In Situ Cranioplasty with Autoclaved Bone Flap in Meningiomas with Potential Bone Infiltration

Hosam A.M. Habib*
Department of Neurosurgery, Menoufia University, Egypt

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INTRODUCTION

Meningiomas are the most common benign intracranial neoplasms, second only to gliomas as the most common intracranial tumors overall. The prevalence of meningiomas in population-based studies is 5–8.5 in 100,000.24

Meningiomas are arguably the most rewarding brain tumor a neurosurgeon might be faced with, because of their mostly benign nature which provides a possibility of cure if totally excised. The degree of resection is regarded as the most significant factor in the rate of recurrence and correlates directly with clinical long-term outcome.16,19

The importance of bone involvement as a prognostic factor per se in benign meningiomas (World Health Organization [WHO] grade I) is debated, but it predicts poor outcome in atypical meningiomas (WHO grade II). Failure to address the hyperostosis provides a nidus for the re-growth of the tumor.10,26 The goal for successful treatment in meningioma surgery is to achieve a Simpson grade I excision of the tumor (macroscopically complete removal, including excision of the dura attachment and aggressive resection of all involved bone), whenever it can be accomplished without increased morbidity.19

This is usually accomplished with Convexity meningiomas, unless venous sinus or bone involvement is present. At the end of the surgical procedure the bone flap is to be repositioned, unless it shows signs of bone reaction or infiltration, where it is either discarded or debridement of the infiltrated parts is done, followed by a performing cranioplasty for cosmetic issues.

An optimal cranioplasty material is a substance whose physical properties are as close to those of bone as possible, must fit the cranial defect achieving complete closure, radiolucent, resistant to infections, minimal expansion with heat, withstand bio-mechanical stresses, resilient enough to be easily shaped, inexpensive, non-reactive to the tissue it will be incorporated into, must be non-resorbable, and ready to use. Unfortunately, there is still no perfect material to fit all these criteria.8

PATIENTS & METHODS

The calvarial bone flaps of twelve patients with convexity meningiomas were autoclaved before being...
repositioned for potential tumor invasion. The study was conducted at the neurosurgical department, of Menoufia University.

In ten cases intra-operative detection of bone involvement was found in the form of hyperostosis with frank bone infiltration, or the presence of bone reaction. None of the former cases were planned for a cranioplasty, as preoperative imaging failed to reveal the bone affection. One case had infiltration of both inner and outer tables of the bone overlying the tumor, and another case of meningioma en plaque had diffuse expansion and hyperostosis of squamous temporal bone. In these two cases, cranioplasty using artificial materials was not done for pure financial reasons, as both patients lacked medical insurance coverage.

Preoperative magnetic resonance imaging (MRI) and/or computed tomography of the head, with sagittal and coronal reconstructions, were obtained for all patients to determine the extent of the tumor and to identify any associated bony changes. At the time of surgery, once the bone flap was raised, it was inspected for signs of bone reaction, hyperostosis, or frank bone infiltration; if present, portions of the hyperostotic bone were removed and sent for pathological evaluation, and then the bone flap was sent for autoclaving for 20 minutes at 134°C. The excised tumor and its dural attachment were also sent for pathological evaluation (table 1). The dural defect was closed with an epicranial graft. The autoclaved flap is then repositioned and when needed a high speed drill was used to remodel the bone flap, removing hyperostotic areas which might cause asymmetry reducing the cosmetic outcome.

All patients were followed clinically and with serial neuroradiological examinations to assess infection, bone resorption and tumor recurrence. The visual analogue scale was used to assess the patient’s satisfaction with final cosmetic outcome.

RESULTS

Nine women and three men (mean age 52.2 years ± 6.7, range 42–65 years) underwent gross total tumor resection of meningiomas invading the skull, for which their bone flaps (mean area of flap 54.2 cm² ± 27, range 20–120 cm²) were autoclaved. Table 1 presents an overview of patient characteristics, surgical and pathological data, as well as post-operative and radiological follow-up findings.

In seven of the cases (58.3%) the hyperostotic fragments sent for pathology did reveal the infiltration by tumor cells, but this could be an underestimate since only portions of suspicion of infiltration were submitted for analysis while the rest of the flap was autoclaved.

