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Case report

Streptococcal periorbital necrotizing fasciitis: Case series on a rare but potentially life-threatening entity☆

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ABSTRACT

Objective: Periorbital necrotizing soft tissue infection (NSTI) is a rare entity caused either by polymicrobial infection (type 1) or Streptococcus pyogenes and/or Staphylococcus species (type 2). A high level of clinical suspicion is necessary to make the diagnosis. We present 3 cases of NSTI illustrating our diagnostic and therapeutic approach.

Patients and methods: The main outcome measures were laboratory and clinical findings at initial presentation, microorganism cultured, predisposing conditions and the number of debridements needed as well as final outcomes.

Results: Biomarkers of inflammation in blood samples were elevated at admission and Streptococcus pyogenes was cultured in all three cases. Clinical suspicion of this rare disease and prompt surgical treatment was crucial to confirm the diagnosis.

Imaging and laboratory workup, however, did not prove to be diagnostically helpful in our cases. We performed early and consequent debridement of necrotic tissue to control the infection alongside adequate systemic antibiotic therapy including clindamycin in all cases of suspected NSTI. As intraoperative findings revealed necrotic tissue even in an apparently quiet situs, we decided to debride the wound daily after the first surgery until there is very little or no necrotic tissue to debride seen intraoperatively.

Conclusions: Based on the negative experience with our first case, we developed a more aggressive surgical plan for cases with periorbital NSTI. After early debridement, the patient is surgically reevaluated on a daily basis until surgery is deemed to have been unnecessary. We follow this approach, as necrotic tissue is sometimes identified intraoperatively from a lack of resistance to manipulation rather than from its clinical aspect alone. At a later point, plastic surgery may be required when the infection is under control.

1. Introduction

Periorbital necrotizing fasciitis, a form of necrotizing soft tissue infection (NSTI), is considered a very rare clinical picture [1,2]. Due to its rare occurrence, there is a risk that the diagnosis will be delayed. This is problematic as rapid surgical treatment is crucial for a favorable prognosis.

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Considering this possible differential diagnosis in well-known and apparently mild soft tissue infections as preseptal cellulits is the first step to prevent the devastating sequelae of NSTI. If these seemingly uncomplicated infections progress unexpectedly quickly, the indication for surgical intervention should be made promptly. Possible complications from NSTI range from disfigurement, loss of vision, septic shock and even death [3].

The causative microorganism identified most often are Streptococcus pyogenes (group A streptococcus) [1–3]. However, Streptococcus pyogenes are causative for various infections including acute pharyngitis and infections of the skin such as erysipelas and cellulitis [4]. It has been previously reported that the incidence of infections caused by Streptococcus pyogenes in Europe increased in 2022 and 2023 [5–9].

At initial presentation, it is often difficult to distinguish relatively mild courses of infection from life threatening entities like NSTI or toxic shock syndrome.

This paper will focus on the diagnosis and indication for surgery as well as differentiation from cases of infections with Streptococcus pyogenes to be treated conservatively. We describe three cases of periorbital NSTI that presented to our clinic from 11/2023 to 04/2024 that were treated surgically. We suggest an approach to manage cases of soft tissue infections including microbial diagnostic from conjunctival or wound swab, hospitalization and close surveillance with the help of marking of the affected areas. We describe our surgical approach, which includes daily debridements of the wound until the surgery is deemed to have been unnecessary by the surgeon.

2. Case series

According to the guidelines of the responsible ethics committee, approval is not required for case reports. Written informed consent was obtained from all patients involved in this case series.

Table 1 shows the patient characteristics of cases 1–3. CRP: c reactive protein.

Microorganisms were identified by routine culture methods.

2.1. Case 1

2.1.1. Presentation

A 65-year-old patient presented to our emergency department in the morning after referral from a district hospital with left eyelid swelling that had been present since 4 a.m. the same day, with a feeling of tension in the eye area and nausea with one episode of vomiting. He denied injuries or previous surgery at the eye region. The referring district hospital had already administered Metoclopramid, Decortin 100 mg and Dimetindenmaleat 8 mg.

