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Prolonged and intermittent discharges from surgical sites in patients with history of craniotomy: Delayed diagnosis

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Abstract

This study aims to evaluate characteristics of delayed and prolonged surgical site discharges and their prognostic significance after craniotomies. Postoperative infections after craniotomy are potentially serious complications warranting vigilance and intervention. Prolonged and delayed surgical site discharge is an overlooked and seldomly reported entity in the neurosurgical literature. We have treated several cases with prolonged discharges from their craniotomy sites in a delayed fashion even years after their surgeries. The tertiary referral center database was reviewed for cases involving surgical site discharges. We found 164 cases of infection following neurosurgical procedures between 2010 and 2020, of which nine involved discharges. Four of these patients were excluded upon the second evaluation, and finally, five cases were included for further analysis. Our cohort comprised three females and two males aged 13–46 years (mean: 28.8 years). The initial surgeries were performed a mean of 61.2 months ago. Subtle discharges from surgical sites began as early as 1 month or as late as 15.5 years following surgery. The culture results implicated *Pseudomonas aeruginosa* in one case, coagulase-negative *Staphylococcus* in one, and normal skin flora in two. One case was inconclusive. All patients were operated on, and the surgical site was irrigated. In two patients, the bone flap and the cranioplasty material were also removed. The patients were followed up for a mean 40.8 months and there were no further discharges from the surgical site. Non-purulent, sticky discharges from surgical sites are an overlooked entity in neurosurgical practice. Recognition and familiarity with the natural course of this condition can make earlier exploration of the surgical site possible, with favorable outcomes compared to long-term antibiotic therapy.

Keywords: Craniotomy, non-purulent discharge, culture-negative, propionibacterium, skin flora, surgical site infection

Introduction

Postoperative infections after craniotomy are potentially serious complications that need to be identified and treated immediately. Although their clinical presentation is variable, meningitis, subdural empyema and cerebral abscess formations are the most reported features of these infections [1]. Prolonged and delayed surgical site discharges is an overlooked and seldomly reported entity in neurosurgical literature, which has mainly focused on surgical site infections (SSIs) and their characteristics, risk factors, and causative agents. Indeed, the reports on infections, although mentioning, mostly exclude patients with surgical site discharges without prominent rise in infectious parameters

The incidence of SSIs after intracranial surgery was reported to be around 6.2% [2]. Narotam et al. classified the infections based on the extent of involvement: superficial, if only the scalp is involved, and deep, if all the tissues beneath the galea are involved [3]. In case of bone flap involvement, the infected tissues are removed and discarded, followed by long-term antibiotic therapy [1].

Surgical site discharges are commonly encountered, and yet, an overlooked entity because of their benign appearance. Infectious parameters are not necessarily elevated in every patient. Mostly, any specific microorganisms, other than skin-colonizing bacteria, cannot be detected in the cultures. Clinician treated these patients with antibiotics and even these discharges ceases temporarily. Clinical vigilance is important because the patients will continue living with these sticky discharges with cosmetic complications and there is also a risk for prolonged infection affecting deeper structures.

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Delayed SSIs have been examined in non-neurosurgical literature before. They were caused by agents, mostly skin-colonizing bacteria from the clinic, that got inoculated at the time of surgery but became active at a later period [3,4]. On the other hand, another report suggested that postoperative deep and intracerebral infections were acquired from distant infection sites, not the skin flora [5].

Prolonged infections after cranial surgery have seldomly been reported and there is no data about non-purulent, sticky discharges, which cause cosmetic distress and demoralization in patients. The infections associated with these discharges only respond intermittently to antibiotics and frequently recur, leading to delayed diagnosis, sometimes years after discharge begins. This study aimed to determine the general characteristics of such patients and the prognostic factors for delayed diagnosis. A retrospective analysis was performed.

