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Management of infected hydroxyapatite cranioplasty: Is salvage feasible?

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ABSTRACT

Introduction: The use of hydroxyapatite cranioplasties has grown progressively over the past few decades. The peculiar biological properties of this material make it particularly suitable for patients with decompressive craniectomy where bone reintegration is a primary objective. However, hydroxyapatite infection rates are similar to those of other reconstructive materials.

Research question: We investigated if infected hydroxyapatite implants could be saved or not.

Materials and methods: We present a consecutive series over a 10-year period of nine patients treated for hydroxyapatite cranioplasty infection. Clinical and radiological data from admission and follow-up, photo and video material documenting the different phases of infection assessment and treatment, and final outcomes were retrospectively reviewed in an attempt to identify the best options and possible pitfalls in a case-by-case decision-making process.

Results: Five unilateral and four bifrontal implants became infected. Wound rupture with cranioplasty exposure was the most common presentation. At revision, all implants were ossified, requiring a new craniotomy to clean the purulent epidural collections. The cranioplasty was fully saved in one hemispheric and 2 bifrontal implants and partially saved in the remaining 2 bifrontal implants. A complete cranioplasty removal was needed in the other 4 cases, but immediate cranial reconstruction was possible in 2. Skin defects were covered by free flaps in 3 cases. Four patients underwent adjunctive hyperbaric therapy, which was effective in one case.

Discussion and conclusion: In our experience, infected hydroxyapatite cranioplasty management is complex and requires a multidisciplinary approach. Salvage of a hydroxyapatite implant is possible under specific circumstances.

1. Introduction

The use of hydroxyapatite (HA) cranioplasty has progressively gained acceptance in neurosurgical practice over the past few decades (Stefini et al. 2013; Fricia et al. 2019). The unique biological properties of this material (especially its microporous structure aiming at osteointegration and its self-repairing ability in case of breaks) make it suitable for cranial reconstruction after decompressive craniectomy (DC), particularly in young patients (Staffa et al. 2012; Iaccarino et al. 2015). However, though several solutions have been proposed to avoid dislocations/mobilizations, HA cranioplasties are difficult to adequately anchor to the surrounding skull. They are also usually thicker than other implants but practically no longer adjustable once placed, as any intraoperative modification could cause micro-fractures in the still fragile prostheses (Rienzo et al. 2012; Stefini et al. 2013; Lindner et al. 2017).

Although the microporous structure of HA is considered protective against bacterial colonization, infection rates ranging from 1 to 14% have been reported (Iaccarino et al., 2018; Zanotti et al. 2018).

Effective management strategy in cases of HA implant infection is a matter of debate. Most authors suggest that complete cranioplasty removal is the only safe option for achieving a quick field sterilization, despite potential complications such as sinking flap syndrome. Variable rates of successful conservative treatment have been reported by a handful of other authors. (Johnson et al. 2000; Ashayeri et al. 2016; Di Rienzo et al. 2016, 2020, 2021; Iaccarino et al., 2018; Still et al. 2018) It should be emphasised that any attempt to salvage an infected implant may turn disastrous due to the potential further, multidirectional spreading of germs inside and/or outside the cranioplasty. (Johnson et al. 2000; Di Rienzo et al. 2016, 2020, 2021; Iaccarino et al., 2018; Still et al. 2018)

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We present our experience in the management of nine patients with HA cranioplasty infection. The decision to maintain or remove (completely or partially) the implant in each case was strictly tailored according to the patient's clinicoradiological features, producing mostly successful results.

Moreover, we reviewed the few main series on the topic and compared our results with the literature to highlight some of the solutions that allowed us to optimise the management of such complex situations.

2. Materials and methods

We retrospectively reviewed records of patients surgically treated for HA cranioplasty infections at our institution from January 2009 to December 2018. Pertinent clinical and radiological information was registered. Pre-, intra- and post-operative pictures and videos were collected for every procedure after obtaining appropriate consent from either the patient or a legally authorised representative.

In cases of open wounds, the head was entirely shaved to properly inspect the involved area and its surroundings for the presence of further lesions. Swabs were then taken. All patients underwent an emergent contrast-enhanced CT head, except in case of renal insufficiency. Brain MRI was performed on one patient.