The affected left eye showed a bulging swelling of the eyelids with hyperthermia, bloody secretion without pus. It was not possible to open the eye due to the marked eyelid swelling. Sonography showed free motility and an attached retina. Findings in the right eye were unremarkable with full visual acuity.

2.1.2. Imaging findings

CT imaging revealed diffuse periorbital soft tissue swelling on the left without involvement of the adjacent intraorbital structures and without evidence of a suspected abscess. CT imaging findings were consistent with a preseptal eyelid cellulitis.

2.1.3. Course

A conjunctival swab was taken, and the patient was hospitalized for administration of intravenous antibiotics (Cefuroxime).

During the following night, marked systemic symptoms were observed: the patient's temperature increased to 39 °C and his blood pressure was 95/62 mmHg with a heart rate of 120. Two pairs of blood cultures were obtained and as vital parameters could not be stabilized, the patient was transferred to the intensive care unit at 11 p.m. for management of systemic inflammatory response syndrome [10].

Antibiotic treatment was changed to Piperacillin/Tazobactam and Azithromycin.

As dermal lesions of whitish colour appeared, we suspected NSTI and wound debridement was performed in the eyelid and orbital region on the day following admission. The lesions were first noticed at 9 a.m. the day following admission and surgery was performed

Table 1
Patient characteristics.

	Age	Sex	Predisposing conditions	Cultured microorganism	Laboratory parameters at presentation	Number of debridements required
Case 1	65	male	none	Streptococcus pyogenes	CRP 1.66 mg/dl (norm 0–0.5) Leucocyte count 4.49/nl (norm 3.0–10.0)	4
Case 2	47	male	Drug abuse	Streptococcus pyogenes	CRP 14.90 mg/dl (norm 0–0.5) Leucocyte count 14.54/nl (norm 3.0–10.0)	3
Case 3	81	male	none	Streptococcus pyogenes	CRP 13.70 mg/dl (norm 0–0.5) Leucocyte count 28.62/nl (norm 3.0–10.0)	3

2 h later at 11 a.m. Fig. 1 shows the findings at the time of first surgery. The surgery was performed by an experienced ophthalmic surgeon as well as a colleague from the ENT department. Overtly necrotic tissue of the eyelids and orbit were debrided and affected areas of the face including temporal, supraorbital and nasal region were debrided. Multiple drainages were inserted. Fig. 2 shows the situs at the end of surgery.

At the end of surgery after removal of the draping, a spreading of the necrotic areas to the neck region was observed. Therefore, neck dissection was performed by the ENT surgeon and debridement of the parotid region and hairy scalp was performed immediately.

Streptococcus pyogenes was cultured from the initial conjunctival swab. The antibiotic regimen was therefore changed to penicillin and clindamycin administered intravenously.

Three further necrosectomies were performed four, nine and thirteen days later. Blood cultures revealed septicemia with multidrug-resistant gram-negative bacteria 11 days after initial surgery. The source of this infection remained unknown. The Antibiotic therapy was therefore escalated to Meropenem. General condition then deteriorated rapidly leading to multiple organ failure and the patient died at 2 weeks after initial presentation.

2.2. Case 2

2.2.1. Presentation

A 47-year-old patient presented to our emergency department with swelling of the left eyelid. The patient reported that he had fallen on his head the day before. The patient had been treated at the emergency department multiple times for falls under influence of alcohol and other drugs in the past. Fig. 3 shows the initial presentation with marked swelling of the left upper eyelid making lid opening impossible and purple-colored lesions at the upper eyelid (see Fig. 4).

2.2.2. Imaging findings

CT imaging showed extensive eyelid phlegmon without evidence of an abscess or melting. Morphologically unremarkable visualization of the ocular bulb and the retrobulbar space was described by the radiologist without evidence of foreign bodies or osteodestruction. The findings were consistent with preseptal cellulitis.

