



## Cranioplasty after 25 Years of Implant Rejection

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**Abstract:** Cranioplasty is a common neurosurgical procedure performed to reconstruct cranial defects. Failure of cranioplasty may be early or delayed and further can be attributed to the surgical procedure itself or to the reconstruction material used for the procedure. We reported a 54-year-old man came to the clinic with wound and defect in his scalp. He had previous craniectomy 25 years ago due to an accident that caused a head injury. The size of the wound was 10 x 10 cm with granulation tissue at the base of the wound. There was no discharge at the site of the wound. In physical examination, vital sign was normal, laboratory examination showed slight leukocytosis. Cranioplasty surgery was performed to reconstruct the scalp defect. Implant failure was found characterized by pain at the implant site, erythema, and fever. Therefore, cranioplasty implant rejection was diagnosed. Reconstructive cranioplasty with titanium mesh was done a week later. Thirty years ago, PMMA maybe the most available biomaterial, however, disadvantages may occur such as infections, extrusion, decomposition, fracture of implant in larger defect, and lack of integration to the bone. Spontaneous implementation of the biomaterials leads to CIR, and without proper resolution under two weeks it leads to a foreign body response (FBR) and chronic inflammation. Hence in this study, the use of titanium mesh can overcome those disadvantages, with lower risk of infection, non-corrosive, non-inflammatory, good cosmetic results and great potential of osseointegration. In conclusion, materials in cranioplasty should be considered and follow up regularly and well. Cranioplasty implant rejection was a known complication risk that can leads to chronic inflammation. Associated symptoms including pain, erythema and fever. Using synthetic implants with non-inflammatory and great osseointegration characteristics can lead to great results as shown in this case.

**Keywords:** cranioplasty; implant; rejection

## INTRODUCTION

Cranioplasty is defined as the surgical repair of a defect in the cranium by insertion of an object (bone or non-biological materials such as metal or plastic plates). Repairing the cranial bone is one of the oldest neurosurgical practices dating back to ancient Egypt. Replacing the cranium is not only a protective and cosmetic procedure but may also reverse the altered physiological state that occurs following craniectomy and improve electroencephalographically abnormalities, aberrations of cerebral blood flow and cerebrospinal fluid dynamics.<sup>1</sup>

Recently, an increased interest in analysing possible factors associated with complications has emerged in order to improve modalities of the procedure. Various potential risk factors have been identified: Cranioplasty timing, optimal cranioplasty material (autologous vs alloplastic), bone resorption rate using autologous cranioplasty's, or possible risk factors that may influence the implant survival. Possible factors such as hydrocephalus, patient age (<30 years), and segmented bone flaps may lead to significant higher rates of complications and bone flap resorption. A combination of an autologous implant and a younger age seems to play an important role due to a high number of bone flap resorption. In cases of bone flap resorption in children and adolescents, subsequent revision is necessary in up to 50% of cases.<sup>2</sup>

The ideal material used for cranioplasty should have the following properties; biocompatibility, low cost, malleability to fit different defect shapes, and resistance to infection. Although autologous bone grafts fit many criteria of the ideal graft, they have a high resorption rate that may necessitate revision surgery and application of alloplastic material. Therefore, bone grafts have been replaced by other materials to decrease resorption rate and donor site morbidity.<sup>3</sup>

## CASE REPORT

A 54-year-old man came to the clinic with wound and defect in his scalp. He had previous craniectomy 25 years ago due to an accident that caused a head injury. The size of the wound was 10 x 10 cm with granulation tissue at the base of the wound. There was no discharge at the site of the wound (Figure 1). In physical examination, vital signs were normal, laboratory examinations showed slight leucocytosis. Cranioplasty surgery was performed to reconstruct the scalp defect, however, implant failure occurred characterized by pain at the implant site, erythema, and fever. Therefore, the implant in this patient was removed, and a week later, a reconstructive cranioplasty with titanium mesh was performed to repair the scalp defect. Using synthetic implants with non-inflammatory and great osseointegration characteristics can lead to great results as shown in this case (Figure 2-6).

## DISCUSSION

Cranioplasty is defined as a reconstructive procedure that is used to repair skull defects and restore the skull anatomy. To repair the bone defect, numerous natural and artificial materials have been used by neurosurgeons.<sup>4</sup> The other aims of cranioplasty is protecting the brain from mechanical assault and cosmetic reasons. Based on its timing, cranioplasty can be divided into early and late cranioplasty depending on its timing after decompressive craniectomy.



