurement or asymmetrical skull growth (Fig 2E–G). The most common symptom at presentation was headache, and the meningiomas were commonly located at the frontal region and the extracranial growth at the paranasal sinuses (Fig 2H–K) and parietal bone invasion (Fig3A–D). Pathological reports revealed atypical features in six patients. The most common reported histological subtype was meningothelial meningioma (Table 1).

Total tumor resection was performed in six patients. Cerebrospinal fluid (CSF) leakage, sinus invasion, and aesthetic problems were the main reasons to avoid total tumor resection. Excessive blood loss was managed through simple scalp clips, intraoperative transfusion, and conservative approach for tumor extensions into paranasal sinuses. The most common complication was CSF fistulas beneath the scalp. No cranial base CSF fistulas developed in any patient. Calvarial reconstruction (Fig 3E) was performed using polymethyl methacrylate (PMMA) cement where needed. No perioperative mortality occurred, and all patients except one were followed up for at least 1 year. Four patients with residual mass (Fig 3F–G) or diagnosed with atypical meningioma underwent radiotherapy. Tumor progression was detected in two patients at follow-up; one received radiotherapy whereas the other refused treatment.

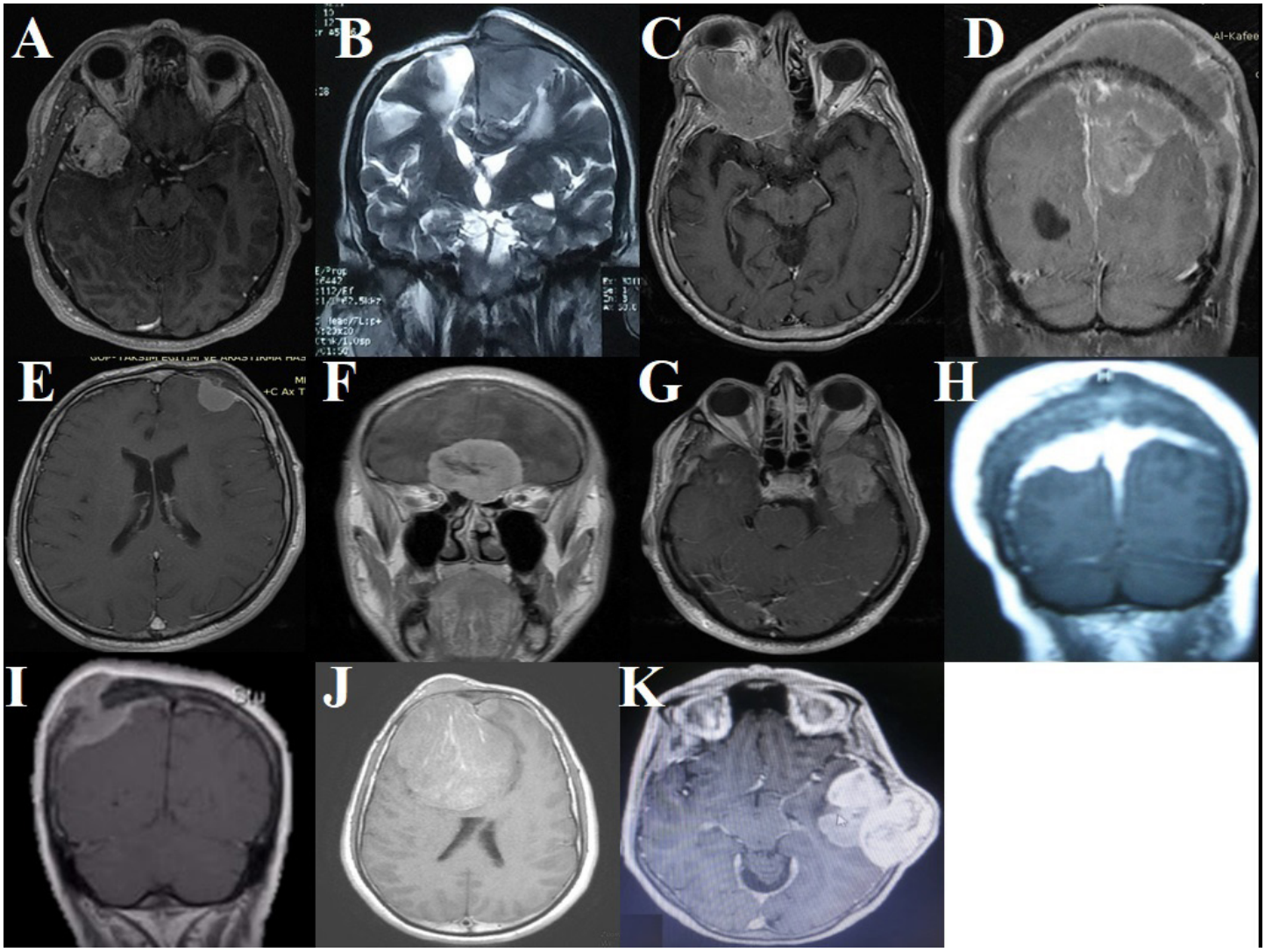

Figure 1: Cranial MR sections showing extracranial invasion in patients

Surgical Challenges

The most commonly encountered surgical challenges were large calvarial and cranial base defects due to bone erosion, dural defects due to invasive tumor growth, and managing the superior sagittal sinus with parietal tumors (Fig 3H–K). Cranial base defects and CSF fistulas were avoided by leaving residual tumors in place in three patients showing paranasal invasion; fibrin glue