None of the cases had post-operative bone infection, or extrusion or radiological signs of sequestration. There was excellent flap alignment, with minimal or no bone resorption in all patients (Fig 1-3).

Most of the patients had an excellent cosmetic outcome (visual analogue scale for cosmesis [VASC] 90 ± 9, range 70–100). No Signs of recurrences were detected till the end of the follow up duration (mean follow up duration of the cases was 35.5 months ± 10.4, range 18 – 52 months) in any of the cases.

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Gender</th>
<th>Bone Flap Size (cm²)</th>
<th>Tumor Pathology</th>
<th>Tumor cells detected in bone biopsy</th>
<th>Post Operative Infection</th>
<th>Bone resorption</th>
<th>Recurrence</th>
<th>Visual analogue scale for cosmesis</th>
<th>Follow up Duration (Month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 45 F</td>
<td>5×4 = 20</td>
<td>Fibroblastic (WHO G I)</td>
<td>present</td>
<td>absent</td>
<td>non</td>
<td>non</td>
<td>9</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>2 52 F</td>
<td>7×6 = 42</td>
<td>Meningothelial (WHO G I)</td>
<td>absent</td>
<td>absent</td>
<td>non</td>
<td>non</td>
<td>9</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>3 48 F</td>
<td>8×6 = 48</td>
<td>Meningothelial (WHO G I)</td>
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<td>absent</td>
<td>mild</td>
<td>non</td>
<td>10</td>
<td>30</td>
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</tr>
<tr>
<td>4 48 M</td>
<td>12×10 = 120</td>
<td>Metaplastic (WHO G II)</td>
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<td>absent</td>
<td>minimal</td>
<td>non</td>
<td>9</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>5 56 F</td>
<td>9×8 = 71</td>
<td>Atypical (WHO G II)</td>
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<td>absent</td>
<td>non</td>
<td>non</td>
<td>7</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>6 49 F</td>
<td>6×5 = 30</td>
<td>Meningothelial (WHO G I)</td>
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<td>absent</td>
<td>non</td>
<td>non</td>
<td>8</td>
<td>26</td>
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<tr>
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<td>8×7 = 56</td>
<td>Angiomaticous (WHO G I)</td>
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<td>non</td>
<td>non</td>
<td>9</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>8 65 F</td>
<td>9×7 = 63</td>
<td>Atypical (WHO G II)</td>
<td>absent</td>
<td>absent</td>
<td>minimal</td>
<td>non</td>
<td>9</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>9 58 M</td>
<td>6×5 = 30</td>
<td>Meningothelial (WHO G I)</td>
<td>absent</td>
<td>absent</td>
<td>non</td>
<td>non</td>
<td>10</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>10 52 F</td>
<td>10×8 = 80</td>
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<td>absent</td>
<td>minimal</td>
<td>non</td>
<td>9</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>11 42 F</td>
<td>7×7 = 49</td>
<td>Fibroblastic (WHO G I)</td>
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<td>absent</td>
<td>non</td>
<td>non</td>
<td>10</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>12 51 F</td>
<td>7×6 = 42</td>
<td>Meningothelial (WHO G I)</td>
<td>present</td>
<td>absent</td>
<td>non</td>
<td>non</td>
<td>10</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Demographic, pathological characteristics, and complications.
**Fig. 1:** (a) Pre-operative MRI showing full thickness infiltration of bone which prevented adequate remodeling as a central egg shell outer table was left. (b) Post-operative CT 18 month later with a viable flap.

**Fig. 2:** (a) Preoperative MRI failed to reveal any bone affection, which was only detected intra-operatively. (b) Post-operative CT 38 months later showing Mild bone resorption mainly affecting the inner table with minimal effect on the overall cosmetic appearance.

