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Review Article

Nasal surgery in patients with systemic disorders

Abstract

Multisystemic disorders represent a heterogenous group of diseases which can primarily manifest at the nose and paranasal sinuses as limited disease or secondarily as part of systemic involvement. Rhinologists therefore play an important role in the diagnostic but also therapeutic process. Although therapy of multisystemic disorders is primary systemic, additional rhinosurgery may become necessary. The spectrum of procedures consists of sinus surgery, surgery of the orbit and lacrimal duct, septorhinoplasty and closure of nasal septal perforation. Since the prevalence of most systemic diseases is very rare, recommendations are based on the analysis of single case reports and case series with a limited number of patients only. Although data is still limited, experiences published so far have shown that autologous cartilage or bone grafts can be used in nasal reconstruction of deformities caused by tuberculosis, leprosy, Wegener's granulomatosis, sarcoidosis and relapsing polychondritis. Experiences gained from these diseases support the concept that well-established techniques of septorhinoplasty can be used in systemic diseases as well. However, a state of remission is an essential condition before considering any rhinosurgery in these patients. Even under these circumstances revision surgery has to be expected more frequently compared to the typical collective of patients undergoing septorhinoplasty. In addition, experiences gained from saddle nose reconstruction may in part be of value for the treatment of nasal septal perforations since implantation of cartilage grafts often represents an essential step in multilayer techniques of closure of nasal septal perforations. Aside from the treatment of orbital complications sinus surgery has been proven beneficial in reducing nasal symptoms and increasing quality of life in patients refractory to systemic treatment.

Keywords: systemic disorder, rhinoplasty, nasal septal perforation, saddle nose, sinusitis

Florian Sachse[1]
Wolfgang Stoll[1]

1 University of Münster, Department of Otorhinolaryngology Head and Neck Surgery, Münster, Germany

1 Introduction

Systemic disorders represent a heterogenous group of diseases which can primarily manifest at the nose and paranasal sinuses as limited disease or secondarily as part of the systemic involvement. In general, therapy is systemic but often requires a multidisciplinary approach with participation of several different specialists. The role of the rhinologist is very important since she/he may discover a multisystemic disease at an early stage when the disease is still localized. In this case, early systemic therapy can ideally prevent or at least diminish fatal organic damage. In addition, systemic therapy is usually essential before rhinosurgery is intended. This review provides a selection of systemic diseases with nasal manifestations and their rhinosurgical options of treatment. Because of the rare prevalence of most of the diseases recommendations are mainly based on the analysis of single case reports or case series with a limited number of patients. Provided that rhinosurgical techniques have been reported for a specific disease, they are described and discussed at the corresponding section.

2 Infectious diseases

2.1 Tuberculosis

Epidemiology/pathogenesis: Even today tuberculosis is still one of the most frequent infectious diseases worldwide. According the German Robert Koch institute (RKI) in 2007 the incidence of tuberculosis in Germany was 6.1/100,000. In most cases the disease is caused by *Mycobacterium tuberculosis*. Tuberculosis often coincides with HIV or AIDS. Clinically, primary nasal involvement can be distinguished from secondary involvement as a result of pulmonary tuberculosis. The diagnosis of nasal tuberculosis is based on medical history, nasal endoscopy, histological evidence of typical tubercular granuloma in the nasal mucosa, PCR-detection of mycobacterial DNA and cultivation of *Mycobacterium tuberculosis* from

the nasal mucosa. Overall, nasal tuberculosis is very rare with predominance in females [1], [2], [3].

Nasal symptoms: Symptoms are in general non-specific and include obstructive and rhinitis-like complaints, epistaxis and crusting. Suspicious findings such as easily bleeding membranes and crusts may be observed at the anterior part of the cartilaginous septum and at the inferior turbinates [3], [4]. Nasal septal perforation can occur as a first symptom of the disease [5]. Involvement of the sinuses and nasopharynx has been reported [6], [7], [8]. Recently, we ourselves could observe all these findings in a patient with nasopharyngeal tuberculosis (Figure 1). Nasal polyps may be observed as well in those patients and are considered suspicious for nasal tuberculosis when originating from the inferior turbinates [9], [10].

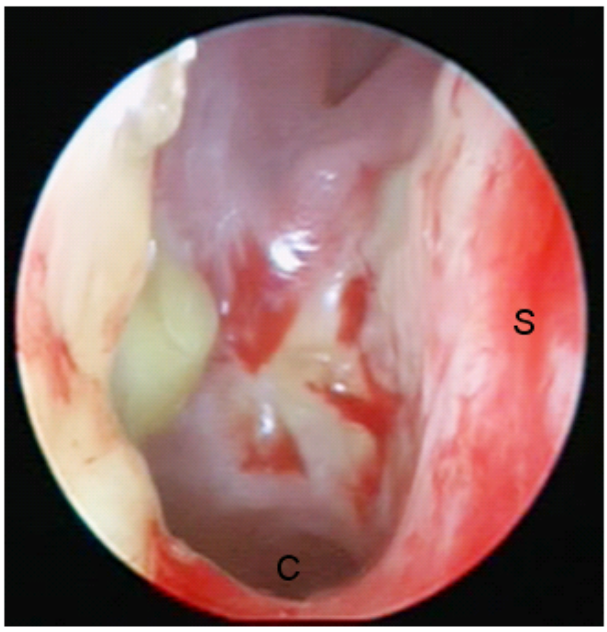

Figure 1: Nasal tuberculosis. Region of the nasal choanae (C). Easily-bleeding membranes are visible in the nasopharynx and at the dorsal septum (S).

Rhinosurgery: Aside from mucosal involvement the nasal skin may be involved as well. Such cutaneous manifestations of tuberculosis are designated "Lupus vulgaris". It has been reported that invasion at the mucocutaneous junction, nasal vestibulum and dorsal nasal skin can result in fissures and contractures of the nasal cartilages [11]. After a 6-months course of systemic therapy, reconstructive rhinosurgery was performed using an auricular composite graft [3].

Sinus surgery may be indicated in patients with involvement of the sinuses refractory to systemic treatment. To our knowledge the indication for closure of nasal septal perforations due to nasal tuberculosis has not been discussed in the literature so far. However, following a successful course of 12-months systemic therapy with unsuspicious clinical and negative microbial findings conditions for closure of nasal septal perforations seem to be acceptable.

