Efficacy of Direct Ethanol Sclerotherapy in Management of Low Flow Congenital Vascular Malformations

Thesis submitted for partial fulfillment of
MD degree in Vascular Surgery

By
Mohammed Hassan Aly Abou Mansour

M.B.B.Ch, M.sc, of General Surgery

Supervised by

Prof. Dr. Mostafa Soliman Mahmoud

Professor of General and Vascular Surgery
Faculty of medicine - Ain Shams University

Prof. Dr. Tarek Mohammed Radwan

Professor of Vascular Surgery
Military medical academy

Dr. Nader Mohammed Mohammed Hamada

Lecturer of Vascular Surgery
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2019

Acknowledgment

*Before all and above all thanks to **ALLAH,** for without his blessing, this work would have never been accomplished.*

*I would like to express my deepest and most sincere thanks and gratitude to **Prof. Dr. Mostafa Soliman Mahmoud,** professor of Vascular Surgery Faculty of Medicine –Ain Shams University for his valuable assistance and support.*

*I am most obliged to **Prof. Dr. Tarek Mohammed Radwan,** professor of vascular surgery, military medical academy, for generous and most helpful contribution, advices, and for his marvelous support.*

*To **Dr. Nader Mohammed Hamada**, lecturer of vascular surgery, Faculty of Medicine –Ain Shams University, I would like to thank you for your generous and nonstop contribution.*

*Thanks to **prof. Dr. Wayne Yakes**, who I learned so much from him about vascular anomalies.*

*To **my all family & to my friend Dr. Abd Elwahab Hashem**, for their support and effort and their endless nonstop help through the whole way, I ask Allah, to give them what they wish.*

*To the **patients with vascular anomalies**, their families, and colleagues who participate in the care of and research in this field.*

Mohammed Abou Mansour

List of Contents

List of Abbreviations

AM	Arterial malformation
AVM	Arterio-venous malformation
AVF	Arterio-venous fistula
BCMSP	Bogota Congenital Malformations Surveillance program
CBC	Complete blood count
CLVM	Cappilary lymphatico-venous malformation
CM	Cappillary malformation
CT	Computed tomography
CVM	Congenital vascular malformation
dceMRI	Dynamic contrast enhanced MRI
DIC	Disseminated intravascular coagulopathy
DMSO	Dimethyl sulfoxide
DUS	Duplex ultrasound
EUROCAT	European Surveillance of Congenital Anomalies
EVOH	Ethylene vinyl alcohol
FR	French
GLOVES	Congenital lipomatous overgrowth with vascular, epidermal and skeletal anomalies
HLM	Hemolymphatic malformation
IBCA	Isobutyl 2-cyanoacrylate
ICU	Intensive care unit
IMC	International Medical Center
INR	International normalized ratio
IPEH	Intra vascular papillary endothelial hyperplasia
ISSVA	International Society for the Study of Vascular Anomalies
KTS	Klippel-Trenaunay syndrome
LIC	localized intravascular coagulation
LM	Lymphatic malformation
MRI	Magnetic resonance imaging
mTOR	mammalian target of rapamycin
NBCA	N-butyl cyanoacrylate
NSAID	Non-steroidal anti-inflammatory agents
PAP	Pulmonary artery pressure
PKB	Protein kinase B
POL	Polidocanol
PT	Prothrombin time

PTT	Patial thromboplastin time
PVA	Polyvinyl alcohol particles
RBCs	Red blood cells
SD	Standard deviation
SPECT	Single-photon emission computed tomography
STIR	Short-tau inversion recovery
STS	Sodium tetradecyl sulfate
TALPS	Trans arterial lung perfusion scintigraphy
TIE2	tyrosine-protein kinase receptor
VAR	Veno-arteriolar reflex
VM	Venous malformation
WBBPS	Whole-body blood pool scan

List of Figures

List of Tables

Abstract

Background: Congenital vascular malformations (CVMs) may contain venous, capillary, lymphatic, or arterial components in any combination and have been associated with various dysmorphic syndromes. CVMs appear at birth, persist through life and have slowly progressive course and some of them may be temporary hidden due to their deep location.

Aim of the Work: to evaluate the efficacy of ethanol sclerotherapy in management of low flow congenital vascular malformations and to report any possible adverse events related to this modality of treatment.

Patients and Methods: This case series prospective study was conducted on 40 patients having low flow CVMs at the department of Vascular Surgery at the International Medical Center (IMC), Cairo Egypt, during the period from April 2017 to April 2019.

Results: all patients showed good response as regard clinical improvement which was represented in patient's satisfaction, as 87.5% were satisfied and 12.5% were very satisfied. All patients showed good radiological response which was obvious in comparison of pre and post procedure MRI, as 5% were completely cured and 95% were markedly improved. All patients had no major complications, but 42.5% of patients had one or more minor complications which were subsided spontaneously or with nominal therapy without consequences or hospital admission.

Conclusion: Ethanol sclerotherapy is highly efficient method in treatment of low flow CVMs, but accompanied with many local complications which could be minimized when management was done by multidisciplinary team.

Key words: Ethanol Sclerotherapy, Low flow congenital vascular malformations

Introduction

The blood vascular system develops in two distinct, consecutive stages vasculogenesis & angiogenesis both of them are regulated by biomechanical factors. When any defect is happened to them, it will lead to vascular malformations. When defective development occurs in the early stage of embryonic development, it will produce an extra truncular malformation, but if it happens in later stage it will produce a truncular malformation **(Lee, 2008)**.