Material and Methods

Study Cohort

This study was based on our observation of several cases with long-term extended discharges from their surgical site, even years after their initial cranial surgeries. Acting on this observation, we retrospectively searched the hospital database between August 2010 – May 2020 for cranial infection cases. We found 164 cases and analyzed all their relevant documents to determine those having prolonged discharges from their surgical sites. Our search yielded nine such cases, of which four were excluded upon second evaluation. The remaining five cases were analyzed for their demographic features, infectious parameters, surgical histories, and treatments. Informed consent from each and every patient was obtained before the procedures. This study was approved by the local institutional review board (AEAH-IRB no: 20/22-22.12.2020). All patient data were identified and kept confidential. Informed consent was documented using a written consent form and signed and dated by the patient or the patient's legally authorized representative at the time of consent. A copy of the signed and dated consent form was given to the person signing the form.

Exclusion Criteria

The reasons for excluding the four patients are provided here. The first patient, who was operated for subdural hematoma one month ago, was excluded because his surgery was recent and the discharges began soon after, without any delay. Moreover, the diagnosis was not delayed as well. He was operated early for surgical site exploration and repair. Antibiotic therapy management resulted in a good outcome and the culture for this patient revealed a "coagulase-negative *Staphylococcus*" infection. A blood test revealed that infection parameters were high after the initial surgery. The second patient, who was operated for an arteriovenous malformation, was excluded for her recent medical history. She had operated 3 weeks ago and the discharges from the surgical site had begun soon after the surgery. There was no delay or hesitation regarding the diagnosis. The third patient, who was operated for a posterior fossa tumor 10 years ago, was later diagnosed with an abscess in the posterior fossa; however, she was excluded because there were no skin-related discharges. The fourth patient, who was admitted for sarcoidosis, was excluded because there was no history of a previous intracranial surgery at the drainage site. Finally, a total of five cases were included for further analysis.

Results

The general features of the five patients are summarized in Table 1. They comprised three females and two males aged between 13–46 years (mean: 28.8 years). The initial surgeries involving the particular discharge sites were performed an average of 61.2 months ago (range: 9–192 months). After the initial surgeries, the time taken for the onset of subtle discharges from the surgical sites varied from 1 month to 15.5 years (Figures 1 and 2). The duration of initial surgery and beginning of the disharges were variable. These five patients with prolonged discharges constituted 3% of the overall intracranial infection cases.

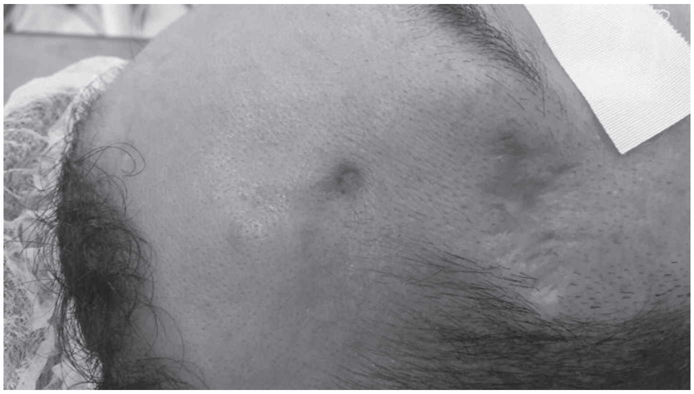

Figure 1. Intraoperative view from the surgical site. Leak from this dimple is variable from patient to patient. Some will have non-purulent, (meaning culture-negative results from the leak) sticky discharges in their hair without obvious dimple