was used in one of them. Dural defects were primarily repaired or using galeal grafts in eight patients. Bovine pericardial patches were used for dural repair in three patients. An orbital tumor was completely removed in one patient; in another patient, the residue was left as is and treated by gamma-knife radiosurgery. Preoperative embolization was attempted in four patients, which proved difficult (Fig 4A–C); proper embolization was achieved only in one patient (Fig 4D). In the patient who underwent embolized intracranial sectioning, the intraorbital extension was difficult to penetrate (Fig 4E). Excessive blood loss was managed through intraoperative transfusion in six patients. Further blood loss was avoided by not prolonging the surgery to remove tumor extensions into paranasal sinuses in four patients. No perioperative mortality occurred. The most common complication was CSF fistulas beneath the scalp in five patients. In all patients, CSF fistula was resolved by pressure wrapping and no surgical intervention was needed. No cranial base CSF fistula developed.

Another challenge was calvarial reconstruction. Cranial defects were repaired using PPMA cement in four patients, and no calvarial repair was required in four patients. Calvarial repair was also planned for two patients who refused any further treatment. Two patients showed a small craniotomy area and calvarial defects that did not require reconstruction. In two patients, the bone flap was placed back after drilling away the eroded part without covering the defect through cranioplasty. In one patient, the frontal craniotomy area was reconstructed using the healthy remaining part of the bone and a PPMA patch (Fig 4F). No mortality occurred, and favorable outcomes were achieved in all patients. Subcutaneous recurrence was noted in the patient who did