Treatment was patient-tailored based on neurological status, inflammatory markers and neuroimaging. Four surgical treatment schemes were used:

1) ***emergency implant removal and debridement***, for patients with impaired consciousness and CT evidence of surgical site infection;
2) ***partial cranioplasty removal and debridement***, in cases without neurological compromise but with an open wound, pus leakage, exposed implant, face/head tissues swelling, raised inflammatory markers and CT demonstrating surgical site infection. The amount of implant removal was preoperatively planned in relation to the evidence of a circumscribed CT extension of any epidural collection. Again, intraoperative confirmation was always obtained, carefully inspecting the whole cranioplasty surface and starting with a targeted implant removal to be expanded up to find macroscopically uninvolved dura;
3) ***flap re-opening, debridement, irrigation with vancomycin, and flap repair***, for asymptomatic patients with an open wound, exposed implant, no pus leakage, no face/head swelling, no or slightly altered inflammatory markers, no CT evidence of epidural/subdural abscess, and no intraoperative evidence of cranioplasty surface abnormality (erosion, thinning, cavitation, pus accumulation either above the implant or in its immediate surroundings);
4) ***implant removal, aggressive debridement up to expose the dural layer re-sutured at the moment of DC, immediate cranioplasty***, for patients that were showing focal thinning of the skin flap (typically over the pterional region), face/head swelling, raised inflammatory markers, and with contrast enhanced head CT revealing the presence of epidural abscess. In these cases, wound was not found open, cranioplasty was not found exposed, and pus leaking was never observed.

Samples for microbiology were collected intraoperatively from multiple sites. Cranioplasty fragments were also sent for analysis. Once toilette was completed, the field was irrigated with hydrogen peroxide and iodine solutions.

Wound repair options were pre-operatively evaluated with our plastic surgeon team based on size of defects, infection severity, and potential donor-site morbidity and included: 1) circumferential, epi-galeal flap detachment and direct repair; 2) advancement flap; and 3) free flap.

Twelve weeks of intravenous antibiotics were administered in every case, either targeted or broad-spectrum (2 g meropenem three times a day plus 1 g vancomycin twice a day). In patients who underwent partial or total implant removal, cranial reconstruction was never considered earlier than 6 months and only after normalisation of inflammatory markers, complete wound healing, and CT negativity for infection signs.

A non-contrast post-operative CT scan was performed within 24 h after surgery to rule out complications. Contrast CT scans were also planned for 4, 12 and 24 weeks post-surgery, and non-contrast scans were planned for 12 and 24 months.

Following appropriate informed consent, to monitor any significant change in wound appearances, pictures and videos of the flaps were taken pre-operatively and then post-operatively at 3-week intervals and sent to us through a dedicated hospital e-mail.

Minimum follow-up was 14 months and maximum was 9 years.

Ethical approval was waived by our local ethics committee due to the retrospective nature of the study and because all procedures were performed as part of routine care.

3. Results (Table 1, Figs. 1 and 2)

From January 2009 to December 2018, we implanted 43 HA cranial prostheses in patients previously treated by DC. In the same period, 283 patients underwent post-DC reconstruction by autologous bone, 20 by polyetheterketone (PEEK), 12 by pre-formed titanium meshes, 15 by customised polymethyl methacrylate (PMMA), and 5 by customised titanium plates.

Nine HA cranioplasties (20.93%) became infected. Six of these 9 patients had been treated by DC for TBI, two for SAH, one for meningoencephalitis with severe intracranial hypertension refractory to maximal medical therapy. At the time of infection 6 patients harboured a ventriculo-peritoneal shunt, implanted either simultaneously with first cranioplasty (4) or shortly after (2).

HA had been selected as first cranial substitute in one case (due to traumatic bone fragmentation). It replaced a resorbed bone flap in the other 8 patients.

Six implants were made of a single piece, 3 of 2 pairing pieces. Five implants were unilateral (surface area >100 cm^2 and <150 cm^2), four bifrontal ($1 > 150$ cm^2 and <200 cm^2; $3 > 200$ cm^2).

Mean age of the infected patients was 36.4 years, with a male to female ratio of 8:1.

The shortest interval between cranioplasty and infection was 18 months, the longest was 106 months.