2.2.3. Course

The patient was hospitalized and as clinical deterioration with livid discoloration of the medial eyelid appeared, immediate debridement of the wound was performed within the next 6 hours. Intraoperative presentation confirmed the diagnosis of periorbital NSTI. Streptococcus pyogenes was cultured from the conjunctival swab. Antibiotic therapy was escalated to Penicillin and Clindamycin.

Fig. 4A and B shows the intraoperative situs. Due to several discussions with various specialized departments (trauma surgery, plastic surgery, ENT, microbiology) and their expertise with NSTI concluding in a different finding in clinical examination vs surgical finding, we scheduled daily surgical revisions regardless of the clinical picture. Two more surgical debridements were performed the following two days. At the final surgical revision, no more necrotic material could be identified intraoperatively and the "daily surgical schedule approach" was stopped. After one week, a stable wound without progressing necrosis had been achieved and therefore the wounds were closed. Fig. 5A and B show the postoperative results at 3 weeks postoperatively. The patient survived without severe disfigurement. He had spent more than 3 weeks in our inpatient department.

2.3. Case 3

2.3.1. Presentation

A 81-year-old patient presented to our emergency department reporting lid swelling that he had first noticed less than 24 hours ago. The skin of the upper eyelid showed livid discoloration as shown in Fig. 6.

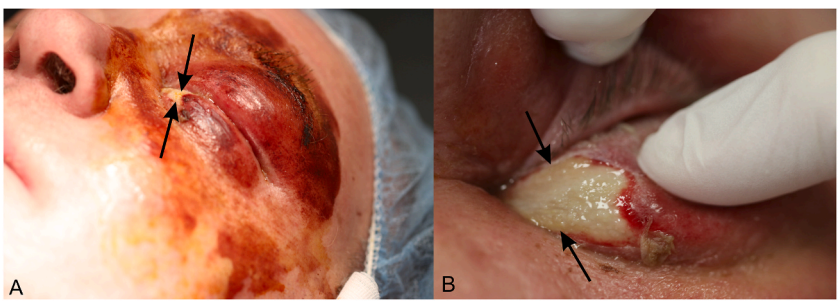

Fig. 1. Clinical presentations prior to first surgery with overtly necrotic tissue (arrows) (A). Note the whitish lesion at the lower medial canthus (arrows) (B).

Fig. 2. Situs at the end of surgery with multiple drainages inserted.

Fig. 3. Initial presentation of case 2 with marked swelling of the left upper eyelid and purple-colored discoloration (arrows) of the skin at the medial upper eyelid.

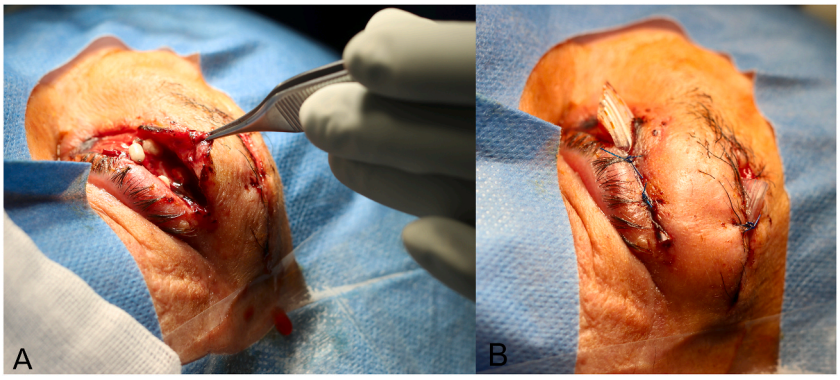

Fig. 4. Situs during surgery after debridement of necrotic tissue and insertion of antibiotic pellets (A) and at the end of surgery with drainages inserted (B). Vital skin was spared during debridement.