2.2 Leprosy

Epidemiology/pathogenesis: Leprosy (Hansen's disease) is an infectious disease caused by *Mycobacterium leprae* and involves the skin, mucosal surfaces and peripheral nerves. Although it is a very rare disease in Europe, leprosy still belongs to the most frequent infectious diseases worldwide with an annual incidence of 250,000 new cases. Clinically, five subtypes can be distinguished due to the patient's immune status, clinical and histological findings. In addition, PCR diagnostic may be useful [12].

Nasal symptoms: In general, early stages are characterized by unspecific nasal symptoms with the exception of a reduced sense of smell [13]. Sinonasal symptoms can occur and can be refractory to systemic treatment [14], [15]. The clinical spectrum ranges from localized involvement of the external nose and extensive destruction of the septal cartilage and bone resulting in nasal septal perforation and saddle nose deformity [16], [17], [18]. Moreover, destruction of the anterior nasal spine and of nasal turbinates is not uncommon. Thus, the degree of destruction is often more extensive compared with other systemic diseases discussed in this review. In severe cases only the nasal skin and he lower lateral cartilages are preserved [18]. Principally, systemic treatment should precede any local surgical procedure.

Rhinosurgery: Menger and coworkers reconstructed 24 saddle nose deformities of different severity caused by leprosy [18]. In all cases an external approach was used. A V-Y procedure was used in four patients in order to lengthen a retracted columella. The nasal septum and upper lateral cartilages were reconstructed by implantation of a dorsal onlay graft. An absent anterior nasal spine was reconstructed by implantation of a caudally extended columella strut. The authors exclusively used autologous costal and auricular cartilage. Wound infection, extrusion or warping of implants was not observed in any patient. Functional and aesthetic improvement was observed in 15/17 patients. The rate of implant resorption was dependent on the implant site. Least resorption was observed for dorsal onlay grafts (4/17). Moderate resorption was observed for columella strut and shield grafts (7/17). In general, conchal cartilage grafts were associated with less resorption than costal cartilage grafts. Overall, advantages are dominating so that the authors advocate reconstruction of saddle nose deformities in leprosy using autologous cartilage grafts [18]. Aside from cartilage grafts bone grafts have been used by another group. However, the rate of complications such as wound infection and graft resoprtion was 50% [19].

3 Immune deficiency

Immune deficiency can be broadly classified in primary immune deficiency syndromes that are very rare and those acquired secondarily during life. As a consequence, these patients may suffer from opportunistic bacterial, viral, fungal or parasite infections. At the nose and the

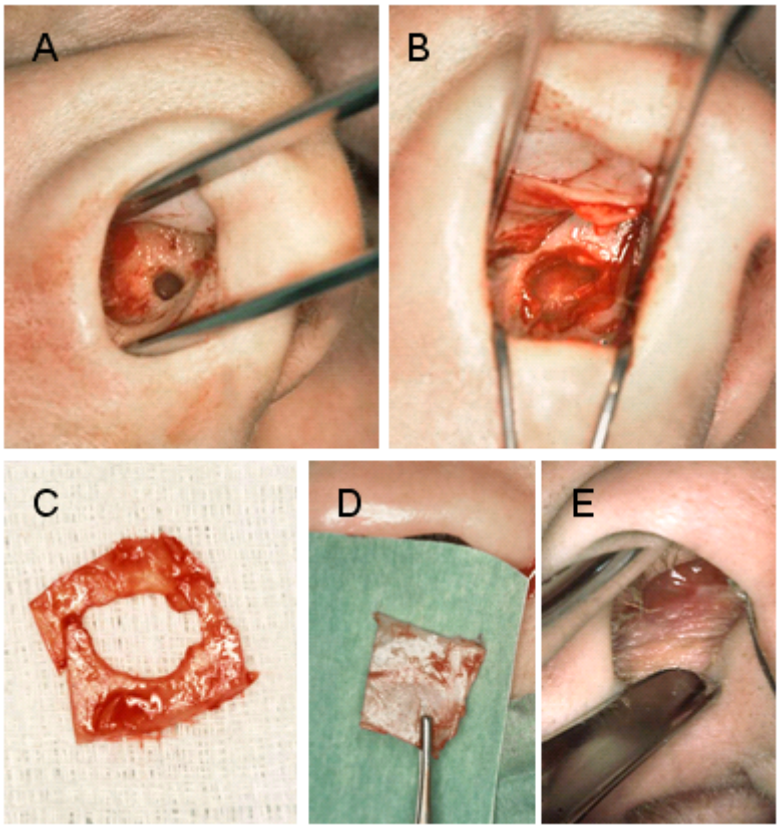

Figure 2: Closure of a small nasal septal perforation (type A) in a HIV positive patient by cartilage exchange. Demonstration of the small perforation (A). Cartilage resection at the borders of the perforation (B, C). Dorsal septal cartilage graft (D). Closed perforation (E).

sinuses infections generally manifest as acute/chronic sinusitis or nasal septal perforation. As already mentioned numerous diseases may be associated with an immunosuppressed condition. As an example we discuss the impact of immune suppression and the role of rhinosurgery in patients with HIV/AIDS and primary nasal NK/T-cell lymphoma.

3.1 HIV/AIDS

Epidemiology/pathogenesis: According to the RKI 3,000 new infections per year have been observed in Germany since 2007. Causative pathogens are several types of the human immune deficiency virus (HIV).

Nasal symptoms: Rhinitis-like symptom can be observed frequently in this group of patients. Porter and coworkers interviewed HIV positive patients and found sinonasal symptoms in 66% of cases. Sinusitis was reported by 54% of patients. Allergic rhinitis like symptoms were reported by 80% of patients [20]. Similar observations were reported by Prasad and coworkers who investigated sinonasal symptoms in 968 HIV positive patients. They found that sinusitis complaints were predominating in their patients [21].

Aside from bacterial sinusitis invasive fungal sinusitis is a serious threat for immunosuppressed patients. Therapy has to be initialized immediately and consists of extensive surgical removal of involved tissue and application of Amphotericin B [22], [23]. Nasal septal perforations associated with invasive fungal sinusitis have been reported [24].