At inspection, a well-defined dehiscent area with exposure of the underlying cranioplasty was observed in 6 cases (along the line of flap incision in 4 subjects, within the flap in 2). In 2 patients skin was intact but thinned and translucent over the pterional area. In the last case in our series there was no wound abnormality but both face and neck on the side of the infected cranioplasty were massively swollen at hospital admission.

Fever was observed only in the 3 patients with intact skin. Inflammatory markers were always raised (CRP in 6 cases, ESR in 8, procalcitonin in 4, leucocyte count in 7), although in different combinations.

Only 4 of the 6 preoperative swabs (always obtained by open wounds) came positive (Table 1: Corynebacterium striatum, A. Baumanii, S. Epidermidis, Methycillin resistan S. Aureus). Intraoperative swabs were positive in 6 cases (Table 1: P Aeruginosa, E. Coli in 2 cases, A. Baumanii, K. Oxytoca, Methycillin resistan S. Aureus).

Swabs were performed in all patients presenting with an open wound. These samples were concordant with intraoperative results only in 2 cases, where antibiotic therapy was left unchanged. In the remaining 4 cases antibiotic therapy was modified according to the results of intraoperative samples.

Contrast CT at admission revealed an epidural abscess in 6 cases (with epidural air penetration in 2). Maximal enhancement involved the dural layer in 7 cases. No contrast was administered in 2 cases due to creatinine levels above the normal range.

A 2 weeks preoperative course of antibiotic therapy was adopted in 7 patients. This strategy was not possible in the 2 subjects experiencing

Table 1
Patient demographics, craniotomy type, clinicoradiological features, inflammatory markers, germs isolated from culture, surgical treatment, and final outcome.

Patient	Age, y	Sex	Craniotomy	Time from cranioplasty to infection, months	Admission GOS	Inflammatory markers	Open wound	Epidural pus	Dural enhancement	Pre-operative swab	Intra-operative swab	Surgical treatment	New cranioplasty material	Flap repair	Final GOS
1	17	M	Left F-T-P	32	5	CRP+, ESR+, PCT-	Yes	Yes	Yes	–	–	Implant removal + immediate cranioplasty	PEEK	Direct repair	5
2	56	M	Right F-T-P	106	5	CRP+, ESR+, PCT+	No	No	No	Corynebacterium striatum	*Pseudomonas aeruginosa*	Toilette		Advancement flap	5
3	19	M	Bi-frontal	18	4	CRP+, ESR+, PCT-	Yes	No	Yes	–	*Escherichia coli*	One-side implant removal	PEEK	Direct repair	5
4	48	M	Right F-T-P	45	3	CRP+, ESR+, PCT+	Yes	Yes	Yes	Acinetobacter baumannii	Acinetobacter baumannii	Implant removal		Advancement flap, trapezius muscle free flap	1
5	19	M	Bi-frontal	20	3	CRP+, ESR+, PCT+	Yes	Yes	No	–	–	One-side implant removal	HA	Direct repair	4
6	49	M	Left F-T-P	40	4	CRP-, ESR-, PCT-	No	Yes	Yes	–	–	Implant removal + immediate cranioplasty	PEEK	Direct repair	5
7	58	M	Bi-frontal	38	3	CRP-, ESR+, PCT-	Yes	No	Yes	–	*Escherichia coli*	Toilette		Radial forearm free flap	3
8	43	M	Right F-T-P	20	3	CRP+, ESR+, PCT+	No	Yes	Yes	Staphylococcus epidermidis	Klebsiella oxytoca	Implant removal	PEEK	Direct repair	3
9	19	F	Bi-frontal	22	4	CRP-, ESR+, PCT-	Yes	Yes	Yes	Methicillin-resistant*Staphylococcus aureus*	Methicillin-resistant *Staphylococcus aureus*	Toilette		Radial forearm free flap	5

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; F, female; F-T-P, fronto-temporo-parietal; GOS, Glasgow Outcome Scale; HA, hydroxyapatite; M, male; PCT, procalcitonin; PEEK, polyetherketone.

rapid neurologic deterioration, where immediate surgery was considered the only safe option.

In all cases, HA implants were found fully ossified at surgery, making necessary a redo craniotomy and aggressive drilling of the surrounding borders (where residual HA appeared intertwined with autologous bone) to reach the epidural collections.