2.3.2. Imaging findings

CT imaging was performed and showed extensive preseptal soft tissue phlegmon on the left periorbital region without evidence of abscess formation. Mucosal swelling in the maxillary sinuses on both sides (left > right) were described, but without mirror formation.

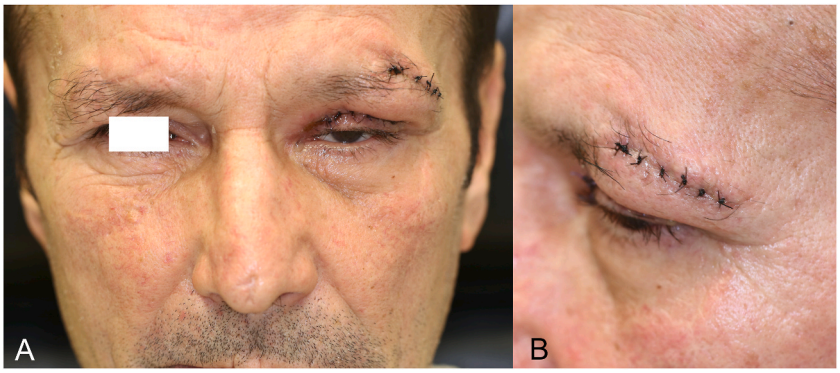

Fig. 5. A and B: Postoperative result at 3 weeks postoperatively.

Fig. 6. Findings at presentation to our emergency department. Note the necrotic lesion (arrows) on the upper medial canthus.

2.3.3. Course

Immediate necrosectomy was performed 3 hours after initial presentation to our emergency department**.** Initial antibiotic treatment was Piperacillin/Tazobactam and Clindamycin, which was switched to Penicillin/Clindamycin after Streptococcus pyogenes was cultured from the initial swab. Again, we applied our consented "daily surgical schedule approach". Two more debridements were performed the following two days until at the last surgical revision a clean stable wound was present. As extensive debridement of the skin was necessary, an experienced oculoplastic surgeon performed wound closure with a free skin graft 6 days after the last debridement. Fig. 7 shows the early postoperative findings after necrosectomy and free skin graft. Fig. 8 shows the final results after wound closure. This patient showed full recovery without major disfigurement and good lid function.

3. Discussion

We modified our management of cases presenting with soft tissue infection according to the cases described. We want to emphasize, that periorbital NSTI should be suspected in every case of soft tissue infection and adequate follow-up is necessary to make the correct diagnosis. We perform conjunctival swabs or wound swabs in every patient as this proved helpful to culture a microorganism in our case series. Immediate hospital administration and marking of the lesions allow for intravenous antibiotic therapy as well as close surveillance of the infected area and vital parameters. In case of rapid progression despite systemic antibiotic treatment, immediate surgical intervention is carried out. We schedule daily surgical debridements regardless of the clinical presentation until the

Fig. 7. Situs after free skin graft.