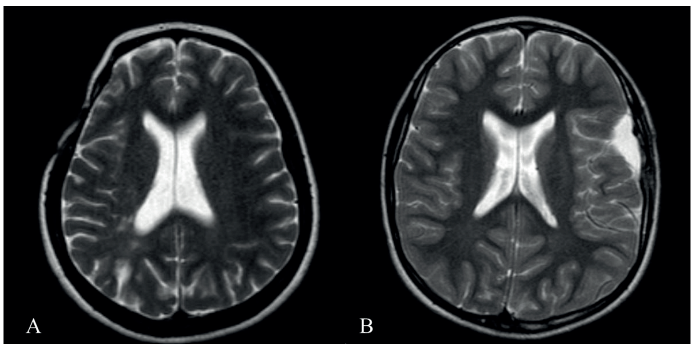

Figure 2. T2-weighted magnetic resonance images of patient number 1 and 3. In both, there was no obvious abscess formation in the intracranial region

The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, and white blood cell (WBC) count of all the patients were measured in preoperative blood tests. The ESR was in the normal range (20 mm/h) for all patients, except patient 4, who had a slightly higher value of 24 mm/h. The mean rate was 15.2

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mm/h (range: 7–24 mm/h). CRP levels were slightly high in two patients, the highest being 7 mg/L (normal range: 0–5 mg/L). The mean CRP level was 4.41 mg/L (range: 2–7 mg/L). Another infection parameter, WBC count, was in the normal range for all the patients (range: 5500–7700/mm^3, normal range: 4.5–11000/mm^3) (Table 1).

Table 1. Summary of the study population

	Age/ gender	Initial surgery	Discharge duration from the surgical site	Preoperative blood test	Co-morbidity	Recent treatment	Bone involvement	Culture	Outcome
1	38y, F	5 years, Pterional craniotomy for aneurysm	Started 1 Month after initial surgery, intermittently continued 5 years	ESR: 13 mm/h (N), CRP: <3.45 mg/L (N), WBC: 7700/mm^3	no	Exploration and irrigation	no	Skin flora	Good,no discharges, no complications
2	46y, F	16 years, arachnoid cyst	15.5 years after initial surgery, continued 6 months	ESR: 13 mm/h (N), CRP: 7 mg/L (H), WBC: 7700/mm^3 (N)	Operated for colon cancer 9 months ago + systemic chemotherapy	Exploration and bone removed	Osteomyelitis lytic appearance	Pseudomonas aeruginosa	Good, no discharges, no complications
3	13y, M	9 months, arachnoid cyst	2 Month after initial surgery, intermittently continued 7 months	ESR: 19 mm/h (N), CRP: 2 mg/L (N), WBC: 7400/mm^3 (N)	no	Exploration and irrigation	no	Culture (-)	Good, no discharges, no complications
4	25y, F	9 months, temporal lobectomy and hippocampec-tomy for epilepsy	2 Month after initial surgery, intermittently continued 7 months	ESR: 24 mm/h(H) CRP: 6.14 mg/L (H), WBC: 6800/mm^3 (N)	no	Exploration and irrigation, debridement	no	Coagulase-negative Staphylococcus	Good, no discharges, no complications
5	22y, M	3 years, cranioplasty	2.5 years after initial surgery, intermittently continued 6 months	ESR: 7 mm/h (N), CRP: 3.45 mg/L (N), WBC: 5500/mm^3 (N)	no	Exploration and irrigation	Cranioplasty material removed	Skin flora	Good, no discharges, no complications

ESR: erythrocyte sedimentation rate (0-20 mm/h), CRP: C-reactive protein (0–5 mg/L), WBC: white blood cell (4000-10500/mm^3), N: normal, H: high

All patients were operated on, and cultures were obtained from the surgical sites. None of the patients received preoperative antibiotic therapy. There was no anaerobic culture. Normal skin flora was reported in two patients. The culture results for the others were: *Pseudomonas aeruginosa* in one, coagulase-negative *Staphylococcus* in one, and no microorganism detected in patient 3.

The surgical site was irrigated in all the patients. In two patients, the bone flap and cranioplasty materials were removed additionally: patient 2 had osteomyelitis while patient 5 had cranioplasty material. There was no bone involvement in the other three patients. The patients were followed for an average 40.8 months (range: 24–60 months) and there were no further discharges from the surgical site.

