L24. Local treatments of subglottic and tracheal stenoses in granulomatosis with polyangiitis (Wegener’s)

Stenoses of the respiratory tract from the larynx to the bronchi are severe and potentially life-threatening disease manifestations of granulomatosis with polyangiitis (Wegener’s) (GPA). The fundamentals are given in two recent reviews [1,2] with specific sections dedicated to subglottic stenosis (SGS) in vasculitis/GPA. However, the true nature of these stenosing conditions is obscure, hampering the therapeutic access to a cure.

Etiology

The subglottic area represents the junction of two embryological buds, but this does not readily explain the pathological process. The subglottic area is also the site for development of acute laryngitis in children (pseudo croup) usually caused by parainfluenza virus type 1. This would suggest a primary viral infection of this tissue as the initial event, but this has not been documented. Gastroesophageal reflux does not appear to be responsible for SGS [3] as originally proposed in 1985 [4].

Clinical presentation

There are two characteristic variants of SGS: the acute, initial and the late chronic. The acute, initial variant may involve the vocal folds causing hoarseness in addition to stridor (figure 1a). The macroscopic appearance is like the acute, initial lesion in the nose, responding within weeks to traditional corticosteroid treatment (figure 1b). The late chronic variant may be detected in relation to an exacerbation, but has probably been on its way for some time, as this variant appears to have its own life, usually being detected in patients without signs of vasculitic activity. This phenomenon has been referred to as “compartmentalized disease activity” [5]. The late chronic variant usually has a pale, smooth surface (figure 2a), starts 1 or 2 cms below the glottis and biopsies frequently only reveal small bits of scar tissue. This finding could be due to that the initial lesion may cause coughing but not hoarseness or stridor, whereas we observe the chronic fibrotic reaction weeks or months later when stridor brings the patient to our attention. As ¼ of patients with SGS also develop stenoses further down the trachea and the bronchial tree, stridor may not only reflect SGS.

SGS is seen more frequently in young women and has a widely variable course. A few patients only have one episode of SGS whereas another few may have relapses every second month.

Detection

In a recent cross-sectional, systematic study, we found 22% of 121 GPA patients to suffer from SGS, identified by flexible nasolaryngoscopy [6]. This prevalence is in the high end (not including small, selected series from ENT departments treating SGS [7]), probably reflecting that non-symptomatic patients and some patients with stridor/breathing difficulties are not identified as having SGS without sufficient visualization. Even so, flexible nasolaryngoscopy may not always yield a sufficient view of the trachea. Standard X-ray examination of the thorax may not be sufficient either, as the subglottic area may not be included – or the SGS may be misinterpreted to represent the glottis or vice versa. CT-scans – especially with reconstructions of the trachea and bronchi – are better suited but deliver...
radiation. Frequent MRI-scans – although currently still expensive – done routinely could solve the problem, detect additional tracheobronchial stenoses and explore the character and development of the SGS lesion using edema sensitive sequences [8].

**Local treatments**

Recognizing that SGS frequently develops despite optimal systemic therapy and/or while the disease appears to be in remission, several local treatments have evolved over time. When comparing results of various treatment modalities, it must be considered that SGS is relatively rare yielding small study populations and that differences in the composition of the patient materials regarding acute versus chronic lesions, no scarring from previous procedures versus established scarring and frequently versus infrequently relapsing patients are decisive for the results.

**Figure 1**
a: acute, initial subglottic stenosis in a young female before treatment; b: same patient after 3 weeks of treatment with oral corticosteroids, inhaled corticosteroids and methotrexate

**Figure 2**
a: late, chronic subglottic stenosis in middle aged male before treatment; b: same patient after dilatation with laser tracheoscope for 15 minutes (without laser treatment), peroperative methylprednisolone bolus and postoperative inhaled corticosteroids
Trachéostomie

Ce traitement, impliquant une condition permanente avec une trachéostomie de silicium ou de matériau artificiel pour assurer l’ouverture de la trachéostomie, était la solution simple au problème pendant les années 1980 [9]. Il peut être relevant pour les situations d’urgence et pour les cas rares avec destruction sévère de la larynx et/ou de la trachée garantissant un airway, mais avec la description du bénéfice de l’effet de l’intratrachéale dilatation et de l’utilisation de mitomycine-C injection en 1996 [10], les trachéostomies ont été closes et ne plus considérées comme un problème important.