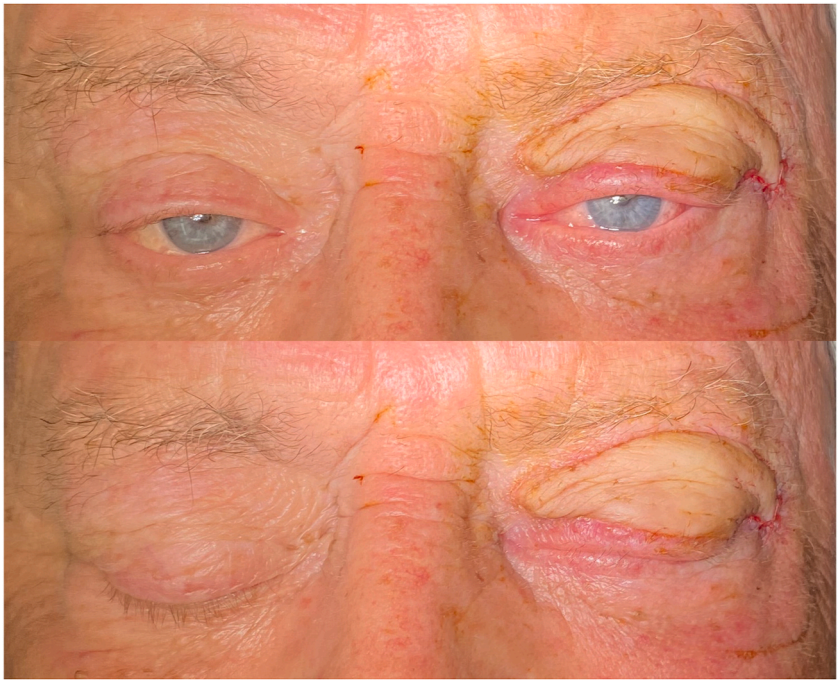

Fig. 8. Final result three weeks after wound closure with a free skin graft.

intervention is deemed to have been unnecessary intraoperatively. Only when a stable clean wound is achieved wound closure – if necessary, using skin grafts – is scheduled. We recommend waiting 5–7 days after the last surgical debridement before closing the wound.

Necrotizing soft tissue infection (NSTI) is defined as a spreading infection of soft tissues including skin, subcutaneous tissue, fascia or muscle leading to necrosis of the involved tissue and resulting in the need of surgical debridement [11]. It is often associated with the early onset of shock and organ failure [4]. The diagnosis is mostly based on clinical features [2]. Two types of NSTI are distinguished according to the causative microorganism: Type 1 is polymicrobial whereas type 2 is caused by either streptococcus or staphylococcus [12]. We found streptococcus pyogenes in all cases we reported on. Thus, all our cases were classified as periorbital NSTI type 2. It has been reported, that only 10 % of NSTI cases affect the head and neck area, which might be due to the good blood

supply in this area [1]. Minor trauma and herpes zoster as well as minor surgeries or the use of immunosuppressive medication have been reported to predispose to this disease [2,4].But not in all cases, predisposing factors can be identified [1,2]. In cases 1 and 3, no predisposing factors were identified, while in case 2 drug abuse may have predisposed to severe infection. Furthermore, the patient reported trauma to the head which we considered to be blunt trauma. It has been shown that blunt trauma is associated with an elevated risk for NSTI caused by Streptococcus pyogenes [13–16]. It has been previously reported, that low antibody titers to bacterial exotoxins or membrane M proteins in otherwise healthy patients increase the risk for invasive streptococcal infection, but they do not modify disease severity [1,17]. We do not routinely include these parameters in laboratory workup of patients presenting with periorbital soft tissue infections, therefore it remains unknown if low antibody titers were present in our patients.

3.1. Diagnosis

At presentation NSTI may resemble cellulitis with diffuse tense swelling of the affected tissue. Periorbital erythema and edema are typical, often with an initial lesion in the medial canthal region. Fluid filled bullae and reddish discoloration of the skin that progresses to a dark blue or gray color are clearly diagnostic [1,4], but not always present. Overtly necrotic skin may be seen. In all our cases of NSTI, either a livid or a whitish discoloration of the skin were visible indicating necrosis of the (sub)cutaneous tissues. In the periorbital region, the skin infection seems to become apparent earlier than in other parts of the body [1].

Pain out of proportion and soft tissue crepitus may be present. Rapid progression despite use of systemic antibiotics is indicative of necrotizing disease. In all our cases of NSTI the rapid progression within hours confirmed initial suspicion of this devastating disease. Therefore, we recommend close surveillance of patients with suspected cellulitis every 3 h marking the involved areas to allow for objective assessment of disease progression even if different physicians are involved.