**Fig. 3:** (a) Preoperative C.T. bone showing diffuse thickening of the squamous temporal bone overlying a case of meningioma en plaque, which was remodeled by drilling before insertion. (b) Post-operative of the same case 48 months later showing absence of graft resorption.
DISCUSSION

The ultimate goal of a neurosurgeon in meningioma surgery is complete excision of the offending tumor and repositioning of the raised craniotomy flap, as it gives the best cosmetic results with a shorter operative time.\(^3\) The standard treatment for infiltrated bone flaps is bone flap discarding or debridement of the affected portions followed by cranioplasty. Another option, in cases where the flap is invaded by the tumor cells, is repositioning the bone flap after autoclaving it, without lengthening of the surgical procedure or compromising the completeness of tumor resection.\(^3,5\)

Although a primary intra-osseous meningioma of the skull is uncommon, the reported incidence of meningiomas secondarily involving the calvaria provoking osteoblastic and less common osteolytic reactions is 49%.\(^4\)

The exact cause of associated hyperostosis in meningiomas, was always a point of controversy, whether this represents a secondary change of the bone without tumor invasion versus direct infiltration of the bone by tumor. Theories, proposed over the years, for meningioma-associated hyperostosis have included preceding trauma,\(^26\) vascular disturbances of the bone caused by the tumor,\(^10,14\) irritation of the bone by the tumor without bony invasion,\(^26\) stimulation of osteoblasts in the normal bone by factors secreted by the tumor cells, production of bone by the tumor itself and tumor invasion of the bone.\(^26\)

The most widely accepted theory for the association of hyperostosis with meningiomas, is tumor invasion of the bone.\(^3,26\) Predominantly a specific histological pattern of growth can be determined. However, a relationship between bone invasion and pathologic grade or size of the meningioma has not been found.\(^19\)

Tumor location is one of the most important factors affecting operative and long-term morbidity and mortality. It was especially noted that those involving the cranial base, such as the parasellar region, had a higher likelihood of incomplete tumor resection, unlike convexity lesions where completeness of excision is usually feasible. Kallio et al.\(^16\) reported that the rate of mortality was dramatically increased in patients who underwent incomplete resection of their tumors as compared with those who underwent complete resection. Jääskeläinen\(^5\) reviewed 657 patients who were treated during a 20-years period and found that the overall rate of recurrence in this population was 19%. Factors associated with an increased rate of recurrence in this series were invasion of bone, incomplete resection of the dural attachment (i.e., simple coagulation of the dura), and a soft consistency of the tumor. Marks et al.\(^20\) found, in their review of 53 patients, a rate of recurrence of 9.5% after complete resection versus 18.4% after subtotal resection. More recently, Miller\(^22\) showed that the extent of resection and mitotic index of the tumor were "powerful" factors for predicting recurrence.

Failure to address calvarial hyperostosis in meningioma surgery through limited bone resection, causes an increase in the rate of recurrence.\(^1\) On the other hand, poor cosmetic outcome is evident if aggressive bone resection is done. Cranioplasty has the theoretical potential of negating the cosmetic consequences of an aggressive extensive craniectomy in patients with hyperostosis of the cranial vault, in order to maximize radical tumor resection and decrease recurrences.\(^8\)

The first use of a cranial bone autograft was in 1821 by Von Walther.\(^4\) It then gained wide popularity.\(^1,7,28\) Orthopedicians have used autoclaved devitalized bone in their practice for more than 60 years. Naffziger\(^23\) in 1936 first described re-implantation of an autoclaved, tumor infiltrated bone flap in neurosurgical practice, and the idea was later implemented by Ray and Parsons in 1947.\(^30\)

Cryopreservation of autoclaved flaps for delayed implantation, was performed in several studies that concluded that the rate of bone resorption increased dramatically if the two processes were combined,\(^25\) due to marked destruction of the bone structure and significant reduction of its osteogenic properties. Wester\(^25\) emphasized the low complication rate met with re-implanting autoclaved bone flaps and that this technique effectively kills all tumor cells infiltrating the bone. Since then the procedure has been widely applied by others and used to facilitate treatment of cranio-facial skeletal tumors.\(^3,22\)

Autogenous bone grafts as Split rib or calvarial grafts are the best choice of an intra-operative in situ cranioplasty bone graft, as they have similar resilience, brittleness, and rigidity to the resected calvarial bone.\(^17\) They enjoy a high local take and compatibility with minimal or no host reaction in addition to minimal donor-site side effects, especially for split calvarial grafts if the operative site allows.\(^15\) The drawbacks of this technique is extended time of an already prolonged operation together with added morbidity and increased blood loss of a second incision as well as difficulty of reforming the bone resulting in suboptimal cosmetic results.\(^8,31\)