Radiological Findings

In our cohort, no specific radiological findings were consistently associated with the non-purulent discharges from the surgical sites, aside from the usual postoperative changes observed in T2-weighted and post-contrast MR images. We consider MRI an essential tool for distinguishing between abscess formation and localized infections, which are typically associated with more pronounced radiological features, and the more subtle non-purulent discharges from surgical sites. The absence of characteristic findings on MRI in cases of prolonged discharges could be interpreted as a diagnostic indicator. This observation underscores the diagnostic challenges posed by these discharges and highlights the importance of clinical vigilance when radiological evidence is inconclusive.

Statistical Analysis

Descriptive statistics were used to summarize the data. The results were reported as means, SDs, and percentages. No inferential statistical analysis was performed due to the small sample size.

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Discussion

The classification of SSIs by the Center for Disease Control was modified by Korinek et al. as scalp infections, bone flap osteitis, brain abscess and subdural empyema, and meningitis. Scalp infections were defined by the presence of either purulent discharge from the surgical site or the determination of a bacterium from a serous discharge or a decision made by the neurosurgeon based on clinical findings. On the other hand, bone flap osteitis went one step further, necessitating either surgical diagnosis of bone involvement or the presence of fever with associated local signs and discharge, yielding culture results and radiographic features suggesting the diagnosis [6]. The Center for Disease Control has criteria for superficial and deep SSIs involving specific durations: 30 days for superficial and 30–90 days for deep SSI. Moreover, there may be signs of inflammation such as localized pain or tenderness, swelling, erythema, or heat [7].

These classifications obscure the diagnosis of prolonged, non-purulent, intermittent, and inconspicuous leaks, which manifest only as sticky hair near the surgical sites. The patients in our cohort admitted that they had mentioned their clinical presentations to the attending neurosurgeons and as expected, mostly blood and culture tests were ordered, which did not indicate a serious infection. Moreover, these patients had been treated with broad spectrum antibiotics several times, which were successful for a while but the discharges recurred several weeks or months later.

The diagnosis of SSIs after craniotomies is not always straightforward. The duration between the craniotomy and the diagnosis varies drastically – anywhere between days to years. This is not compatible with the hypothesis that all SSIs are caused by skin-colonizing bacteria inoculated perioperatively [3]. Sheh-Arbib et al. have suggested that prolonged, deep SSIs may be acquired from distant sites of infection in the postoperative period [5]. However, it is an undeniable fact that antibiotic prophylaxis in the perioperative period reduces the incidence of SSIs [8].

In our study group, most of the patients realized the sticky discharges from their wound within a couple of months. However, two patients experienced discharges years after their initial craniotomies, the longest being 15.5 years after surgery. In all cases, the discharges continued intermittently despite long-term antibiotic treatments. Some delayed infections have previously been reported: Barazi et al. [9] and Levitt et al. [10] presented cases experiencing infections 18 months and 23 years after their surgery, respectively. Although both these patients had *Propionibacterium acnes*-related infections, the former had intracerebral abscess and the latter had osteomyelitis, diagnosed incidentally during the surgery.

SSIs are caused by various microorganisms. They may have a cutaneous (*S. aureus*, coagulase-negative *Staphylococci, P. acnes*) or non-cutaneous origin (*Enterobacteriaceae, P. aeruginosa, Acinetobacter spp., Streptococci, Pneumococci, Enterococci*). Indeed, perioperative antibiotic prophylaxis was efficient in preventing methicillin-sensitive *Staphylococci*, most other Gram-positive cocci, *P. acnes*, and anaerobic microorganisms [6]. Korinek et al. presented their experience over 6243 craniotomies and demonstrated that SSIs dropped from 8.8% to 4.6% due to antibiotic use [8].