Rhinosurgery: Functional endoscopic sinus surgery can reduce symptoms in HIV positive patients with the exception of improvement of a reduced sense of smell [25], [26]. Nasal septal perforations have been rarely observed but may be the first symptom of the disease. Sometimes, the cause of a nasal septal perforation can be identified. Bennett and coworkers detected *Mykobakterium kansasii* in a HIV positive patient with nasal septal perforation [27]. Prior to any rhinosurgery, HIV positive patients and those suffering from AIDS require long-term stabilisation of their immune system and strict control of opportunistic infections. Only in this situation closure of a nasal septal perforation should be planned [27], [28]. In the past, mortality of AIDS was tremendously higher than today. That is why rhinosurgery was contraindicated or had less priority in these patients. We ourselves have closed a small perforation in a HIV positive patient using an autologous septal cartilage graft combined with bilateral mobilisation of mucosal flaps (Figure 2).

3.2 Primary nasal NK/T-cell-lymphoma

Epidemiology/pathogenesis: Immunophenotyping and modern moleculargenetic studies revealed that destructive midline lesions actually represent manifestations of sinonasal Non-Hodgkin lymphomas of the type “Primary nasal NK (natural killer cell)/T-cell lymphoma” or destruc-

tive processes caused by Wegener's granulomatosis [29], [30], [31]. An association of Epstein-Barr-Virus with primary nasal NK/T-cell lymphoma has been reported [32], [33]. The incidence for western Europe and the United States has been estimated to be below one percent per year [34].

Nasal symptoms: Locally NK/T-cell lymphoma initially presents with unspecific symptoms including nasal obstruction, purulent rhinorrhea, epistaxis, crusting and local inflammation of the nose and face and sometimes ophthalmologic complaints. Disease progression is associated with mucosal ulceration, nasal septal perforation and destruction of the hard palate formerly summarized by the clinical term "lethal midline granuloma". Disseminated disease is characterized by metastasis into the skin, visceral organs, and general illness and by so called B-symptoms. Agressive NK/T-cell leukaemia is associated with very fast disease progression and lethal outcome. Therapy of NK/T-cell lymphoma is dependent on tumor stage as defined by the Ann-Arbor classification. For stages I and II radiotherapy alone is the therapy of choice. Chemotherapy and chemotherapy combined with radiotherapy are options for progressive tumor disease. The 5-year survival rate for stages I and II does not exceed 50%. Disease progression is associated with lethal outcome within weeks or even days in the case of a leukaemic course of disease [29], [35].

Rhinosurgery: Because the prognosis of primary nasal NK/T-cell lymphoma is very poor, rhinosurgery has just low priority and may be considered in a persistent state of remission. At any rate, local wound healing would probably be impaired following radiotherapy. In the case of extensive destruction of the nose, hard palate, sinuses and face prosthetic rehabilitation is an alternative option for these patients [36].

4 Multisystemic diseases

4.1 ANCA associated vasculitis

The term "ANCA associated vasculitis" summarizes Wegener's granulomatosis, microscopic polyangitis and Churg-Strauss Syndrome because these diseases share some clinical, pathogenetic and immunologic findings. In general, this group of vasculitis involves small vessels (small vessel vasculitis).

4.1.1 Wegener's granulomatosis

Epidemiology/pathogenesis: Wegener's granulomatosis (WG) is characterized by granulomatous inflammation of the respiratory tract, necrotizing vasculitis of the small- and medium-sized vessels and by necrotizing glomerulonephritis [37]. The disease usually begins not before the fourth decade of life. An annual incidence of 10/1,000,000 in Germany has been reported [38]. Classically the upper respiratory tract, the lungs and the kidneys are involved. However, localized WG has been observed in 10–15% of patients presenting with head and neck involvement only [39].

The diagnosis of WG can be made according to the criteria of the American College of Rheumatology (ACR) [40]. Nasal tissue biopsies reveal typical histopathologic signs of WG in the majority of patients [41]. Serologic detection of antineutrophil cytoplasmatic antibodies with cytoplasmatic fluorescence (cANCA) and ELISA (Enzyme-linked Immunosorbent Assay) reactivity against proteinase 3 (anti-PR3) is an important finding in WG. In addition, it has been observed that superantigens derived from *Staphylococcus aureus* are associated with the production of PR3-ANCA [42]. Clinically, colonization of the nasal mucosa by *Staphylococcus aureus* is considered as a risk factor for relapse [43]. There is much variability of the spectrum of systemic manifestations as musculoskeletal, neurologic and skin manifestation can occur, too. Although renal manifestations are rarely observed initially, 75% of patients have renal involvement during disease progression [44].

Nasal symptoms: In the head and neck region WG can manifest with sinonasal, auricular, laryngotracheal, ophthalmologic and/or salivary gland complaints. In the generalized phase the nose and the sinuses display the highest degree of disease activity [45], [46]. Mucosal edema, granulation and massive crusting are typical findings for WG (Figure 3). Sometimes, a mucosal pattern of cobblestoning can be observed [47]. The anterior part of the nasal septum (Kiesselbach's area) is one of the most frequently involved areas. With disease progression mucosal erosions and formation of scars may be visible. Finally, extended disease may present with nasal septal perforation or saddle nose deformity [41], [48]. Nasal endoscopy is important since it has been reported that disease activity can be evaluated by the inspection of the nasal mucosa [49].

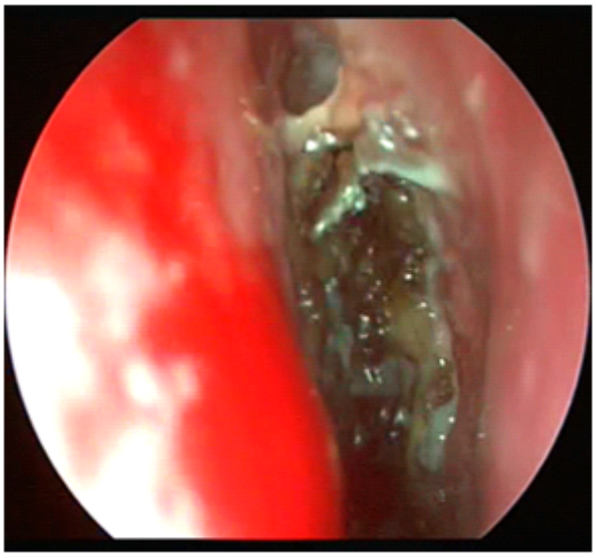

Figure 3: Active Wegener's granulomatosis. Massive crusting and inflammation of the nasal mucosa.