Although rare in immunocompetent individuals, mucormycosis is a differential diagnosis that should be considered in cases of periorbital soft tissue infection [18]. In our patients, mucormycosis was ruled out by intraoperative biopsy of the necrotic tissue and microbiological culture.

In case 2 and 3 we found elevated leukocytic count and CRP at initial presentation. In case 1 however, only slightly elevated CRP was noted at initial presentation even though in this case, marked systemic symptoms quickly developed. We conclude from this, that initial laboratory findings are not predictive of clinical course. It has been previously reported, that laboratory parameters show poor sensitivity in the diagnosis of NSTI and should therefore not be used to rule out this entity [19].

Imaging studies were reported to be helpful in identifying the tissue involved, but they are not confirmatory of the disease [20]. CT and MRI may show soft-tissue edema infiltrating the fascial planes even prior to cutaneous signs. CT imaging has been proposed as a useful tool to guide debridement [21]. In all our cases, the diagnosis was made clinical and from intraoperative findings, CT imaging did not guide diagnosis or therapy. CT imaging can be used to detect fascial gas, which shows good sensitivity and specificity in the diagnosis of NSTI. However, imaging should not delay surgical treatment [19].

3.2. Complications

The orbicularis muscle and eyelid marginal arcades are thought to protect the tarsal plate, conjunctiva and lid margins from necrosis even in cases with deeper involvement of the orbit or skin necrosis [1,22]. This observation is in good agreement with findings in our patients as in all cases, the lid margins and tarsal plates were spared by the infection. The orbital septum which separates intraorbital fat from eyelid fat and the orbicularis oculi muscle seems to be a barrier preventing spreading into the orbit. However, in cases following trauma or surgery spreading of the infection into the orbit is possible [22]. We observed spreading of the infection into the orbit in case 1 even without prior trauma.

Bilateral involvement is common as there is no barrier to spreading of the infection in the nose area [1,23–25]. Retinal arterial occlusion is a rare complication from NSTI. Several factors contribute to the pathomechanism: Severe perivascular involvement can cause thrombosis, systemic hypercoaguability is discussed as a contributing factor and increased intraorbital pressure from edema may also aggravate ischemia [1]. Exotoxins released by Streptococcus pyogenes such as streptolysin O may stimulate intravascular accumulation of platelet-leucocyte aggregates and lead to vascular occlusion [26]. In our case series, no patient suffered from retinal arterial occlusion and all cases showed unilateral involvement.

3.3. Therapy

The distinction between cellulitis and periorbital NSTI, although difficult to make in early stages of the disease, is of utmost importance, as the latter requires prompt surgical debridement of the necrotic tissue to avoid spreading along fascial planes. In contrast to cellulitis, the disease cannot be controlled with systemic antibiotic therapy alone [4]. Surgical treatment is confirmatory in cases with suspected periorbital NSTI. When case 2 and 3 presented to our clinic, we had a higher level of suspicion, therefore, appropriate treatment was established sooner and both patients had a more favorable outcome.

It has been previously reported, that delayed treatment negatively affects the prognosis [2,20,27]. Therefore, surgery with least delay is recommended in various studies including necrotizing infections of various locations [28,29].

The recommended therapeutic regimen consists of a beta-lactam antibiotic i.e. penicillin in combination with clindamycin. Clindamycin is particularly beneficial as it inhibits the synthesis of streptococcal toxins. Clindamycin should not be used as monotherapy, however, as there are reports of Streptococcus pyogenes resistant to Clindamycin, in contrast to penicillin G [30]. NSTI leads to marked systemic symptoms including septic shock and organ failure. Source control is achieved by prompt and repeated surgical

debridement. It lowers the bacterial load and reduces the exotoxins released, which are causative for the systemic reaction. Our approach is to perform debridement daily until the surgery is deemed to have been unnecessary, as necrotic tissue at the fascial plane is best recognized during surgery as described above. The daily surgical debridement is an approach already accepted in other surgical disciplines [26,31] but not yet widely used in ophthalmology.