Dilatation/dilatation

Tous les types de procédures ont été utilisés – principalement avec plus ou moins la même réponse favorable. La procédure original décrite [10,11] utilisait la dilatation sérielle avec un bougie dilatateur et cette procédure est encore utilisée avec succès [12]. Cependant, comme ces dilatateurs sont solid, cette procédure nécessite une interruption de l’apnée. On peut l’éviter en utilisant un laser trachéoscope avec un diamètre augmentant légèrement à la pointe. En pénétrant la trachéoscope dans le SGS, il est dilaté, et le patient peut être ventilé pendant les 15 minutes, le trachéoscope est en place. Cette procédure permet également l’utilisation additionnelle de CO2-laser dilatation si désiré [12]. Le trachéoscope dilatation processus a été amélioré par le développement du Groningen Dilation Trachéoscope [13,14], qui apparaît comme plus effectif que la bougie dilatation. La dilatation peut également être effectuée en utilisant un ballon comme le Fogarty cathéter ballon [11]. Cette procédure également permet l’interruption de l’apnée quand elle est utilisée dans la trachéa. Avec la technologie évolutrice de ballon dilatation, ce traitement alterner plus attrayant, en particulier en cas de lesions plus sévères avec l'utilisation additionnelle de trachéobronchial sténoses [15–17]. Cependant, en opposition au SGS, où la larynx cartilage fournit un cadre pour maintenir l’espace glottique, la trachéa et les bronches seulement ont un cartilage semi-circulaire cartilage support, et si ces cartilages sont endommagés, la dilatation ne sera pas suffisante dans une perspective plus longue [15]. Dans de tels cas, stenting ou reconstruction chirurgicale seront requis.

Stenting

Pour le colaps de la trachée, un T-tube de silicone est approprié, comme cela peut être toléré au trachéostoma pathological, et possible crusts or viscous secretions can be removed through the part of the tube passing from the trachea through the skin just below the larynx. This “tissue” tube is usually closed by a simple silicone cork, permitting the patient to breathe normally through the mouth and speak without having manually to close the “tissue”, as it is frequently necessary if a standard trachéostomy tube is used. In some cases with distal tracheal stenoses and/or additional bronchial stenoses, stenting using the fast developing technologies applied for vascular stenting have gained access to the airways. With the advent of highly flexible and removable stents, prior problems of stenting with formation of granulation tissue, displacement and perforating of the airway wall [18] are presumably diminished.

Surgical reconstruction

Cela suit les principes pour dire que la post-intubation trachéale sténose inclut des resections du sténose et end-to-end anastomosis of the trachea [19]. En opposition au post-intubation related lesions, SGS in GPA patients may still relapse, which will eventually limit the possibility to perform further resections of the trachea.

Laser treatment

Avant l’introduction de la dilatation, lasers – principalement CO2-lasers – étaient utilisés pour retirer les sténoses avec des résultats variables [20,21]. Un motif important pour les résultats moins favorables est que le laser évaporation/tissue excision laisse un open wound. Circumferential lesions like most SGS will therefore tend to re-stenose and even progress as they heal, unless microflaps are raised to cover the wounds as originally [22] and recently [23] described. The open wound problem may to some extent be prevented by only performing radial incisions, which may be effective for short, shell-like stenoses, but with larger stenoses a combination with dilatation is required. The radial incisions, however, can also be performed with microlaryngeal scissors or knives as originally described [11,12].

Intralesional corticosteroid injection

Ce traitement a été introduit pour combattre le mal sur le site, en particulier la maladie post-intubation apparaissait inefficace [10]. L’injection intralesionnelle qui suit la dilatation est indiquée pour prévenir la cicatrisation et la récidive. Elle est fréquemment – en particulier dans la chronic type – difficile à injecter de manière efficace dans le sténose tissu et le matériel peut le mieux sortir que décrit primitivement [10]. Un alternative is postoperative inhalation of glucocorticoids for a month (like in severe asthma) as the inhalation procedure may result in subglottic deposition of clobetasol due to turbulence. In both cases, the local treatment is supported by systemic bolus methylprednisolone injections at the operation. The effect of local glucocorticoid treatment may therefore be limited et it was not found to be effective in one study [24].

Mitomycin-C

Le même résultat [24], cependant, a trouvé un effet significatif de l’utilisation de mitomycine-C, supporté par un essai clinique randomisé prouvant que deux applications de mitomycine-C est meilleure que une application sur une 2-year basis, mais est non effectif sur a 5-year basis [25]. Animal studies on the other hand find application of mitomycin-C to be potentially dangerous due to crust formation [26] which has also recently been reported in patients where no positive effect of mitomycin-C was observed [17]. As stated in the reviews [1,2], the role of mitomycin-C is therefore still open for discussion.

Monitoration

En ordre évaluer les résultats du traitement local, il a été difficile de définir la meilleure réponse pâtente due to the wide
variability in relapse rate. So far, the number of required interventions over a given time and the corresponding intervals between treatments have been used. Video laryngoscopy, as illustrated in figures 1 and 2, is well suited to document treatment effect, and imaging – especially 3D reconstructions – yields precise spatial information. Other options are the use of serial peak-flow measurements, which can be performed frequently by the patients [13], or the use of flow-volume curves [21] or other pulmonary functional tests [15].

Conclusion

This review describes the many local treatment modalities and combinations of these. Due to the usually small and selected patient populations, the results may be difficult to compare. However, most authors, irrespective of treatment modality, find an average of three interventions per patient to be necessary. This calls for multi-center randomized clinical trials based on harmonized criteria for diagnosis, type of SGS and monitoring of treatment results in order to substantiate the effect of any single treatment modality and improve the outcome of local treatment.

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References


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