Rasmussen as well as Cannady and coworkers examined patients with WG and evaluated nasal symptoms. Nasal

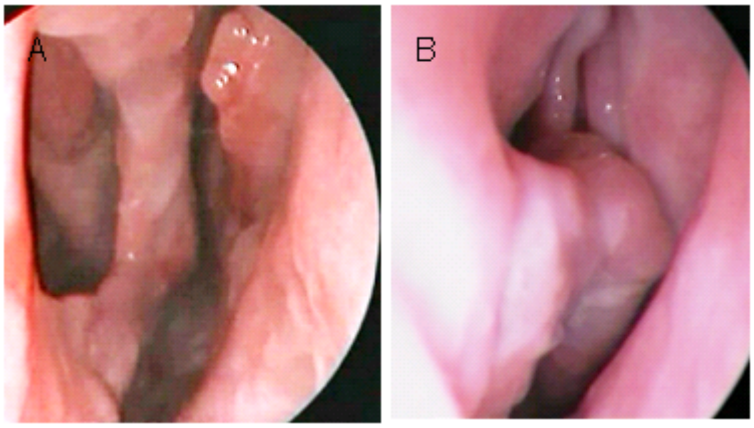

Figure 4: Wegener's granulomatosis in remission. Large nasal septal perforation (type C). No signs for inflammation or crusting are visible (A). Closure of the perforation by (bilateral) inferior turbinate flap (B) and costal cartilage interposition graft (not shown).

obstruction was reported by 54–58% of patients, recurrent epistaxis and foetor by 50–52% of patients, massive crusting by 56–69% and sinonasal involvement by 33–61% of patients [50], [51]. According to Cannady the frequency of a nasal septal perforation was 33% and 28% for saddle nose deformity. The rate of ophthalmologic symptoms such as epiphora and pseudotumor orbitae are 13% and 3% respectively [50].

Rhinosurgery: Rhinosurgery in WG aims to eliminate or at least reduce complaints caused by nasal septal perforation or saddle nose deformity. Surgery should be performed only if remission (ideally complete remission) was achieved or a minimum of disease activity is left [45], [52], [53]. Perioperative induced flare ups of disease activity and impaired wound healing are considerations that may argue against an operation.

Frequently, structural cartilaginous and mucosal defects can be observed in WG. To solve this problem Duffy and coworkers have suggested a technique using bilateral facial artery based musculomucosal flaps [54]. Recently Congdong and coworkers published a series of cases of WG patients undergoing reconstructive rhinosurgery and analyzed the long-term follow up. Twelve saddle nose deformities were corrected in a state of stable remission. Two patients required revision rhinoplasty (primary success rate 77%, overall success rate 92%). For reconstructions costal cartilage (39%) and temporoparietal bone (calvarial bone graft, 26%) were implanted in the majority of cases. In addition, irradiated allogenous rib (7%), irradiated dura (7%), autologous conchal cartilage (7%), iliac crest (7%) and bony septum (7%) were used. In one case an auricular composite graft was used for the reconstruction of an ala rim defect. Nishiike and coworkers reconstructed a saddle nose deformity using autologous iliac crest [55].

As evaluated by Congdon and coworkers rhinosurgery does not induce a flare-up nor does it influence the course of the disease. However, disease severity contributes the success rate in saddle nose reconstruction due to the observation that patients with localized WG had an overall success rate of 88% whereas those with involvement of the lungs had just 60%. It is worth to mention that resorption was always observed with irradiated materials (transplant success rate: 0%), whereas least resorption was seen for autologous transplants (transplant success rate costal cartilage: 83%/calvarial bone graft: 75%). Overall, saddle nose reconstruction in patients with WG is safe even if an increased rate of revision surgery has to be expected compared with a typical collective of septorhinoplasty [53].

Shipchandler and coworkers reconstructed four saddle nose deformities using an external rhinoplasty approach by implantation of a split calvarial bone L-shaped strut. This L-shaped strut consisted of a dorsal onlay graft and a columella strut fixed together with a titan screw. The strut was placed in a subcutaneous pocket under the skin of the nasal dorsum and fixed between the medial crura of the alar cartilages. Wound infection, extrusion or dislocation of transplants did not occur. During a follow-up period of 21 months no resorption of transplants was observed [56].

Closure of nasal septal perforations in WG has been traditionally refused or considered as contraindication since the chronic course of the disease and flare-ups prevent successful wound healing. In addition perforations are often very large [51], [52]. However, we have successfully closed a large nasal septal perforation in a WG patient in remission and well-cared nasal mucosa. Closure was achieved by bilateral mobilization of inferior turbinate pedicled mucosal flaps and interposition of costal cartilage (Figure 4). In the case of persistent active disease or failed closure of a perforation implantation of a septal button is an alternative option of treatment.

Functional sinus surgery including decompression of the orbit and the optical nerve may become necessary for some patients although data are very limited so far [50], [55], [57]. Furthermore, patients with involvement of the nasolacrimal duct may require drainage surgery [50], [58], [59].

4.1.2 Microscopic polyangiitis

Epidemiology/pathogenesis: Microscopic polyangiitis (MPA) is a necrotizing vasculitis characterized by low or

absent deposition of immune complexes involving small vessels (necrotizing glomerulonephritis, pulmonary capillaritis). Involvement of medium sized arteries has been observed, too. Further definition criteria do not exist. Distinction from panarteriitis nodosa has been made for a few years only [37]. An annual incidence of 3/1,000,000 in Germany has been reported [60]. Antineutrophil anticytoplasmatic antibodies with a perinuclear fluorescence pattern (pANCA) that are directed against myeloperoxidase (anti-MPO) can be detected in MPA. The diagnostic golden standard still is histological evidence preferentially gained by renal biopsy. Nasal biopsy is usually unsuccessful [41]. Systemic therapy is analogous to that of WG [61].

Nasal symptoms: In general, sinonasal manifestation of polyarteriitis nodosa and MPA are very rare. According to the studies of Paulsen and Rudert only Rhinosinusitis with crusting may be considered a frequent symptom [41]. Metaxaris and coworkers found nasal symptoms such as epistaxis and sinusitis in 8/18 patients [62]. We ourselves have observed bilateral prominent vessels at the Kiesselbach area in a patient with MPA who reported frequent episodes of epistaxis (Figure 5). Interestingly, this area is predominantly involved in WG, too. Nasal polyps and nasal septal perforation have been observed, whereas to our knowledge saddle nose deformities have not been reported so far [41], [63], [64], [65], [66].