Table 1: Demographic, clinical, and radiological data of the patients

Patients	1	2	3	4	5	6	7	8	9	10	11
Gender	Male	Male	Female	Male	Male	Male	Male	Female	Female	Male	Female
Age	44	55	78	57	45	41	63	48	55	53	70
Symptoms	HA, Epilepsy	hemiparesis	HA, exophthalmos	HA, hemiparesis, blindness	HA, protrusion on forehead	HA, Epilepsy	Exophthalmos	Headache	Headache, protrusion	Headache, behavioral change, protrusion on forehead	Headache, protrusion
Pathology type	Grade 1 Meningothelial	Grade 2 Atypical Meningothelial (Ki67 15%)	Grade 2 Atypical Fibrous	Grade 2 Atypical Meningothelial	Grade 1 Meningothelial	Grade 1-Mikst	Grade 2 Atypical Meningothelial	Intraosseous Meningioma	Grade 1 Meningothelial	Grade 2 Atypical Mikst	Grade 2 Atypical Meningothelial
Localization	Sphenoid Wing	Convexity	Orbital	Biparietal	Frontal	Olfactory	Orbital	Biparietal	Parietal	Frontal	Temporal
Surgical approach	Pterional	Frontoparietal	Frontotemporal	Parietal	Frontal	Bifrontal	Pterional	Parietal	Pterional	Pterional	Temporal
Complications	CSF fistula	Hemiparesis	-	CSF fistula	-	CSF fistula, Over hemorrhage	Serebral edema	Flap necrosis, CSF fistula	CSF fistula	CSF fistula, Over hemorrhage	CSF Fistula
Cranium reconstruction	Original bone	Partially original bone	Original bone	Partially original bone	Original bone	Original bone	Original bone	PMMA	Original bone	Partial original bone + Partial PMMA	PMMA
Size(mm)(X-Y-Z)	40-39-44	50-58-53	50-73-59	118-80-106	27-24-25	48-49-43	39-89-72	85-80-55	38-43-45	75-93-75	56-63-66
Excision	Total	Subtotal	Subtotal	Subtotal	Total	Subtotal	Subtotal	Total	Total	Total	Total
Invasion/ extracranial growth	Temporal Bone	Parietal Bone	Orbit	Orbit	Paranasal Sinus	Paranasal Sinus	Orbit	Parietal Bone	Parietal Bone	Frontal Bone+ Paranasal Sinus	Temporal Bone
Type of bone involvement	Erosion	Erosion	Erosion	Erosion	Hyperostosis	Erosion	Erosion	Hyperostosis	Hyperostosis	Erosion	Erosion
Tumor volume (mm^3)	23,289	52,149	73,066	339,51	5,496	34.314	84,793	126,9	24,948	177,49	95,68
Radiotherapy	–	+	+	+	–	–	+(gamma-knife radiosurgery)	–	–	+	–
Recurrence/ progression (1 year)	–	Unknown	+	+	–	–	–	–	–	–	–

not undergo cranioplasty at the 3-month follow-up. Minimal progression of the paranasal tumor was noted in the patient with paranasal invasion in the first year of follow-up.

DISCUSSION

Meningiomas arise from arachnoid cap cells. Due to their origin, they initially grow from the arachnoidal planes toward the brain like a cauliflower (1). Some meningiomas, however, may also grow through the dura and into the epidural space, sometimes even penetrating the endosteum and the overlying bone (3%–5% of cases) (3, 7). In this study, It was observed two types of bone involvement with extracranially invading meningiomas: bone erosion (osteolysis) or hyperostosis, both of which eventually lead to bone destruction. Hyperostosis can be radiologically observed as a diffuse thickening of bone over an area proportionate to the dural base of the meningioma (Fig 2B–4G). Osteolysis can initially be detected as scalloping or disappearance of the trabecular structure, followed by the complete destruction of the inner and outer tabulas in the calvarial bones (3, 6, 7) (Fig2A, 2K and 4 H, and I). It was noted bone erosion in eight patients (70%) and hyperostosis in three (30%) (Table1). It was noticed that in patients showing delayed presentation, both types of bone involvement resulted in bone destruction, with the tumor piercing and growing through the calvarial bone.