Two HA implants were removed without considering replacement, due to the rapid deterioration of neurological conditions. In 2 cases the infected cranioplasty was removed and a new implant immediately repositioned. Explant of only one of the 2 pieces of a bifrontal cranioplasty was possible in 2 cases. In the remaining 3 patients the cranioplasty was left in place after an extensive toilette of the infected tissue (Table 1); vancomycin irrigation was used in only one of these patients.

Direct repair of the dehiscent wound was possible in 5 cases. A radial forearm free flap was needed to cover the skin defect in 2 cases (after debridement), an advancement flap in 2 more patients. The advancement flap failed in one case and a trapezius free flap was performed, this time without further complications.

Management was complicated in 2 shunt patients. The first, harbouring a ventriculo-peritoneal shunt contralateral to the infected flap, developed a severely symptomatic sinking flap syndrome since day 5 after cranioplasty removal, although the valve had been reset to 200 mmH_2O immediately after surgery. This dictated shunt removal, evolving into a slow deterioration of neurologic conditions, due to hydrocephalus. Three weeks later the flap was tense and broke, while the patient was host in a rehabilitation facility. At admission, skin was so thin that even with the use of a temporary external drain to reduce local pressure, it was not possible to re-approximate the borders. Our Plastic Surgeons decided for a flap advancement, that was temporarily successful. Two weeks later a dehiscent area appeared in the middle of the advanced flap, so that 2 days later a free transfer from the trapezius took place. In these 5 weeks, the patient's neurological conditions progressively worsened from Glasgow outcome scale (GOS) 3 to GOS 2. A ventriculoperitoneal shunt was re-implanted 6 months later and set at 170 mmH_2O, but 2 weeks later the patient developed a lung infection from *Acinetobacter baumanii*, delaying cranial reconstruction. He died from sepsis 14 months later, without cranioplasty.

In the second case, a patient carrying an adjustable ventriculoperitoneal shunt underwent removal of part of a bifrontal implant. Shunt setting was left at 130 mmH_2O, initially without clinical modifications. However, five months later he developed a sinking flap syndrome and his backup HA cranioplasty, which was still available, was used for cranial reconstruction.

Hyperbaric therapy took place pre-operatively in 3 cases and post-operatively in 1 (the only patient who appeared to benefit from it, as documented by serial CT scans).

Overall, we were able to fully save 3 implants and to remove only part of 2. Although in these last 2 cases further reconstruction was still needed, the new surgical procedure was shorter in duration when compared to the first cranioplasty placement (150 Vs 260 min), allowing to minimize intraoperative blood loss, tissue manipulation and exposure of the intracranial compartment. In addition, in case of explant of the whole cranioplasty, the risks of skin flap retraction would have been increased, thus potentially complicating the subsequent reconstructive procedure.

4. Discussion

The conventional strategy for dealing with cranioplasty infections has historically been based on removing the infected bone/implant and performing a local debridement, followed by a delayed cranial reconstruction after prolonged I.V. antibiotic therapy. Immediate cranial reconstruction after debridement was considered too dangerous due to the risk of recurrent infections and bone resorption. (Di Rienzo et al. 2013, 2021; Zanaty et al. 2014, 2015; Lopez et al. 2016) However, a single-stage surgery could avoid an additional socioeconomic burden for