An overall mortality rate of 10–15 % in patients with NSTI has been reported [16,32]. The mortality rates differ depending on the region involved: While involvement of the eyelids was associated with a 10 % mortality rate, involvement of the lower face and neck was associated with a mortality rate of 32 %. The authors attributed this to the spreading of the infection to vital structures [33]. The optimal extent of debridement needs to be decided upon by the surgeon. Some authors suggest that subcutaneous debridement of overtly necrotic tissue sparing as much skin and orbicularis muscle as possible might be beneficial compared to more extensive debridement [1,22]. The reasoning behind this idea is, that vital orbicularis muscle might be beneficial in terms of blood supply to the orbital region and thus penetration of antibiotics and sparing skin helps prevent disfigured appearance. Wladis et al. found, that a history of immunosuppressant medication was associated with a higher risk of the need for extensive debridement including exenteration surgery [34]. Rothschild et al. found, that older age was associated with more extensive disease at presentation as well as worse final visual acuity [35]. Repeated debridement may be necessary to achieve control of the infection. This was the case in all our patients, with each receiving 3–4 debridements. Reconstructive plastic surgery is only recommended when complete removal of infected tissue has been achieved [20]. Therefore, we assured that a stable clean wound was achieved prior to wound closure in all our patients.

Hyperbaric oxygen therapy has been suggested as a complementary therapeutic measure, but its role remains controversial [2,20,23]. It has been reported, that hyperbaric oxygen therapy reduces mortality and also the number of debridements required [36].

3.4. Epidemiology

Although periorbital NSTI is considered a rare entity, we report on three cases that presented to our clinic within 6 months. This seems like an unusually high incidence. Another university clinic in the same area reported an unusual clustering of cases of NSTI in 2023 [37]. An increased incidence of scarlet fever and invasive infections with Streptococcus pyogenes was reported in different European countries in 2022 and 2023 including Germany [5–9]. It was discussed, if this could be related to a difference in population immunity due to restrictions related to the Covid-19 pandemic [6–9]. This explanation would be in agreement with the evidence on susceptibility to infection in patients with low antibody titer to certain streptococcal antigens [17]. As previously mentioned, we did not investigate immunity to streptococcal antigens in our patients, therefore this suspected connection remains hypothetical. Observation of the incidence in the coming years should shed light on whether the reduced exposure to streptococcal antigens could actually have led to such disease susceptibility.

4. Conclusion

We conclude that a high level of clinical suspicion is needed for early diagnosis of NSTI and to initiate prompt surgical treatment. Imaging modalities are not helpful in the diagnosis but may help to identify involved structures prior to surgery. Laboratory findings were not predictive of clinical course in our case series. Hospitalization is necessary for adequate follow-up and treatment of these cases. The diagnosis of periorbital NSTI is made clinically and confirmed by immediate surgery. It should be considered in all soft tissue infections of the periorbital region. We recommend taking a conjunctival swab and marking the areas involved at initial presentation to allow for close monitoring of the dynamics of the disease. The involved marked area is inspected every 3 h. Progression within hours despite adequate antibiotic therapy is highly suspicious for NSTI and should lead to prompt surgical debridement. CT imaging may be helpful to rule out postseptal involvement and reveal fascial gas.

Early and consequent debridement is essential for treatment success and should be accompanied by adequate systemic antibiotic therapy. We recommend to schedule surgery every day until a scheduled debridement is deemed to have been unnecessary. Plastic surgery by an experienced oculoplastic surgeon is often necessary when the infection is under control.

CRediT authorship contribution statement

Isabella D. Baur: Writing – original draft, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Isabel Habert:** Writing – review & editing, Formal analysis, Data curation. **Monica Markstaller:** Writing – review & editing, Investigation, Data curation. **Kathrin Hartmann:** Writing – review & editing, Data curation. **Arthur Mueller:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Data availability

The data used is available from the corresponding author upon reasonable request.

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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