Histological atypia may also facilitate the invasive behavior of meningiomas. In line with previous literature, the most common histological type in this study was meningothelial meningioma. However, atypical histology has been reported in 6% – 14% of extracranial meningioma cases (3, 4, 6); in this study, 54% of the patients showed atypical features. Late presentation makes the tumor more likely to invade the brain, which qualifies the meningioma as grade II. This may explain the higher rate of atypical histology in this study

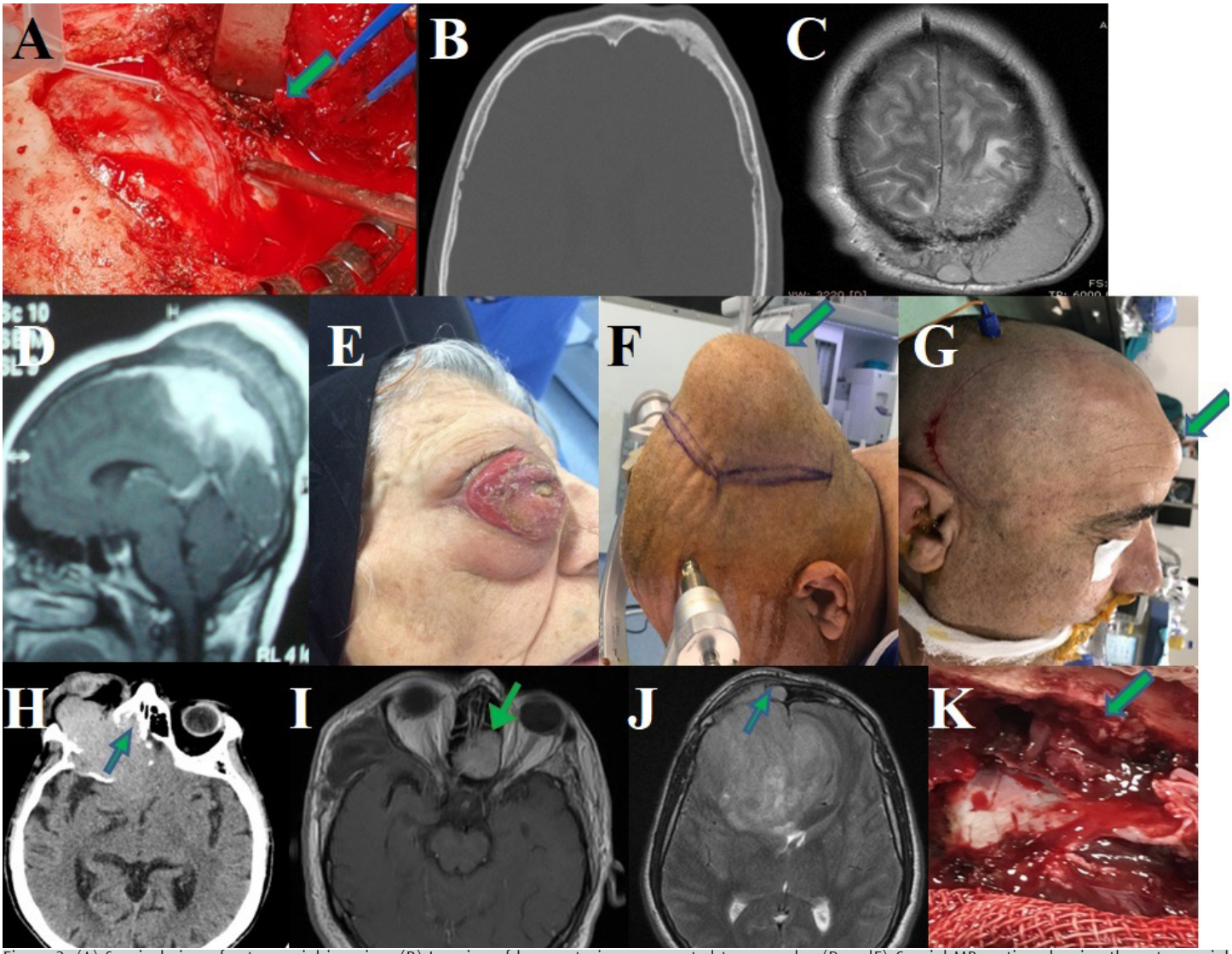

Figure 2: (A) Surgical view of extracranial invasion. (B) Imaging of hyperostosis on computed tomography. (D andE) Cranial MR section showing the extracranial portion of the tumor that is larger than the intracranial portion. (E–G) Facial disfigurement or asymmetrical growth of the skull. (H–K) Extracranial growth along the paranasal sinuses

as one patient with paranasal invasion was diagnosed with grade II atypical meningioma solely based on brain invasion.