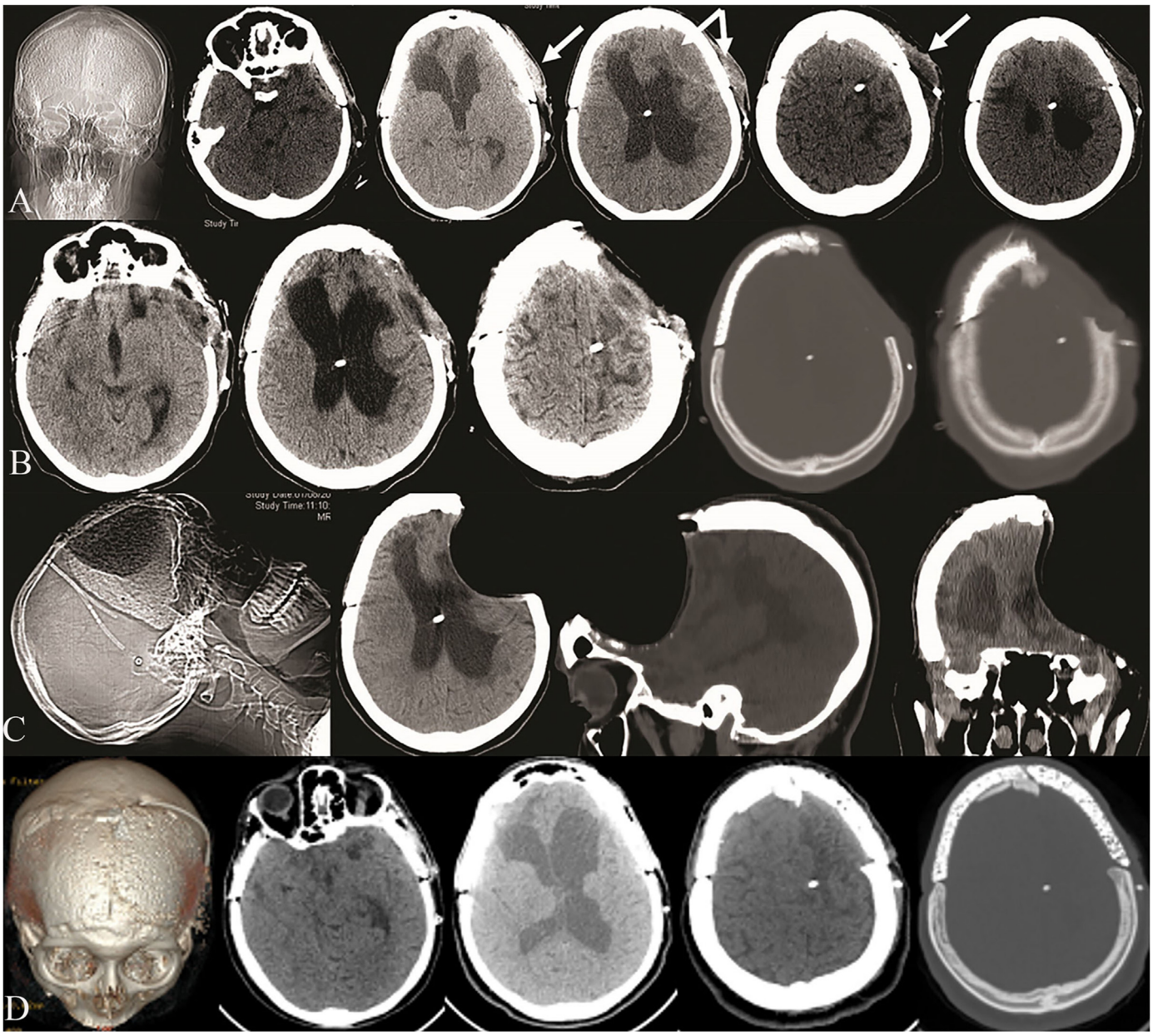

Fig. 1. HA cranioplasty infection in a bifrontal implant (shunted patient)
A: admission CT demonstrating a large subcutaneous and epidural pus collection (white arrows). The intracranial component of the abscess compresses and displaces the left frontal ventricular horn.
B: post-operative CT: the left half of the HA cranioplasty has been removed and the collection debrided. Modest brain expansion can be noted, with full resolution of the mass effect on the ventricular system.
C: Five-months post-operative CT, performed in emergency due to sudden neurological deterioration. Massive sinking flap with severe contralateral brain displacement is evident. Shunt reset at 200 mmH_2O was ineffective, so the still available backup implant was used to fill the defect.
D: CT one year after the implant of the left HA backup cranioplasty. No further surgeries were needed.

the patient (cosmetic deformity, psychosocial distress, lost working days) while potentially reducing the risks and costs of a delayed surgical procedure. (Zanaty et al. 2014, 2015; Lopez et al. 2016; Di Rienzo et al. 2021)

Given these considerations, some alternative management strategies have been proposed by different authors, including intraoperative autoclaving of infected cranioplasties, 'in situ' irrigation with antibiotics (usually vancomycin) of autologous bone flaps/artificial implants, simple debridement, debridement *plus* immediate titanium mesh cranioplasty (Wind et al. 2013; Missori et al. 2016; Wui et al. 2016; Bokhari et al. 2019; Moneim et al. 2020).

