Dear Editors,

A 79-year-old man presented with a one-week history of painful erythema and swelling of the left auricle. Notably, the earlobe was spared (Figure 1a, b). Four weeks earlier, he had undergone micrographically controlled wedge excision at our department for left auricular squamous cell carcinoma. At that time, he had shown no other signs or symptoms. Suspecting a delayed wound infection with cartilage involvement, the patient was started on clindamycin 600 mg IV t.i.d. as well as ibuprofen 600 mg PO t.i.d.. As there was no improvement after six days, the antibiotic regimen was switched to tazobactam (4.5 g IV four times daily) in consultation with our colleagues from the ENT and infectious disease department. Subsequently, the patient experienced recurrent episodes of subfebrile temperatures associated with a normal white blood cell count and a fluctuating increase in C-reactive protein levels (up to 197 mg/L). Blood cultures came back negative. Again, antibiotic therapy was switched, this time to moxifloxacin (400 mg IV once daily). A comprehensive diagnostic workup (chest X-ray, transthoracic and transesophageal echocardiography as well as abdominal ultrasound) intended to rule out any other infectious focus that might have caused the fever yielded no pathological findings. Lymph node ultrasound showed no abnormalities, either, except for inflammatory changes in the left retroauricular region. Due to persistent anemia with hemoglobin levels of 7.5 mmol/L, the patient had undergone a bone marrow biopsy a few months earlier, which had ruled out a systemic hematological disorder.

Upon further questioning, he reported to have experienced several episodes of auricular swelling in the past. In addition, he had had recurrent bouts of conjunctivitis that had been treated with some type of eye drops he could not specify in more detail. Closer examination revealed a slight deformation of the nasal cartilage suggestive of a saddle nose (Figure 1a, black arrow). A biopsy taken from the auricle due to the recalcitrance of the condition revealed inflammatory changes consistent with perichondritis (Figure 2a, b). Serological tests showed a marginally increased rheumatoid factor (18.2 IU/mL; normal range < 14 IU/mL). Urinalysis and urine sediment examination as well as antinuclear and antineutrophil cytoplasmic antibodies (ANA and ANCA) were within normal limits.

Given the histological findings, the recurrence of symptoms and the history of conjunctivitis, we eventually made the diagnosis of relapsing polychondritis, as the extended diagnostic criteria (including histological findings and recurrent conjunctivitis) proposed by McAdam and Damian [1, 2] (Table 1) were met. While our patient’s auricular chondritis was unilateral and – strictly speaking – did not fulfill said

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**Clinical Letter**

**Acute flare of relapsing polychondritis following surgical treatment of auricular squamous cell carcinoma**

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**Figure 1** Deformed nasal cartilage (black arrow) (a); left auricle four weeks after surgery (b).
diagnostic criteria, our clinical suspicion was supported by
the insufficient response to the various antibiotics previously
administered.

Relapsing polychondritis is a rare systemic inflammatory
disorder that may affect cartilaginous structures in various
parts of the body. Areas predominantly involved include the
elastic cartilage of the ears and nose as well as the hyaline
cartilage of the trachea, vertebral bodies and joints [3, 4].
Organs with proteoglycan components such as the eye, heart
and vessels as well as the inner ear may also be affected
[5, 6]. About one-third of cases of relapsing polychondritis
are associated with other systemic disorders such as systemic
vasculitis, rheumatoid arthritis, hematological comorbidity
or lupus erythematosus [7].

Although cartilage trauma (for example, due to ear
piercings) has been reported as a possible trigger of relap-
sing polychondritis [8, 9], to date there have been no reports
of this condition being induced by local surgical procedu-
res. A small case study comparing patients with and without
trauma showed that patients with previous cartilage trauma

Table 1 Diagnostic criteria for relapsing polychondritis (modified after [1, 2]).