Although most extracranial meningiomas are secondary extensions of intracranial tumors spreading through the calvarial bones, perineural spaces, or vascular channels (9), primary extracranial meningiomas are considered to arise from the proliferation of ectopic arachnoid tissue or the perineural cells accompanying the cranial nerves (10). Less than 2% of all meningiomas primarily arise outside the subdural compartment and may destroy the calvarial bones and grow both intra- and extracranially (7, 9). This appears to be the case in the above mentioned patient as she displayed a large orbital mass growing out of her orbit, resulting in the destruction and displacement of the orbital roof toward the brain (Fig 2E–2H). The intraoperative appearance was a mass largely growing inside the orbital cone, which would eventually erode and push on the orbital roof to reach and invade the dura and the brain.

It has been suggested that pure extradural meningiomas arise from residual arachnoid cells or remnant multipotent mesenchymal cells (10, 11, 12). However, as in this study, extracalvarial growth of meningiomas mostly results from direct extension or metastatic seeding of intracranial meningiomas (7). As observed in all this study' patients with parietal meningiomas, the extracranial extension can grow to reach a point that this becomes the main focus of the surgical treatment for the patient (13, 14). Impeded scalp circulation and excessive blood loss is particularly concerning in such patients. The scalp may be stretched too tight to accommodate the underlying growing tumor. Dilated collateral circulation was observed in three patients in this study (Fig 4B–D). Three other patients presented with perioperative scalp problems due to bad circulation. Preoperative embolization wherever possible and simple scalp clips proved to be useful in the management of blood loss during the surgical resection of these kinds of tumors.