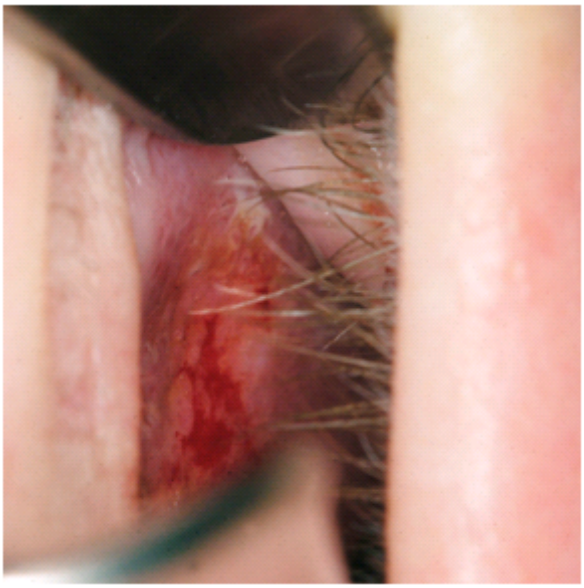

Figure 5: Microscopic Polyangiitis. Prominent vessels at the area II in a patient suffering from recurrent episodes of epsitaxis.

Rhinosurgery: Because of a similar pathophysiology treatment should orientate on WG.

4.1.3 Churg-Strauss Syndrome

Epidemiology/pathogenesis: Churg-Strauss-Syndrome (CSS) was described for the first time in 1951 by Churg and Strauss as allergic angiitis and allergic granulomatosis. An annual incidence of 1/1,000,000 in Germany has been estimated [67]. Diagnosis of CSS can be made according to the criteria suggested by the American College of Rheumatology (ACR) or according to the definition of the Chapel Hill Consenus Conference [37], [68].

The typical histopathological finding of eosinophilic vasculitis and the association with asthma allow distinction from other types of vasculitis. However, histopathologic evidence gained from a nasal biopsy is rarely successful [41]. Hypereosinophilia (>1,500/µl) and detection of pANCA directed against MPO are suspicious of CSS.

Nasal symptoms: Sinonasal symptoms are frequently observed in CSS patients. Actually, one third of patients with CSS consult an Otorhinolaryngologist because of worsening of nasal complaints. Symptoms associated with allergic rhinitis such as obstruction (95%), rhinorrhea (95%), anosmia (90%) and excessive sneezing (80%) are predominant in these patients. Some patients suffer from a milder degree of nasal crusting (75%) and purulent (65%) or bloody (60%) rhinorrhea thereby sharing some symptoms also observed in WG [69]. Nasal polyps may be present in up to 76% of patients [70], [71], [72]. Nasal septal perforation has been observed in CSS [41], whereas saddle nose deformities have not been reported.

Rhinosurgery: Because of a similar pathophysiology treatment should orientate on WG.

4.2 Sarcoidosis

Epidemiology/pathogenesis: Sarcoidosis (Boeck's disease) is a chronic multisystemic disorder of unknown aetiology affecting predominantly young adults and people of middle age. An annual incidence of 10/100,000 has been estimated [73]. Bilateral hilar lymphadenopathy and increased levels of the Angiotensin converting enzyme (ACE) are suspicious of sarcoidosis. The most important histopathologic sign is non-caseating granuloma. Moreover, cervical lymphadenopathy, salivary gland and lacrimal gland hypertrophy, Lupus pernio and ophthalmologic complaints are observed in these patients. Sinonasal involvement can occur as part of systemic disease but can also represent limited disease of the nose and sinuses [74].

Zeitlin and coworkers analyzed 733 cases of sarcoidosis and found that sinonasal involvement often is underestimated. Interestingly, patients with sinonasal involvement frequently required prolonged systemic therapy [75]. In order to standardize the diagnosis of sinonasal sarcoidosis de Shazo and coworkers have developed a number of criteria [76].

Nasal symptoms: Sinonasal sarcoidosis often presents with unspecific symptoms such as nasal obstruction, crusting, epistaxis, postnasal drip, recurrent episodes of sinusitis, facial pain and headache. However, endoscopic examination typically reveals a hyperplastic and friable mucosa with reddish and edematous areas. In addition, small yellowish nodules in the submucosa of the nasal septum and the inferior turbinates are considered suspicious for sarcoidosis [77]. Hyposmia or even anosmia can represent further symptoms of the disease. In add-

ition, nasal polyps, nasal septal perforation and rhinophym may be associated with sarcoidosis. Arrosion of the soft and hard palate due to destructive granuloma as well as saddle nose deformity have been reported [78], [79]. Cranial base involvement and intracranial spread as well as invovlement of the nasolacrimal duct has been observed [80], [81]. Small nodular skin lesions of the nasal ala regions have been reported [82].

Rhinosurgery: Although glucocorticosteroids represent the first choice of drugs in the treatment of sarcoidosis, functional endoscopic sinus surgery has been shown to relief symptoms, to reduce the amount of glucocorticosteroids and to improve quality of life in a group of patients [74], [83], [84]. Kay and coworkers retrospectively analyzed a collective of 86 patients with sinonasal sarcoidosis. Six of their patients (7%) underwent sinus surgery because of anatomic blockage of the osteomeatal complex due to recurrent acute epsidodes of sinusitis, polyp formation or granuloma [83]. Similar observations were reported by Goodmann and coworkers who performed sinus surgery in six patients with refractory sinonasal sarcoidosis [84]. Correspondingly, Zeitlin and coworkers advocate rhinosurgery in patients refractory to systemic treatment [75]. Almost no data exist concerning saddle nose reconstruction in patients with sarcoidosis. Shipchandler and coworkers used a L-shaped calvarial bone graft for saddle nose reconstruction in one patient [56].

4.3 Relapsing polychondritis

Epidemiology/pathogenesis: Relasping polychondritis (RP) is a very rare rheumatologic disease characterized by recurrent inflammation and destruction of auricular and nasal cartilages. In addition, the disease may also involve joints, eyes, the audiovestibular system, the cardiovascular system and the respiratory tract. An autoimmune pathogenesis seems possible since antibodies directed against type II collagen have been detected in cartilages. An annual incidence of 1/3,500,000 has been estimated [85].