| Author          | Criteria                                                                 |
|-----------------|--------------------------------------------------------------------------|
| McAdam et al. [1] | – Recurrent bilateral auricular chondritis                               |
|                 | – Nonerosive inflammatory polyarthritis                                  |
|                 | – Nasal chondritis                                                      |
|                 | – Ocular inflammation (conjunctivitis, keratitis, scleritis, uveitis)    |
|                 | – Respiratory tract chondritis (laryngeal/tracheal cartilage)           |
|                 | – Cochlear and/or vestibular dysfunction (neurosensory hearing loss/tinnitus/vertigo) |
| McAdam et al. [1] | – Three out of six criteria must be met                                  |
| Damiani et al. [2] | – At least three of McAdams’s diagnostic criteria [1]                  |
|                 |  or                                                                      |
|                 | – One or more of the clinical findings included in the McAdam criteria [5], with histological confirmation|
|                 |  or                                                                      |
|                 | – Chondritis at two or more separate anatomic sites, with a response to corticosteroids and/or dapsone |

Figure 2 Auricular biopsy showing fibrosis of connective/adipose tissue and moderate lymphocytic inflammation (a) as well as areas of degenerative changes of hyaline cartilage (b) (hematoxylin-eosin stain, original magnification x 200).
exhibited higher levels of autoimmunity and systemic involvement than those without trauma. It has been proposed that this autoimmune phenomenon is triggered by exposure of a cryptogenic cartilage matrix protein antigen, which requires prior trauma for it to come into contact with the patient’s own (innate) immune system [10]. The adaptive immune system, too, is thought to be activated by surface molecules of the innate immune system, such as toll-like receptors (TLRs) and NOD-like receptors (NLRs). TLRs interact with pathogen-associated molecular patterns (PAMPs) produced by most pathogens. This too explains why infections are able to trigger relapsing polychondritis. Overall, there is an inflammatory response associated with lymphocyte activation and production of IL-1B and IL-18 as well as a prolonged T-cell response and production of autoantibodies directed against cartilaginous tissue [9].

Antigens reported to be involved include cartilage oligomeric matrix protein (COMP), found in the extracellular matrix, and matrilin 1. While antibodies to COMP have been shown to be negatively correlated with disease activity [11], antibodies directed against matrilin 1 have primarily been described in patients with laryngotracheal involvement and show a positive correlation with disease activity [12]. Circulating anti-collagen II antibodies are found in 30–100% of patients, depending on the study [13, 14]. Anti-collagen IX and XI antibodies have also been described. In the present case, antibody tests were not performed, as this had no therapeutic relevance.

Our patient was initially started on prednisolone 50 mg PO once daily. The fact that this intervention resulted in rapid clinical improvement confirmed our diagnosis [6] (Table 1). Combined PET/CT (positron emission tomography/computed tomography) imaging was used to rule out acute and chronic inflammatory changes in the aforementioned tissues typically affected. 18F-FDG PET/CT is superior to conventional CT in that it can distinguish (even tiny) acute inflammatory foci from chronic inflammatory processes associated with advanced tissue destruction. It can therefore show the extent of active inflammation in the body and indicate suitable biopsy sites [15]. The patient continued to experience new flares of conjunctivitis. As the oral prednisolone dose was gradually tapered to 15 mg/day, the patient was subsequently also started on dapsone 50 mg PO once daily.

Given the rarity of the disease, there are no evidence-based guidelines. Besides the above-mentioned treatment options, less severe cases can be treated with colchicine. 0.6 mg PO two to four times a day and nonsteroidal anti-inflammatory drugs [3].

There are numerous differential diagnoses that may present with perichondritis, the most common being trauma and bacterial infection (primarily caused by Pseudomonas aeruginosa). Another common differential diagnosis is borreial lymphocytoma. Rarer causes of perichondritis include furunculosis, malignant external otitis, leukemic infiltration, burns, insect bites and contact allergy [16], but also viral infections (herpesvirus type 1) [17] and cutaneous T-cell lymphoma [18]. Another condition to be considered, if there is a corresponding history, is cutaneous leishmaniasis [17].

The patient’s clinical presentation initially prompted us to consider an infectious origin, similar to a case described by Krumholz et al. [19]. Postoperative wound infections are a common complication in hospitals, accounting for up to 29% of nosocomial infections [20]. Although dermatologic surgery procedures are associated with a comparatively low risk (4.0%) of wound infections [21], they are much more common than a systemic disease such as relapsing polychondritis, whose incidence is estimated at 3.5/1,000,000/year [14]. Nevertheless, the present case clearly demonstrates that this diagnosis should be considered in patients who do not respond to antibiotic therapy and who present with sparing of the earlobe and/or involvement of other organ systems.

Conflicts of interest
None.

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