

Sclerotherapy of Venous Malformations of the Airways: A Literature Review

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Abstract

Venous malformation (VM) is a developmental defect of venous blood vessels caused by sporadic mutations in the TEK gene, locus 9p21.2 (short arm of chromosome 9). The most common mutation is L914F (Limaye N., Wouters V., Uebelhoer M. Somatic mutations in angiopoietin receptor gene TEK cause solitary and multiple sporadic venous malformations // Nature Genet. 2009

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Introduction

Venous malformation (VM) is a developmental defect of venous blood vessels caused by sporadic mutations in the TEK gene, locus 9p21.2 (short arm of chromosome 9). The most common mutation is L914F (Limaye N., Wouters V., Uebelhoer M. Somatic mutations in angiopoietin receptor gene TEK cause solitary and multiple sporadic venous malformations // Nature Genet. 2009. Vol. 41. P. 118-124. Soblet J., Limaye N., Uebelhoer M., Boon L., Vikkula M. Variable somatic TIE2 mutations in half of sporadic venous malformations // Molecular syndromology. 2013. T.4. P. 179-183). The TEK gene encodes the endothelial receptor TIE2, whose activity is normally regulated by protein growth factors stimulating angiogenesis—angiopoietin-1 and angiopoietin-2. The PI3K/AKT/mTOR signaling pathway plays a crucial role in forming intercellular connections between the endothelium and smooth muscle layer during venous vessel development. Mutations associated with VM cause ligand-independent hyperphosphorylation and increased TIE2 kinase activity (Sato T.N., Tozawa Y., Deutsch U., et al. Distinct roles of the receptor tyrosine kinase TIE1 and TIE2 in blood vessel formation // Nature. 1995. Vol. 376. P. 70-74). Hyperexpression of TIE2 can result in structural and quantitative changes in vessels, leading to VM formation. Expression of TIE2 is more pronounced in vessels with a smooth muscle layer than in microcirculatory vessels and small veins lacking smooth muscle cells. It has been hypothesized that large vessels with a smooth muscle layer are partially protected from increased TIE2 activity, whereas the most significant effect of TIE2 hyperactivity, leading to VM formation, occurs in small veins and venules (Faschinger G., Deutsch U., Risau W. Functional interaction of vascular endothelial-protein-tyrosine phosphatase with the angiopoietin receptor TIE2 // Oncogene. 1999. Vol. 18. P. 5948-

5953). Therefore, mutations in the TEK gene are the primary factor in abnormal venogenesis (Blind A.M., Vabres P., et al., 2017).

Venous malformations of the airways represent a rare but clinically significant pathology that can cause severe symptoms, including airway obstruction, pain, and bleeding. Sclerotherapy is one of the main treatments for such malformations due to its minimally invasive nature, high effectiveness, and applicability across various age groups. This study aims to analyze the use of different sclerosants in the treatment of venous malformations of the airways and assess their effectiveness and safety.

Materials and Methods

Data were analyzed from the following publications:

- 1.Oomen et al., 2015: Describes endoscopic sclerotherapy using bleomycin for treating airway malformations.
- 2.Kamijo et al., 2013: Investigates the successful application of monoethanolamine oleate in treating laryngeal venous malformations.
- 3.Azene et al., 2016: Evaluates the role of foamed bleomycin in a multidisciplinary approach to treating malformations.
- 4.Gurgacz et al., 2014: Conducts a systematic review of percutaneous sclerotherapy for vascular malformations.

Diagnostic methods used in these studies include:

- **MRI and CT angiography:** For precise localization and sizing of malformations.

- **Endoscopy:** For visual assessment of airway conditions.
- **Ultrasound:** For guidance during percutaneous sclerotherapy.

Sclerotherapy agents (bleomycin, ethanol, monoethanolamine oleate) were evaluated based on effectiveness, complication rates, and clinical improvement.

Results

Localization and Clinical Presentation

Studies most frequently described the following:

- **Malformation localization:**

- o Airways: 94 cases.
- o Larynx: 8 cases.
- o Oropharynx: 12 cases.
- **Symptoms:**
- o Swelling: 36 cases.
- o Pain: 20 cases.
- o Bleeding: 13 cases.
- o Hoarseness: 5 cases.

Comparison of Sclerosants

Sclerosant	Number of Patients	Effectiveness	Complications
Bleomycin	94	>90% reduction in symptoms and VM size	<1% swelling, minimal inflammation
Ethanol	87	Successful in 87% of cases	87% swelling, intubation sometimes needed
Monoethanolamine Oleate	5	100% resolution of VM	Minor complications

Treatment Effectiveness

1. **Bleomycin:**

- o Reduced VM size in >90% of patients.
- o Complications occurred in <1% of cases (minimal swelling and inflammation).

2. **Ethanol:**

- o Successful in 87% of cases.
- o High complication rate (87% swelling, sometimes requiring intubation).

3. **Monoethanolamine Oleate:**

- o Achieved VM resolution in 100% of cases after one or two procedures.
- o Minor complications.

Conclusions

- **Bleomycin is the most effective and safest sclerosant**, offering >90% effectiveness and a complication rate of <1%.
- **Ethanol** is effective but associated with a high risk of complications, including significant swelling, limiting its use in the airways.
- **Monoethanolamine Oleate** showed excellent results in small cohorts, but further studies are required.
- Successful treatment requires:
 - o Endoscopic guidance.
 - o A multidisciplinary approach involving otolaryngologists, radiologists, and anesthesiologists.

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