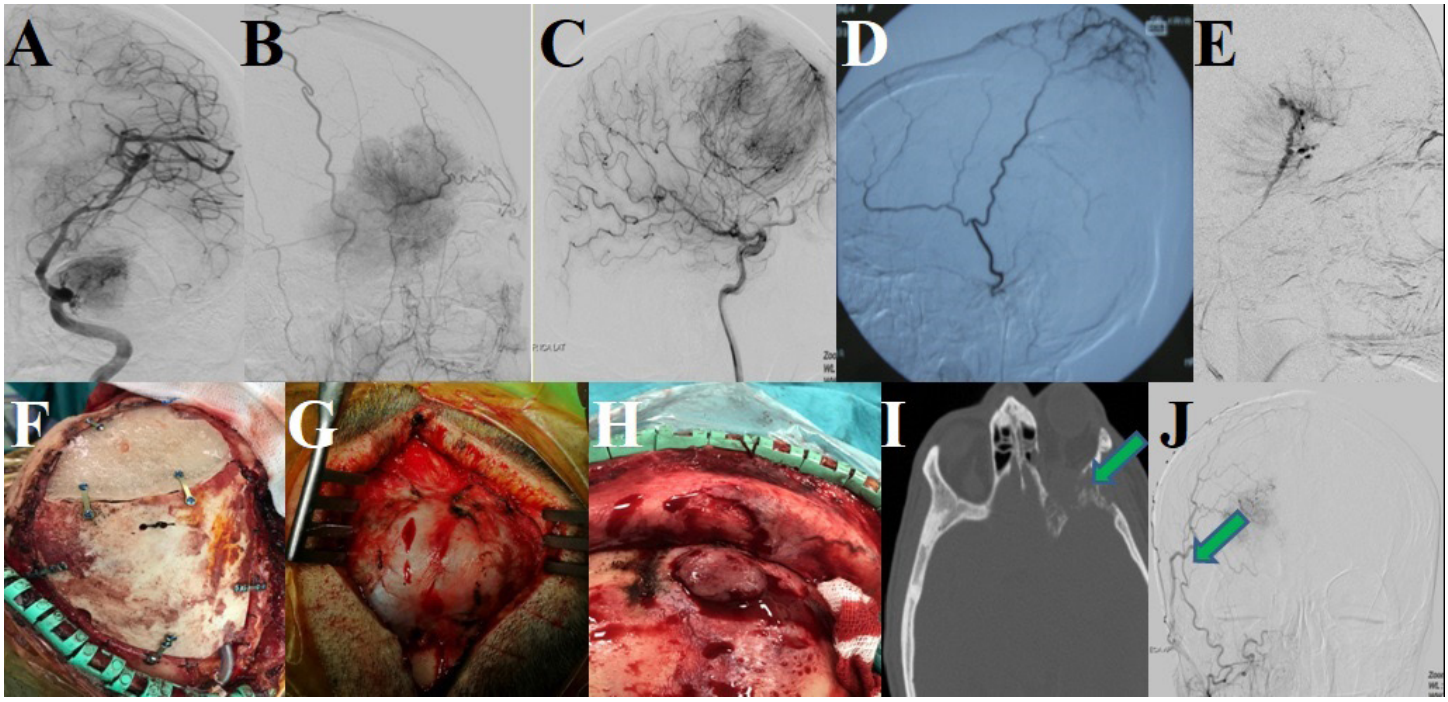

Figure 3: (A–C) Tumor vasculature in cranial digital subtraction angiography (DSA); (D) proper tumor embolization; (E) partial embolization; (F) reconstructed craniotomy area using the healthy remaining bone and PPMA patch; (G) tumor hyperostosis; (H) bone erosion; (I) bone erosion on computed tomography. (J) DSA showing the extracranial portions mostly fed by small distal branches of the external carotid artery.

The size and location of the meningiomas are the main determinants of the clinical symptoms, which may be accelerated by the invasion of the surrounding neurovascular structures and peritumoral edema (3). However, meningiomas with extracranial extension can find empty spaces to grow silently and only be noticed once they grow to large sizes. In this study, 9 of the11 patients presented with giant-sized tumors with an average tumor volume of 92.09 mm3 (Fig 1).

In cases of giant extracranial meningiomas, it is particularly important to conduct a thorough radiological investigation including computed tomography, magnetic resonance (MR) imaging, MR angiography, and digital subtraction angiography (DSA). Preoperative evaluation of neurovascular invasion and feeder vessels can increase the chances of a favorable outcome. These radiological examinations also help in good surgical planning. DSA can also identify feeder vessels and preoperative embolization that can help decrease surgical complications due to excessive bleeding. However preoperative embolization may prove to be difficult and sometimes impossible in meningiomas with extracranial extension (12–16). This is because the extracranial regions are mostly fed by small distal branches of the external carotid artery at the convexity (Fig 4J) or by small perforators directly shooting off the internal carotid artery at the cranial base (Fig 4A). Most endovascular surgeons have no experience with the distal external carotid system or may find it risky to penetrate the feeder perforators at the cranial base. Therefore, preoperative embolization could only be achieved one patient (Fig 4D).

When operating on giant meningiomas, the neurosurgeon may experience prolonged surgical dissection and coagulation. The vascular nature of these tumors can easily lead to excessive blood loss and other perioperative complications. The largest series of extracranial meningiomas including 146 cases was reported by Rushing et al (17). Thompson et al. reported two separate studies on huge meningiomas that included 30 cases with sinonasal tract meningiomas and 36 with ear and temporal bone meningiomas (18, 19). Excessive blood loss, venous sinus thrombosis, meningitis, and CSF fistulas were the major complications, along with giant meningiomas with extracranial invasion (14). Cases of extracranial meningiomas destroying the cranial base with extensions into maxillary, external ear canal, paranasal sinuses, nasal cavity, orbit, middle ear, internal jugular vein, temporal is muscle, and facial and neck soft tissues have previously been reported (10, 14,20–23). Reconstruction of the cranial base was one of the main challenges in the treatment of anterior skull base meningiomas with intra- and extracranial extensions (24). Rhinorrhea was not encountered in this case series. Cranial base defects and CSF fistulas were avoided by leaving residual tumors.