Unlike the first available artificial implants (PMMA and titanium meshes), which required intraoperative free-hand modelling and were characterised by low biocompatibility (with an increased risk of giant cell granulomas development and skin flap damage), the new, customizable titanium, PEEK and HA cranial protheses have high biocompatibility and are individually designed for patients, thus contributing to an excellent anatomical fit and contour. Additionally, the biomimetic properties of HA implants may promote bone integration. Nonetheless, despite the use of custom-made cranial implants, cranioplasty infections remain challenging postoperative complications (Zanaty et al. 2014; Iaccarino et al., 2018; Zanotti et al. 2018).

The first known attempt at preserving an infected HA implant was reported by Johnson et al., in 2000. A cranioplasty with HA cement and titanium mesh was performed in a 43-year-old woman who had

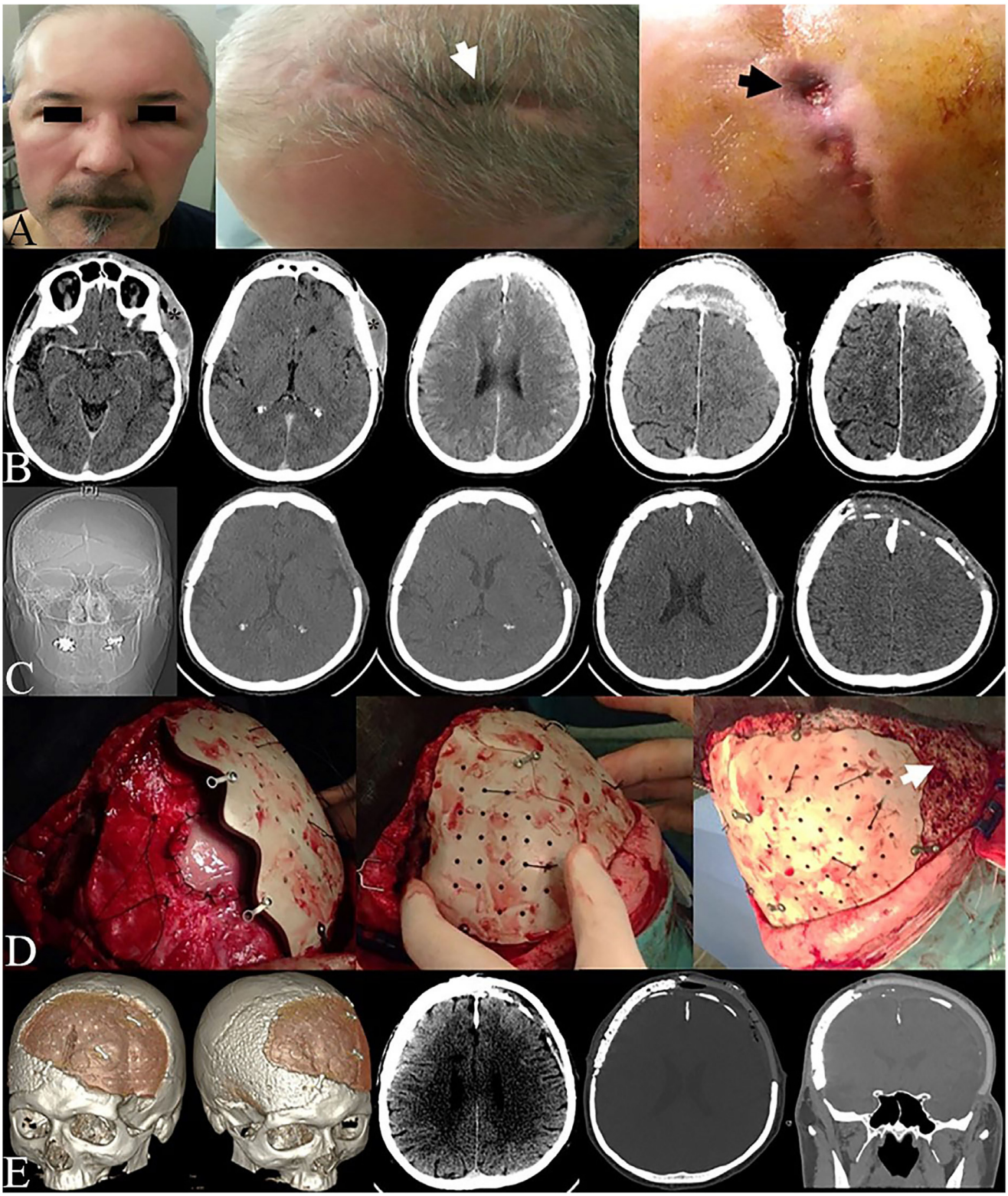

Fig. 2. Another example of HA cranioplasty infection in a bifrontal implant
A: Patient was admitted due to massive facial and scalp swelling. At flap inspection multiple breaks were observed along the bicoronal flap (white and black arrows). Exposure of the cranioplasty became evident after shaving.
B: Admission contrast CT, showing subcutaneous and epidural accumulation of pus. Contrast accumulation within the temporalis muscle was particularly evident and extended to the surrounding tissues (black asterisks).
C: Post-operative CT, showing removal of the left half and part of the right half of the cranioplasty, that was required to allow full debridement of the epidural collection.
D: Intra-operative pictures showing the positioning of the PEEK cranioplasty. Due to the size of the defect, the new implant was realized in 2 pieces. After joining together the 2 PEEK halves, the right implant was fixed with titanium miniplates over the ossified residual HA cranioplasty (white arrow).
E: 1 year later follow-up CT, showing the final result of cranial reconstruction.

undergone a left vestibular nerve section for Meniere's disease through a retrosigmoid route one year earlier. A surgical revision was required due to the development of skin necrosis and wound dehiscence with implant exposure. Wound debridement, targeted intravenous antibiotics and 'in situ' irrigation enabled complete healing (Johnson et al. 2000).

Poetker et al. reviewed a series of 76 HA cranioplasties that were performed after lateral skull base surgeries and reported two cranioplasty infections that ultimately required implant removal (Poetker et al. 2004).