The clinical picture is rather variable and may present as auricular chondritis, nasal chondritis/saddle nose deformity, laryngotracheal chondritis with collapse of the tracheal airway or tracheal stenosis, audiovestibular symptoms, inflammation of ocular structures or polyarthritis or as a combination of these symptoms. The diagnosis can be made according to the criteria defined by McAdam [86] or by Damiani and Levine [87].

Nasal symptoms: Nasal chondritis resembles auricular chondritis in that both often occur acute and are very painful. In addition, nasal fullness of the nose reported as well as epistaxis and rhinorrhea. Following several recurrent episodes of nasal chondritis saddle nose deformity can be the final result.

Rhinosurgery: Rhinosurgery in RP is based on a limited number of case reports only. Rapini refused reconstruction of saddle nose deformities in RP because of the relapsing character of the disease [88]. By contrast, Haug and coworkers successfully reconstructed a saddle nose using iliac crest. A bony implant was chosen because the authors considered it more resistant and less resorpable compared with cartilage [89]. Torossian and coworkers reconstructed a saddle nose deformity in a young patient using calvarial bone graft. The operation was performed 12 months after establishing the diagnosis of RP and in a state of stable remission [90]. Experiences reported by Bell and coworkers argue against a theoretical superiority of bone implants. Usage of cartilage implants is possible in RP if relapsing episodes of nasal chondritis are prevented or reduced to a minimum by immunosuppressive therapy. Bell and coworkers used autologous costal cartilage to reconstruct a saddle nose in 14 years old patient. Although two more episodes of chondritis occurred no signs of resorption of the cartilaginous implant was observed one year after the operation [91].

4.4 Systemic Lupus erythematosus

Epidemiology/pathogenesis: Systemic Lupus erythematosus (SLE) is an autoimmune disorder with potential manifestations at nearly all organs and tissues of the human body. The disease predominantly involves females. An annual incidence of 5/100,000 in Germany has been reported [92]. Oral and nasopharyngeal ulceration are considered as diagnostic criteria for SLE [93].

Nasal symptoms: Nasal symptoms are generally unspecific such as mild episodes of epistaxis or local tenderness or facial pain. The nasal mucosa may appear diffusely reddish and edematous or as atrophic rhinitis. Less than 70 cases of nasal septal perforation have been reported so far worldwide. Nasal septal perforation is even more rarely observed as a first symptom [94]. In a retrospective study of the lupus clinic of the University of Toronto nasal septal perforation was discovered in 40/885 (4.6%) patients with SLE. These perforations usually remain asymptomatic since they are detected after a course of 6.1 years in the mean. In addition, nasal septal perforations occur during exacerbation of the disease or in the context of vasculitis [95]. Oral ulceration often precedes nasal septal perforation.

5 Inflammatory bowel disease

5.1 Crohn's disease

Epidemiology/pathogenesis: Crohn's disease (CD) is an inflammatory bowel disease and can involve all parts of the gastrointestinal tract. An annual incidence of 5.2/100,000 in Germany has been reported [96]. Histopathology reveals non-caseating granuloma as a valuable diagnostic sign that however is detectable in 10% of the cases only. Extraintestinal spread has been observed. Aside from the oral cavity, the nose and the larynx may be involved in the head and neck region [97], [98], [99]. Nasal involvement is extremely rare since less than 15 cases have been reported throughout the world so far

[98], [100], [101], [102], [103], [104], [105], [106], [107].

Nasal symptoms: The spectrum of nasal symptoms consists of nasal obstruction, rhinorrhea, hyposmia, epistaxis and complaints of sinusitis. The nasal mucosa may appear diffusely reddish and hypertrophic and easily starts bleeding. Erosion, ulceration and necrosis of the septum or inferior turbinates may be visible [100], [101], [106], [107], [108]. In addition, nasal septal perforation and saddle nose deformity have been reported [104], [109], [110]. It is worth to mention that nasal symptoms may precede gastrointestinal symptoms [111]. An association with WG and RP has been observed. Book and coworkers retrospectively analyzed 160 patients suffering from inflammatory bowel disease. They observed chronic sinusitis particularly in those CD patients (23%) who suffered from obstructive bowel complications, whereas rhinosinusitis was observed only in 7% of patients without obstructive bowel complications [99].

Rhinosurgery: To our knowledge reconstruction of saddle nose deformities or closure of nasal septal perforations has not been discussed in the literature so far. Partial turbinate resection has been reported [108]. Sinus surgery may become necessary to reduce sinonasal symptoms and to control orbital complications [107].

5.2 Ulcerative colitis

Epidemiology/pathogenesis: Aside from CD ulcerative colitis (UC) belongs to the group of inflammatory bowel disease. An annual incidence of 6/100,000 in Germany has been reported [112]. Although aetiology of UC still remains unclear, an autoimmunepathogenesis has been suggested. An association of UC with chronic sinusitis has been hypothesized in some patients [113].

Nasal symptoms: Nasal septal perforation is a rarity [114].

6 Heriditary hemorrhagic telangiectasia

Epidemiology/pathogenesis: Heriditary hemorrhagic telangiectasia (HHT, Osler's disease) is an autosomal dominant-disease of angiogenesis. The underlying genetic aberrations are associated with formation of endothelial-lined vascular lakes and dilatated vessels. Because the vessel's wall structure is abnormal due to the lack of muscular or elastic support rupture of these vessels already occurs by small trauma. This can lead to substantial bleeding although coagulation factors and platelets are normal because pathologic vessels do not retract or undergo vasospasm. Currently, an incidence of 1/10,000 has been reported [115].

Nasal symptoms: Quality of life is of HHT patients is mainly determined by recurrent episodes of epistaxis [116], [117], although arteriovenous malformations of the gastrointestinal tract, lungs, liver and brain are often associated with higher morbidity and mortality [118]. A variety of treatment options to control epistaxis in HHT patients are available. These include topical therapies, hormonal therapies with estrogens, laser coagulation as well as argon-plasma coagulation [115], [119], [120], [121], [122]. Argon-plasma coagulation, bipolare coagulation as well as anterior and/or posterior nasal packing represent procedures to control acute episodes of epistaxis. Severe epistaxis can be controlled by interventional radiological embolization [123], [124] and surgical arterial ligation [125].