Nadkarniet al. reported a case of a giant meningioma with extracranial extension and invasion of the superior sagittal sinus that weighed 1380 grams despite subtotal excision (14). However, the removal of the largest cranial meningioma was reported by Cech et al. in 1982; the excised tumor mass had an extracranial extension and weighed 2600 grams in total (13,25). These reports described the difficulties of radiological

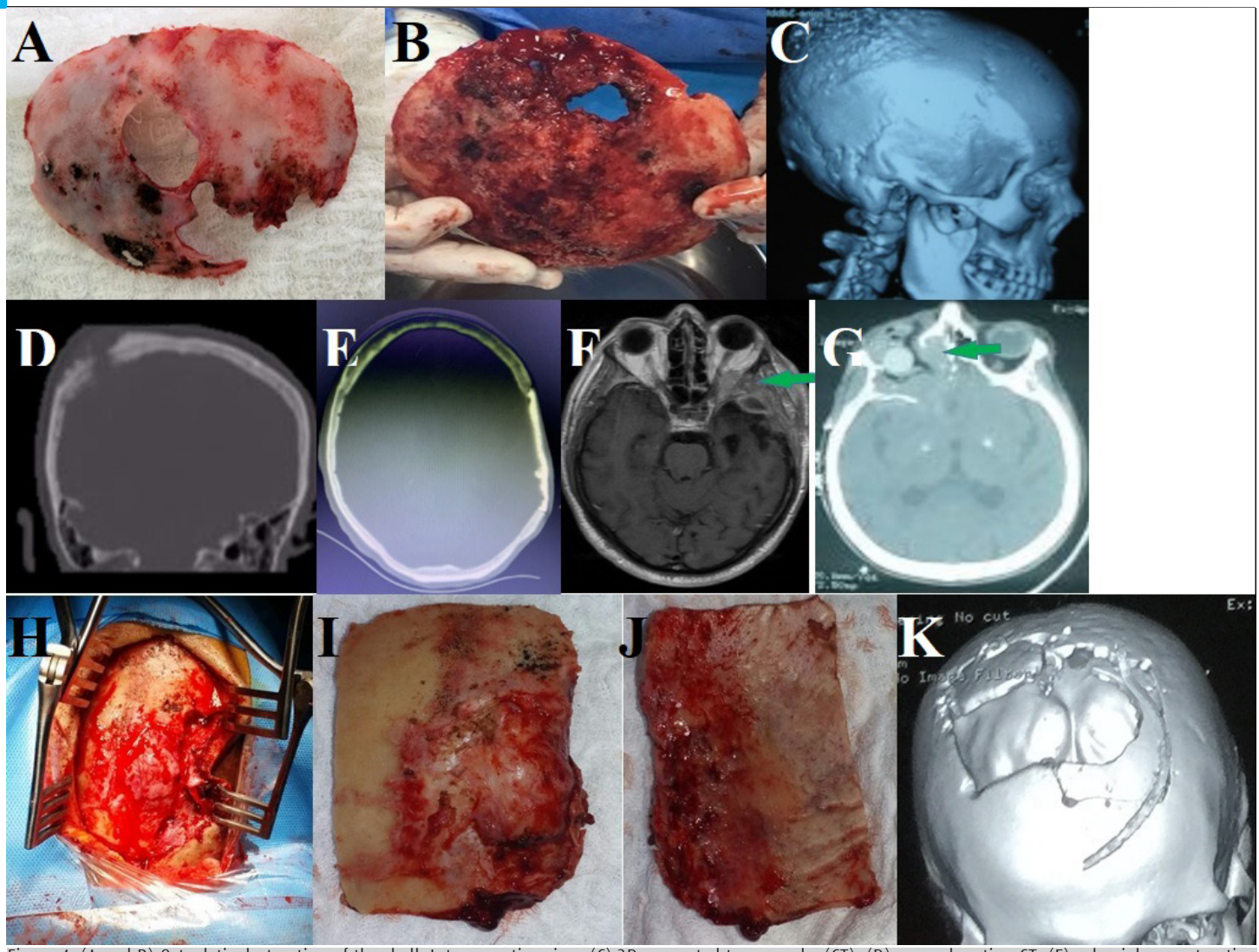

Figure 4: (A and B) Osteolytic destruction of the skull. Intraoperative view; (C) 3D computed tomography (CT); (D) coronal section CT; (E) calvarial reconstruction using polymethyl methacrylate cement on axial section CT; (F, G) residual mass on MRI and CT; and (H–K) large calvarial defect with parietal tumor

evaluation of these patients using standard methods. Similar to this study in parietal extracranial giant tumors, the biggest surgical challenges in these previous studies were excessive blood loss, reconstruction of the calvarium, and repair of the scalp overlying the tumor due to infection or ulceration (26–30).

Primary intraosseous meningiomas have also been reported (31) and should be differentiated from secondary bone erosion of meningiomas. In this study, it was detected two patterns of bone involvement (hyperostosis or osteolysis), ultimately leading to bone destruction as the tumor grew. Hyperostosis is a more common radiological finding than osteolysis as per the literature (12). This is in contrast to this study' findings where in seven patients presented with osteolysis and three presented with hyperostosis where all intraosseous growth was secondary to tumor extension. Moreover, a correlation between calvarial destruction and meningioma malignancy has been suggested (13, 21), especially in association with extracranial soft tissue masses (11). This study do not support such an association; however, further studies are warranted before reaching a definitive conclusion.

The lack of long-term follow-up of the patients is the most important limitation of this study. Long-term patient follow-up was not performed in this study. Therefore, long-term results of the treatments are not available. This study includes the surgical and early results of meningioma cases with extracranial invasion.