**Figure 1.** A 54-year-old man with wound and defect in his scalp. A, Lateral view; B, Posterior view



**Figure 2.** Pre - operative image



**Figure 3.** Intra-operative images



**Figure 4.** Post-operative images



**Figure 5.** One month after surgery



**Figure 6.** Two months after surgery

A time of 2 or 3 months is used as a reference to distinguish between early and late timings.<sup>5</sup> The basic principles of cranioplasty restoring the anatomical cranial architecture to restore the skull protective functions, also improving cranial appearance and function post-craniectomy.<sup>6</sup>

Cranioplasty has a high complication incidence, up to 10–50% although it is a relatively simple neurosurgical procedure. The complications that can occur in cranioplasty are skin breakdown and flap exposure, wound infection, subgaleal pus, intracranial empyema, pyogenic osteomyelitis, hematoma below the replaced flap, intraparenchymal haemorrhage, epidural fluid collection or hygroma below the flap, flap subsidence, flap resorption, implant extrusion, poor fixation flap, incompatible flap size, infection, hydrocephalus, extra-axial fluid collection, seizure,

and bone resorption.<sup>7</sup> Wang et al, create an algorithmic approach of reconstruction for cranioplasty failure based on scalp defect size, location, hairline involvement, reconstruction of soft tissue and reconstruction of skull deformity. When autologous tissue is unavailable or recurrent infection exist, synthetic grafts are used.<sup>8</sup>

The two primary categories of materials used in cranial surgery are biological and synthetic. The ideal material for cranioplasty is lightweight, durable, easily fixable to the skull, malleable, and osteoconductive. Biological materials can also be separated into xenografts, allografts, and autologous grafts. Synthetic materials such as titanium, polymethyl methacrylate (PMMA) and Medpor (porous polyethylene) have many advantages such as mechanical strength and biocompatibility, but none of these materials is perfect cranioplasty material.<sup>4</sup> The graft material choice is multifactorial. Surgeons should consider the age of patients, size, etiology, and location of the defect, also their preferences. Allografts and xenografts are rarely used due to their high rejection, infective complications, and osteonecrosis rates.<sup>9</sup>

Although autologous bone grafts fit many criteria of the ideal graft, they have a high resorption rate that may necessitate revision surgery and application of alloplastic material. Cranioplasty with autologous bone grafts resulting defects requiring replacement by an alloplastic material, meanwhile implanted alloplastic materials can cause an acute inflammatory reaction followed by a chronic inflammatory reaction. Adverse effect of using these materials should always be considered in choosing graft. Foreign body reaction may occur which is characterized by monocytes, macrophages, foreign-body giant cells, and tissue granulation at the biomaterial interface.<sup>4</sup> Also because of its closeness to brain tissues, there may be risk of neurotoxicity. Therefore, to ensure the safety of patients, these materials need to be biocompatible (both locally and systemically), biologically inert, and nontoxic if degraded.

In our case, the implant used in this patient was PMMA. Sign of implant rejection in this patient was pain at the implant site, erythema, and fever. We suggest the implant failure was delayed reaction of chronic inflammatory reaction to the PMMA implant. Thirty years ago, PMMA implant maybe the most available implant in between not much choices. The advantages of using PMMA was strong, radiolucent, non-irritating, and nonconductive, low cost and readily available.<sup>5-7</sup> Despite all the advantages, PMMA also has disadvantages such as higher rate of infection, high risk of extrusion, decomposition, risk of the fracture of the implant in larger defects and a high failure rate in the long-term as a result of lack of integration into bone because of its inert nature.<sup>10-12</sup> Polymethylmethacrylate (PMMA) is used as support wire mesh for large cranioplasties for fracture reduction and more cosmetic resolution. It is a polymerized ester of acrylic acid that strengthly comparable to bone. The use of PMMA may be associated with several complications such as exothermic reaction during the process of curing that may result in local burn and tissue damage. It also has a higher risk of decomposition, extrusion, and infection.<sup>12,13</sup> Autologous bone also has a higher rate of complication compared to allogenic when osteolysis was also considered. Osteolysis occurrence is unpredictable but it has clear risk factors including younger age, bone flap fragmentation, and traumatic brain injury history.<sup>14</sup> In a systematic review conducted by Van de Vijfeijken et al. (2018), PMMA had the highest rates of infection (7.8%), with implant failure occurring in 7.9%. Cheng et al., in 2008 reported a 6.25% failure rate with PMMA cranioplasty, which was similar to Akan et al.'s reported failure rate of 6% rate with PMMA.<sup>15</sup>