Rhinosurgery: Recently, new data have been published analyzing long-term results and quality of life in HHT patients treated by septodermoplasty or nasal closure.

Septodermoplasty

The main principle of septodermoplasty (SDP) is resection of diseased mucosa of septal areas II and III and implantation of an epidermal graft. Elimination of easily bleeding mucosal areas leads to a reduction of the frequency of bleeding within the first two years. After two years however, new formation of telangiectatic vessels dorsal to the epidermal graft is often observed. As a consequence, the frequency of bleeding increases again. Moreover, access to the bleeding vessel then is usually difficult. These arguments have been considered as major points of criticism of this method.

By contrast, recently published studies emphasize the benefit of this method. Levine and coworkers retrospectively analyzed (mean follow-up 3.75 years) 50 HHT patients and found that 86% of patients reported increased quality of life following septodermoplasty although they also complained about impaired sense of smell (78%), crusting (72%), hyposmia (58%) and symptoms of sinusitis (30%) [126]. Harvey and coworkers reported on a collective of 131 HHT patients who were followed up for 60 months. Overall 268 KTP laser procedures were performed. In addition, 33 patients underwent SDP, which was significantly associated with a reduced number of laser procedures postoperatively [122]. Fiorella and coworkers analyzed retrospectively 67 patients who received SDP. Again, a majority of patients (57/67) reported a higher quality of life. In addition, the authors found a significant reduction of blood transfusions with 12 months postoperatively compared with the 12 months period before the operation [127]. Recently, a modification of SDP has been performed by Lesnik. He resected the remaining nasal septum and then performed SDP in nine patients. An increase of quality of life was observed as well as a reduction of the need of blood transfusion [128].

Young's procedure

Taylor and Young introduced the method of permanent closure of the nasal nostrils in 1961. The aim of this procedure is to prevent dryness and traumata of the nasal mucosa thereby reducing the frequency of bleeding. Young himself reported about the problem of permanent breathing through the mouth and re-opened the nasal

Table 1: Survey of the literature

Disease	Closure of nasal-septal perforation	Reconstructive rhinosurgery	Sinus surgery
Tuberculosis		– Alar cartilage reconstruction using auricular comoposite graft [3]	– Caldwell Luc proc., ethmoidektomy in single cases refractory to chemotherapy [3]
Leprosy		– Reconstruction using autologous costal- and conchal cartilage [18], [19] – bone grafts in cases for extensive deformities [19]	
Immunedeficiency HIV/AIDS	may be indicated following prolonged stabilization of the immune system [28]		– extensive sinus surgery in the case of invasive fungal sinusitis [22] – reduction of symptoms in HIV [25, 26]
Wegener's Granulomatosis	contraindication [51], [52] septal button [52]	– reconstruction of saddle nose deformities using autologous costal cartilage/calvarial bone graft [53] – L-shaped calvarial bone strut [56] – iliac crest [55] – surgery in a state of remission [45], [49], [51], [51], [52], [53], [55], [151]	– dacryocystorhinostomy – orbital-/optical nerve decompression in single cases necessary [50], [55], [57], [58], [59] – sinus surgery in cases of sinusitis refractory to medical treatment [50], [52]
Sarcoidosis		– L-shaped calvarial bone strut [56]	– reduction of symptoms [74], [83] – endoscopic and osteoplastic surgical approaches [84] – diagnostic biopsy [75]
Relapsing Polychondritis		– reconstruction of saddle nose deformities using autologous iliac crest [89] or calvarial bone graft [90] – autologous costal cartilge in a state of remission [91]	
Crohn's disease			– ethmoidectomy and orbital decompression in single cases [107]

cavity in five of his patients. Nevertheless, permanent nasal closure may be an option in refractory cases as suggested by several authors [129], [130], [131]. Hitchings and coworkers performed a modified Young's procedure in eight patients with sever bleeding episodes. Complete cessation of bleeding was observed in 88% of patients (mean follow-up 22 months). A detailed analysis revealed that reduction of episodes of bleeding was associated with increased quality of life which was considered even more important than permanent nasal obstruction [117].

Overall, SDP and Young's procedure are options for HHT patients with recurrent severe episodes of epistaxis refractory to local therapies and laser coagulation since in these patients reduction of bleeding obviously determines quality of life more importantly than nasal obstruction.

7 Evaluation of rhinosurgical procedures

Rhinosurgery in patients with systemic diseases may become necessary to reconstruct saddle nose deformities and nasal septal perforations. Sinus surgery plays a role in patients with orbital and intracranial complications. In addition, sinus surgery may be useful in some patients to reduce sinonasal symptoms thereby improving quality of life (Table 1).

Extended diagnostic is mandatory if an underlying systemic disease is suspected and in cases of aetiological unclear saddle nose deformity or nasal septal perforation to prevent failure of rhinosurgery in such patients. Furthermore, non-reflected rhinosurgery may camouflage the symptoms saddle nose or nasal septal perforation as manifestations of a yet localized systemic disease. Thereby, the chance to prevent a potential fatal systemic disease by early treatment could be missed or delayed [132].

Because of the rarity of numerous systemic diseases recommendations on the treatment of nasal deformities caused by systemic diseases are based on single case reports or case series only. Therefore, no specific rhinosurgical techniques have been established so far. However, according the experiences published cartilage and bone grafts haven been implanted with success in stable remission in patients suffering from tuberculosis [3], leprosy [18], [19], Wegener's granulomatosis [45], [49], [52], [53], sarcoidosis [56] and relapsing polychondritis [89], [91].

Experiences gained from these patients suggest that traditionally-proven surgical techniques of rhinoplasty [133], [134], [135] can also be applied in sytemic diseases as far as the underlying disease has been successfully treated previously. Rhinosurgery is performed ideally in a state of complete remission meaning during complete absence of clinical, serologic and radiologic signs of disease. Nevertheless revision surgery has to be expected more frequently compared to a normal collective of rhinoplasties [53]. The question whether cartilage or bone grafts are associated with equal outcomes has not been answered so far since outcome also depends several factors including stage and severity of the underlying disease.