The use of radiotherapy (especially gamma-knife radiosurgery) has become increasingly common for the treatment of recurring residual meningioma. Subtotal resection was performed in five patients, and recurrence was observed in only one patient receiving radiotherapy. In a patient who refused to undergo radiotherapy as recommended, relapse occurred after 3 months. In patients with meningioma with extracranial extension, better outcomes can be obtained when the interventional radiologist, neurosurgeon, and oncologist work as a team (32, 33).

CONCLUSION

In conclusion, giant extracranial meningiomas require detailed preoperative radiological evaluation, and the detection of sinus invasion is of paramount importance. Preoperative embolization should be considered but may prove challenging due to the unfamiliar and distal vascular anatomy resulting from the tumor. Reconstruction of calvarium and scalp may be challenging after tumor removal and should be preoperatively planned. Further, there may be extensive dural and calvarial damage. CSF fistula is the single most common surgical complication of extracranial meningiomas and can be tackled by avoiding superfluous surgical aggressiveness at the cranial base and meticulous dural repair.

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Peer-Review

Externally peer reviewed.

Conflict of Interest:

The authors declare that they have no conflict of interests regarding content of this article.

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Ethical Declaration:

Permission was obtained from the Hatay Mustafa Kemal University, Medical Faculty Clinical / Human Research Ethics Committee for this study, and Helsinki Declaration rules were followed to conduct this study. (01/22 Date: 14/01/2020)

Authorship Contributions

Concept: AG, YA; Design: AG, YA; Supervising: SK; Financing and equipment: NA; Data collection and entry: AG, YA; Analysis and interpretation: AG; Literature search: AG; Writing: AG, YA; Critical review: SK.

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