Stefini et al. reported a 2.05% overall infection rate after HA cranioplasties (33 out of 1608 implants): 31 were removed (18 were later replaced with a back-up device after antibiotic therapy, 8 patients rejected the HA implant), one patient required only medical treatment, and the last patient presented only a limited skin infection (Stefini et al. 2013).

The rate of HA cranioplasty infection recorded by Lindner et al. was 2 in 26 (7.7%, higher than in previous studies); both implants were removed (Lindner et al. 2017).

A higher postoperative HA cranioplasty infection rate (15 out of 109 patients, 13.8%) was reported by Still et al. but it should be noted that a previous surgical site infection was the reason for craniectomy in 53.3% of these patients. A conservative management approach was attempted in four cases, but only one cranioplasty could be preserved (Still et al. 2018).

Unlike the previous reports, Iaccarino et al. described a successful prosthesis retention management with prolonged targeted antibiotic therapy in 4 patients with HA cranioplasty infections ().

Though an in-depth analysis of all 43 HA cranial prostheses we implanted lies beyond the scope of the present study, our series offers some interesting discussion points.

First, our overall infection rate was quite high (20.9%) compared to previous reports. Considering that HA was the first cranial substitute in only one case (due to bone fragmentation) and replaced resorbed autologous bone flaps in the remaining 8, and taking into account that only one patient underwent DC because of infection, we suggest that the impaired vascularization of large DC skin flaps, together with multiple operations and long operative times, played a major role in determining wound dehiscence and surgical site infection. Due to the prevalence of trauma patients in our series (6 out of 9), it could be guessed that the numbers and the severity of injuries might have contributed to a more complex clinical course, exposing these patients to higher risks of infection from multiple sources.

No significant difference in terms of HA implant salvage was found between unilateral and bifrontal cranioplasties.

In the 2 fully salvaged bifrontal cranioplasties, radial forearm free flaps were used to cover the skin defects after debridement. It is well documented that such flaps expose patients to the risk of further complications, including bleeding, flap necrosis and donor-site morbidities. Hence, this invasive procedure was performed only after assessment of the patient's general clinical status and an extensive, multidisciplinary discussion between the team (neurosurgeons and plastic surgeons), patient, and family members. We strongly believe that the removal of non-viable skin overlying the exposed implant and its replacement with fresh, highly vascularised tissue could have facilitated antibiotic penetration, thus leading to infection resolution.