In WG costal cartilage grafts were associated with a better transplant success rate (83%) compared with bone grafts (calvarial bone graft; transplant success rate 75%) [53]. However, Shipchandler and coworkers did not observe complications or resorption in four cases of WG and in one case of sarcoidosis associated saddle nose deformity treated by implantation of a split calvarial bone L-shaped strut [56]. Bone grafts were advocated because of greater availability and less resorption which, however, is not corroborated by the studies of Congdon and coworkers.

In general, infection and resorption is rarely observed following implantation of autologous cartilage [136], [137]. In addition, cartilage grafts display favourable biomechanical properties particularly if used in the tip area [138]. Although alloplastic materials are available in almost unlimited amounts, usage is associated with a high risk of infection and extrusion [139], [140], [141]. Therefore, autologous cartilage is the material of first choice in the reconstruction of saddle nose deformities [19], [134], [140], [142], [143]. According to the data presented in this review this statement seems to be valid for some systemic diseases as well [3], [18], [19], [53], [91].

In the case of nasal septal perforation caused by systemic diseases recommendations on closure of perforations are only theoretical due to missing clinical data. In general, nasal septal perforation occurs as complication following septal surgery, trauma or because of other factors [48], [132], [144], [145], [146], [147]. Aside from these factors systemic diseases can be associated with nasal septal perforation. In many cases series and reviews retrospectively analyzing the outcome of different techniques for closure of nasal septal perforation, included patients were always free of any systemic disease. According to such a selection of patients it can be assumed that active systemic disease is a contraindication for closure of nasal septal perforation.

Closure of asymptomatic nasal perforations is not indicated. In the case of active systemic disease that cannot be controlled implantation of a septal button is an alternative option [146], [148]. In the case of surgical closure the operation is only performed if the mucosa has been fully rehabilitated [132], [145].

Since implanation of autologous cartilage or bone grafts is also an important step in most multilayer techniques for closure of nasal septal perforation, experiences gained from reconstructive surgery of saddle nose deformities should be considered. It is essential to identify, eliminate or at least diminish the aetiological factor causing a nasal septal perforation [132], [144], [145]. Provided that there are optimal conditions the same surgical techniques that have been proven successful in the closure of iatrogenic or traumatic nasal septal perforations can be applied in systemic diseases. According to our personal concept surgical approach and technique are dependent on the localization and the size of a perforation (Figure 6). Small perforations (type A) can be closed by exchange of cartilage as demonstrated in HIV positive patient (Figure 2). Type B perforations can be closed using bipedicled gingivobuccal flaps (Figure 7). Larger perforations (type C) can be closed by cartilage implant and bilateral inferior turbinate flaps as demonstrated in a patient with WG in remission (Figure 4).

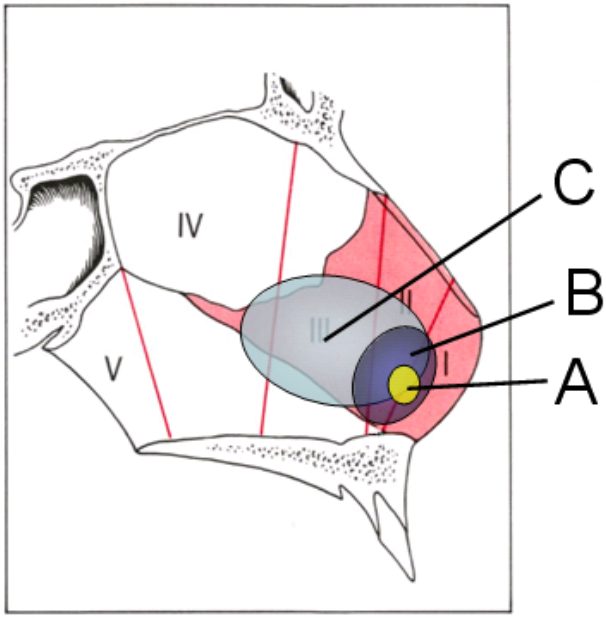

Figure 6: Graduation of nasal septal perforations. Type A: small perforation at the area I (<1 cm in diameter). Type B large perforation at the areas I and II (about 1–1.5 cm in diameter). Type C: Large perforation at the area II and III (>1.5 cm in diameter).

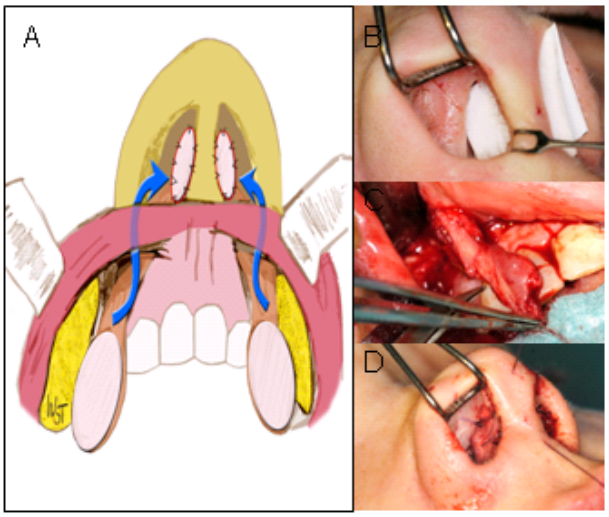

Figure 7: Large nasal septal perforation (type B). Demonstration of the perforation (A). Principle of mobilization of a gingivobuccal pedicled flap (B). Preparation of a gingivobuccal pedicled flap in vivo (C). Closure of the perforation by sutures (D).

In general, successful closure of nasal septal perforation has been observed if a multilayer technique was applied. These techniques have the following steps in common: a) extensive subperichondrial/periosteal dissection and mobilization of the nasal mucosa from the remaining septum, nasal floor and root, b) tension-free closure of mucosal borders, c) interposition of a connective tissue graft such as temporal muscle fascia, periosteum, cartilage grafts with perichondreum or a combination thereof [48], [144], [145], [146], [149], [150].

Overall, reconstruction of nasal deformities and closure of nasal septal perforation associated with systemic diseases has to be always decided in consideration of the type of the disease, severity of the disease, frequency of recurrences and prognosis. Ideally, patients should be in complete remission supported by excellent compliance and long-term medication.

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Corresponding author:
Florian Sachse
University of Münster, Department of Otorhinolaryngology Head and Neck Surgery, Kardinal von Galen Ring 10, 48149 Münster, Germany, phone: +49(0)251/83-56863, fax: +49(0)251/83-56812
sachsef@mednet.uni-muenster.de

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