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Commentary on "Doxycycline Sclerotherapy of Head and Neck Lymphatic Malformations: Intermediate Report of 27 Cases"

Anne Marie Cahill[1]

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Introduction

There are two standard methods of treating macrocystic lymphatic malformations, direct injection and multiday catheter-based therapy. "Macrocystic" has been defined as cysts greater than 1 cm although this varies among providers and practices. For practical purposes, cysts that are large enough to accommodate a pigtail catheter are best suited to catheter-based therapies. To date has been no randomized controlled trials comparing catheter-based and direct injection techniques in terms of outcomes. It would seem intuitive that aggressive upfront catheter-based therapies, using multiple catheters if necessary, would be more efficacious in the short term than direct injection. On the flip side, catheter-based techniques have the following disadvantages: potential need for prolonged intubation for airway protection, multiday painful sclerosant dwell and a longer hospital stay. It is not known if the repeated exposure of macrocysts to sclerosant is more damaging to the endothelium than direct single-day injection. In addition, the sclerosant choice is again very provider dependent and includes mainly doxycycline, sodium tetradecyl foam, ethanol, OK432 or a combination of same [1].

The authors describe their experience with direct injection of doxycycline in a series of 27 patients all defined as macrocystic lymphatic malformations in a mostly pediatric age cohort.

The authors reported a mean number of procedures of 4, with a range of 1–23 and a volume reduction of approximately 50% [2]. In general, macrocystic lesions respond better to sclerotherapy using any sclerosant agent, than either the mixed or microcystic disease type, with reported rates of 76–100% response [3–6].

Symptomatic improvement or complete relief was noted in 85%, but in many of the cases reported, I note the indication was the presence of a neck lesion, and the outcome an esthetic result. This indication is not to be diminished in children, as the presence of a conspicuous neck mass can lead to significant psychosocial issues particularly in the school-aged child. These lesions can also be vexing in that they can swell in response to head and neck infection, get superinfected and undergo intra-cyst hemorrhage with minor trauma, all indications for pre-emptive intervention.

It is important to highlight that in this cohort several lesions were diagnosed at birth but not treated at this time. It is common practice to observe these lesions in the newborn period if asymptomatic, to obviate exposure to general anesthesia and potential neurodevelopmental changes in the first 6 months of life. It is important to determine the timing of intervention with the goals of therapy.

The follow-up period ranged from 6 to 78 months, as it is in many published series, but these lesions are very hormone-responsive and tend to recur again to some degree in puberty when treated in the pre-pubertal period. This hormone response is noted in 3 patients in this series, who

✉ Anne Marie Cahill
cahill@chop.edu

[1] Children's Hospital of Philadelphia, Perelman School of Medicine, University of Pennsylvania, 3401 Civic Center Boulevard, Philadelphia, PA 19104, USA

presented with isolated pubertal lesional conspicuity. Expectations of potential pubertal recurrence are important to communicate to families.

Doxycycline levels were not reported by the authors in their small neonatal and infant cohort. I highlight this because hypoglycemia and metabolic acidosis have been reported in this population, recommending a maximum dose of 250–300 mg per instillation, with preliminary data reporting high systemic absorptive concentrations of doxycycline post-instillation. This has not been validated by other studies to date, but doxycycline dose limits are practiced [4, 5].

As stated prior, there are many different sclerosants reported in the literature, with varying outcomes for lymphatic malformations. A meta-analysis of these agents in over 700 patients reported the best outcomes occurring with macrocystic lymphatic malformations and the use of doxycycline [1].

It is also incumbent upon us to consider the adjunctive use of medical therapies such as the mTOR inhibitor Sirolimus and more recently Alpelisib, targeting the PIK3CA mutation, a somatic mutation associated with overgrowth and lymphatic malformations. These targeted therapies may work synergistically with sclerotherapy to affect a greater response especially in mixed lesions and those that have airway compromise [7].

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Declarations

Conflict of interest The author declares that there is no conflict of interest.

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