These drawbacks gave way to a wide array of inexpensive or expensive artificial materials necessary to maximize implant accuracy and cosmetic outcome, especially if performed intra-operatively in a patient specific cranioplasty technique. Titanium mesh and bone cement are known for their ease to cover skull defects; but quite often, the cosmetic results turn out to be rather disappointing after skin closure, especially when the cranial defect involved the frontal or the temporal areas.\(^36\)

Many reports stated that patients might have histological tumor invasion of the bone, without having
their hyperostotic changes revealed by preoperative neuroradiological imaging. 

In ten patients of the present study, hyperostotic changes were detected during surgery, with no cranioplasty material available to discard the flap and perform a cranioplasty.

In such instances where intra-operative bone involvement is detected, an Intra-operative in situ cranioplasty could be performed, thus avoiding the risks encountered with delayed cranioplasty, especially the occurrence of adhesions of the scalp to dura or brain, and the potential of injuring the non-protected brain during daily exposures to temperature and atmospheric pressure variations as well as traumatic events. This single step technique abolishes the extra burden of another hospitalization, anesthesia; and above all, the cost and possible complications and unbearable psychological stress of a second surgery. 

Several authors had concerns as regards to the use of autoclaved bone flaps, as it is actually denatured dead tissue, that may increase per se the risk of infection, thus not suitable for reconstructing purposes. 

Prolo and Oklund described some cases of aseptic necrosis associated with the use of autoclaved autogenous calvarial bone flaps, but this has not been confirmed by other studies, or in this series.

No cases of infection were met with in this study. The infection rates of this technique are comparable with those for other types of cranioplasty material. Thus, it seems likely that other factors rather than the kind of implanted material play the most important role in reducing the infection rate, particularly the quality of the surgical work. Autoclaving per se does not seem to increase the risk of infection if adequate sterility and aseptic procedures are followed.

A good beveled edge should be made while raising the flap at beginning of surgery. The aim of this is to increase the surface area of graft-to-defect margin contact to avoid fibrous union and assure bone ingrowth into the graft. It is documented that revitalization of the autoclaved bone flap following implantation occurs through a process of revascularization, resorption and new bone formation, progressively replacing the devitalized bone.

Autoclaving does result in loss of osteo-inductive ability of bone, a decrease in its biomechanical properties, and the risk of bone resorption have been of concern to many. None of the cases in this study have shown significant bone resorption, that might compromise the integrity of the flap, nor did they require a second corrective surgical procedure as the cosmetic result was acceptable. In contrast to long bones, the mechanical stresses to which the flap is subjected are minimal. Thus concerns about biomechanical weakness of the bone flap is not substantiated.

In many developing countries, neurosurgical practice is partially governed by the costs and availability of recent medical technology. The lack of medical insurance coverage makes the costs lie upon the patients themselves, who may not afford the seemingly cheapest cranioplasty material. The cost–benefit curve in modern cranioplasty techniques is an asymptotic one. Recent medical technological innovations has placed itself so far out on that curve that a substantial increase in costs only results in a minor, in some cases even microscopic, gain in health.

CONCLUSION

- Failure to address the hyperostosis provides a nidus for the regrowth of the tumor. Thus care must be taken to directly inspect those areas of potential tumour invasion, because the limitation of an adequate preoperative assessment may lead to an unexpected tumor residual in an otherwise complete resection.

- Returning the raised craniotomy flap provides the best cosmetic results, abolishes the time lost for modeling and shaping, if other grafts types are used.

- Although autoclaving severely denatures the organic bone components, it also destroys all tumor cells in calvarial bone flaps preventing possible recurrence.

- This technique reduces the financial burden on the patient, in regions where the lack of medical insurance plays a role in decision making.

The limitation of the present study was the small number of cases presented, and the relatively short follow-up these patients have had; knowing that we are dealing with a tumor of well-known insidious nature (particularly the potential for tumor recurrence and possible bony resorption with time). It is believed that further study of the revitalization process that occurs in the autoclaved bone and the relation between it and size of the flap is needed.

REFERENCES