Goedemans et al.'s found that early cranioplasty defined by within 3 months after decompressive craniectomy associated with more complications.<sup>16</sup> The implantation of biomaterials spontaneously initiates an acute inflammatory reaction, which leads to a CIR. If the CIR does not attenuate after 2 weeks, it becomes pathological, and inflammation is transferred to adjacent tissues. In several studies CIR occurred 30- 53 days after implantation. The causes of toxicity leading to CIR differ between materials and for PMMA, residual monomer generates toxicity. In previous study by Moser et al explained that when using PMMA for cranioplasty with indirect technique may still need fine shaping when implant doesn't fit, and holes are drilled for screw fixation. This adjustment may release residual monomer which causing CIR. Inaccurate

mixture of liquid and monomer may cause residual monomer causing CIR as well.<sup>4</sup>

A foreign body response (FBR) is initiated when a biomaterial is implanted. A complex event cascade will be triggered and it can culminate in the fibrous encapsulation of biomaterial (biomaterial failure) and the unwanted degradation of biomaterial due to the enzymes and reactive species release by immune cells or in an ideal scenario, it can lead to microenvironmental remodelling and tissue regeneration.<sup>17</sup> The host immune response is an essential component of response of implant. Implant materials that evoke a strong chronic inflammatory response or foreign body reaction are logically subject to failure and/or degradation overtime.<sup>18</sup>

Polymethyl methacrylate particles are persistently released after its implantation. It can evoke heightened inflammatory, immune, and osteolytic responses. Inflammatory cellular response including recruitment and activation of myeloid and immune cells such as macrophages, dendritic cells, lymphocytes, and granulocytes is also triggered.<sup>19</sup> Macrophages are the key drivers of the immune response to implanted materials. Aging may be the reason of late implant rejection in this case. Aging affects multiple aspects of immune system. Immunosenescence, macrophage function and polarization dysregulation, and acute immune responses delayed responses are reported in aged-individual. Therefore, aging may affect the host response to implantable materials. Host response to implants is affected by age-related accumulation of cell-intrinsic defects and local tissue microenvironment.<sup>18</sup>

Synthetic implants have shown lower infection rates and absorption rates compared to autologous.<sup>10</sup> Synthetic grafts such as titanium mesh, PMMA, hydroxyapatite, and polyetheretherketone (PEEK) are commonly used in order to avoid the autografts complication, better cosmetic and operative results. Titanium has several advantages including low risk of infection, non-corrosive, non-inflammatory, and very good cosmetic results. It also has perforated nature with a large number of holes that can promote the vascular ingrowth. Therefore, it is considered as a bioactive metal with great potentiality for osseointegration with appropriate texture and porosity.<sup>12</sup>

The mentioned advantages are the reason for using titanium mesh to replace the PMMA. The wound is large with estimated size of 10 x 10 cm and the ability of titanium to promote the vascular ingrowth may increase the wound healing rate to achieve good cosmetic results. It can be used alone or can be combined with another synthetic material, such as MMA or hydroxyapatite, to enhance cosmetic results. It has superior cosmetic results compared with those of other materials used in cranioplasty, it has the lowest infection rate. The disadvantage of this material was found to be heat conductive and is considered expensive. A study by Wesp et al. obtained that a biocompatible Calcium phosphate titanium-enhanced implant seems to be superior to a PMMA implant in terms of surgical site infection and postoperative complications.<sup>20</sup> A retrospective study by Kim et al. described that in-between autologous bone and porous polyethylene, cranioplasty with custom titanium mesh shows benefits in terms of lower post-cranioplasty complication, less intraoperative bleeding loss, shorter operation time, and in-hospital stay.<sup>21</sup>

Another material that may be use for implant that has superiority to titanium and PMMA was PEEK. It can be customized to according to the craniectomy defect with high accuracy to get best cosmetic result. They are also light and nonconductive and do not interfere with imaging modalities. However, it's the most expensive implant and may not easily available.<sup>11,12</sup>

## CONCLUSION

Materials in cranioplasty should be considered and follow up regularly and well. Cranioplasty implant rejection was a known complication risk that can leads to chronic inflammation. Associated symptoms including pain, erythema and fever. Using synthetic implants with non-inflammatory and great osseointegration characteristics can lead to great results as shown in this case.



## Conflict of Interest

The authors affirm no conflict of interest in this study.

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