In the other 2 patients with bifrontal cranioplasties, limited dural involvement and the almost unilateral accumulation of pus (together with the need to minimize the risk of further flap injury due to prolonged skin traction by hooks) guided us to select a partial implant removal. In one of these cases, the replacement PEEK implant was easily fixed with mini-plates and screws to the residual HA cranioplasty because of the latter's full ossification.

In our experience, one of the most interesting aspects of HA cranioplasty infections was the demonstration of their ossification. We always found a complete fusion between HA implants and bone, confirming that infections developed later. In four cases, we had to perform a new craniotomy via burr holes and connecting cuts to reach the epidural abscess lying beneath the cranioplasty. In the remaining 5 cases, HA implants were focally eroded, so surgical drills were used to access the epidural space, after which the cranioplasty was removed in pieces. A surgical drill was also used to completely remove all infected portions of the implants. In fact, the multiple surgical revisions and failures in the only patient who died were associated with recurrent skin ruptures and outflow of pus and HA granules.

Given the complex clinical history of most of our patients and the unsuccessful results reported in the literature, we never performed a 'simple' wound debridement and skin approximation (Still et al. 2018). We believe that such attempts in cases of HA implant infection should be avoided due to their low effectiveness, high risk of neurological deterioration and additional required surgeries, and associated additional psychological burden for patients.

Regarding the use of hyperbaric treatment, we could not find any significant benefit in our patients when it was performed preoperatively. The only patient who seemed to benefit from it received the treatment post-operatively. According to the observations above and due to the small numbers in our series, we cannot support hyperbaric chamber as a valid treatment option in these cases.

One of the unsolved questions is if HA is really more prone to infection than other materials. Although this was not the topic of our research, our intraoperative findings suggest that its microporous calcium matrix may be a risk factor. Subcutaneous tissue growth into HA pores, a common finding in reopening surgeries, might cause localised flap retractions and skin thinning, thus leading to wound ruptures, similarly to what happens with titanium meshes. Additionally, in cases of infection, implant porosity might theoretically facilitate bacterial colonization of the cranioplasty. Conversely, experimental studies suggest that bioceramics could reduce biofilm formation ().

In addition, it is still an open debate if it is possible to save an infected HA cranioplasty. Although our sample size was small, these preliminary data seem to confirm that HA implants, with the help of their unique biomimetic properties and an optimised management strategy, may survive an infection. It can be easily argued that such attempts represent a significant risk, either by the clinical and the medico-legal point of view. Nonetheless, the results coming from the several small series reported coincide with our experience and all seems to point in the same direction. This is the main reason we feel that our patients with an infected cranioplasty need to be fully informed about the possible risks and benefits of an alternative approach. Based on implant preservation, supported by modern, powerful antibiotic therapy and considering the improved biocompatibility properties of the new customized implants. Finally, saving a cranioplasty would translate in allowing an individual to go back to his/her life without the need of further surgeries and without experiencing again the lack of confidence, the neurological compromise and the fear of never going back to normal again that accompany most of decompressed patients in the pre-cranioplasty time interval. As a final consideration, we want to highlight the importance of teamwork with our plastic surgeons in dealing with cranioplasty infections. We recommend that regular patient follow-up and a multidisciplinary approach are vital in selecting an optimal management strategy (choosing the right patient and the right timing for a free flap, deciding between an aggressive and more conservative treatment, etc.) and augmenting the chance of a favourable outcome.

As discussed above, the main limitations of our study reside in its retrospective nature and small sample size; the latter, of course, depends on the aetiology of the phenomenon, which does not allow us to willingly increase the numbers. Moreover, the adopted treatment modalities differ too much to allow for the suggestion of a 'best management strategy'. However, we believe that the effectiveness of some of the proposed solutions is a good starting point for the management of these high-risk patients. Further series are needed to corroborate the findings of the current study.

5. Conclusion

In our experience, infected hydroxyapatite cranioplasty management is complex and requires a multidisciplinary approach. Salvage of a hydroxyapatite implant is possible under specific circumstances.

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Disclosure statement

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Ethical approval was waived by our local ethics committee in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Informed consent

The research data analysis had no effect on the participants or their medical care, and did not require additional informed consent.

Consent was obtained from all the patients/next of the kin for the publication of Figs. 1 and 2, as well as for the medical information reported in the relative figure legends.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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