Infections after craniotomies are not attributed uniformly to the different candidate microorganisms. In a case series by Dashti et al. [2], *Staphyloccus spp*. were responsible for 36% of the cases, followed by *Pseudomonas spp*. (8%) and *Propionibacterium spp*. (4%). Interestingly, the incidence of culture-negative cases was 12%. The frequency of purulent discharge and wound infections was 34% and 52%, respectively. Despite these high proportions, the authors excluded cases with sole wound infections from their cohort, indicating that surgical site discharges were considered relatively benign by the authors. McClelland et al. emphasized in their case series on 1587 cranial operations that the incidence of central nervous system infections after neurosurgical procedures would be higher than the reported 5–7%. *Staphylococcus aureus* was responsible for 42.9% of these cases, followed by *Propionibacterium acnes* (28.6%) [11]. In another study of 2944 patients, 117 (4%) had SSIs and among these, wound infections comprised 25% of the cases while bone involvement was observed in 11.9%. Although the number of culture-negative cases was also high (31 cases, 26%), the main etiological agents were *Staphylococcus spp* [12]. In our case series, culture reports indicated skin flora in two patients, *Pseudomonas aeruginosa* in one, *Staphylococcus* in one, and a negative result in one.

Among these causative microorganisms, *Propionibacterium acnes* needs special emphasis. Nisbet et al. emphasized its indolent presentation and further warned that detecting Gram-positive bacilli in Gram stains of neurosurgical specimens should not be interpreted as contamination [13]. Although there were no specific cases of *P. acnes* in our case series, the two cases of skin flora may involve P. acnes since it is a common member of the skin microbiome. In their study, Kelly et al. reported P. acnes in 4.2% of infections following neurosurgical procedures [14]. Their patients had swelling and purulent discharges from surgical sites. Like our observations, most of their patients reported symptoms two months after surgery [14]. Similarly, Kranick et al. presented a case of brain abscess arising 10 years post-surgery. They speculated *P. acnes* to be the most likely cause of infection due to its prevalence in skin flora, residing under hair follicles in an anaerobic milieu [15].

The patients in our study had a favorable prognosis, despite their long-lasting social distress regarding the appearance of their hair, which had improved intermittently with antibiotic treatments but regressed later. Moreover, two of our patients had bone involvement later in the course of the disease, which may cause potential complications arising from these presumably benign discharges. All our patients were operated on, and their surgical sites were explored for any collections. However, except in one patient, there was no collection or infectious region on the scalp and subcutaneous tissue. The spot on the scalp was removed and the wound was explored, irrigated, and rinsed with 0.9% saline. There were no discharges after a mean 40 months of follow-up. Similar favorable results have been reported for wound debridement [14].

Clinical Implications/Future Directions

This study has demonstrated that surgical site discharges may begin months to years after craniotomy and these may prevail for a long time with intermittent nature. Variability of this duration warrants clinical vigilance during follow-ups in patients undergoing craniotomies. Mostly specific microorganisms cannot be detected however, a skin-colonizing bacteria, *Propionibacterium acnes* may warrant anaerobic cultures from surgical site discharges. Moreover, patients should be followed even if they did not seek for medical consultation, because they may fell desperation regarding these discharges. Surgical exploration and irrigation of the surgical site is effective even if any collection was observed. Future studies may demonstrate exact incidence of this entity and more specific microorganisms can be demonstrated on cultures without administering empirical antibiotic treatment.

Conclusion

Postoperative infections following craniotomies are accepted as a serious complication necessitating intervention. However, when the clinical presentation is subtle and culture results do not indicate significant pathogens, patients generally receive intermittent antibiotic treatments which only have short-term benefits.

Therefore, being vigilant, recognizing non-purulent, sticky discharges from surgical sites, and following-up with patients after antibiotic therapy is stopped may make early surgical exploration possible. Subsequently, wound debridement and irrigation of the surgical site can provide a favorable outcome, preventing progress of the infection and alleviating patient stress.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
Ethics committee approval (AEAHIRB no: 20/22) was obtained from the ethics committee of Antalya Education and Research Hospital on 22.12.2020.'

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