Congenital vascular malformations (CVMs) may contain venous, capillary, lymphatic, or arterial components in any combination and have been associated with various dysmorphic syndromes. CVMs appear at birth, persist through life and have slowly progressive course and some of them may be temporary hidden due to their deep location **(North PE, 2010).**

The incidence and prevalence of the CVMs were confused through the previous decades due to so much confusing definitions and classifications, the extra truncular venous malformation (VM) is the most frequent type of CVMs **(Mattassi R, et al., 2015).**

Difference between hemangioma and CVM according to previous several classifications was not clear until Judah Volkman in 1982 demonstrated that hemangioma is a lesion that has endothelial hyperplasia while CVMs have normal endothelial. 'Biological' classification divided CVMs into high-flow and low-flow lesions according to hemodynamics adding syndromes of complex cases in a group of combined complex defects. Stevan Belov in 1988 proposed 'Hamburg' classification influenced by 'Biological' classification based on morphology as well but adding more criteria. He divided CVMs into 'truncular' group which are defects related to main vessels and 'extratruncular' group which are peripheral defects that could be present into diffuse and infiltrating forms of the single type **(Mattassi R, et al., 2015).**

The International Society for the Study of Vascular Anomalies (ISSVA) published 'ISSVA' classification in 1996. Several updates were published in the last years and the most recent one -Updated ISSVA- was published in 2018 adding several subgroups to include all new discoveries **(Adams and Ricci, 2019)**.

Low flow CVMs are extremely variable in type, site, extension and secondary effects so, their diagnosis should be done by multi-disciplinary team, taking detailed history, making good clinical examinations and doing necessary images under standard protocols via radiologists who have good experience about CVMs **(Lee BB, et al., 2014).**

Unfortunately there are no widely used standard methods or protocols in treatment of CVMs. There are so many different methods in treatment of CVMs; either surgical, endo-venous laser ablation, sclerotherapy using different substances or conservative treatment according to personal experience and facilities **(Lee BB, et al., 2014).**

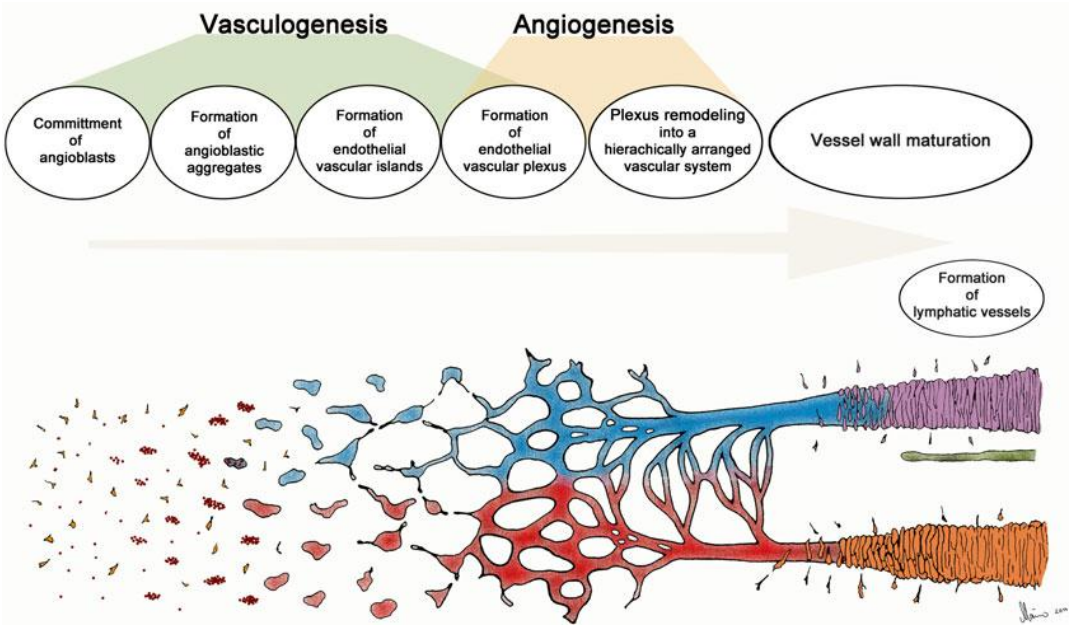
Occlusion of vessels could be achieved by injecting different substances in the vessels like ethanol, bleomycin, particles, coils, glue and others. Ethanol is an excellent sclerotherapy agent for all varieties of the extratruncular CVMs. In experienced hands ethanol sclerotherapy is associated with minimum morbidity. Patients injected with ethanol require close perioperative monitoring to manage its adverse events. The most of ethanol sclerotherapy complications could be managed by conservative measures **(Lee et al., 2003, Mendonca et al., 2010)**

Aim of the work

The aim of this study is to evaluate the efficacy of ethanol sclerotherapy in management of low flow congenital vascular malformations and to report any possible adverse events related to this modality of treatment.

CVMs embryology & genetic aspect

The blood vascular system develops in two, consecutive stages (Fig. 1): firstly (vasculogenesis) differentiation of blood vessels from mesoderm-derived precursor cells, and secondary (angiogenesis) the remodeling of vessels to form arteries and veins **(Flamme et al., 1997)**.



(Fig. 1) Vascular system development **(Xu, K. & Cleaver, O. 2011)**

Vasculogenesis first occurs in the yolk sac. Structures called blood islands form as hemangioblasts differentiate into endothelial and red blood cells. The endothelial cells

migrate from the blood islands and form a random vascular network called the capillary plexus. Meanwhile, the dorsal aorta forms inside the embryo; eventually, it connects the heart to the capillary plexus of the yolk sac thus completing the circulation loop **(Suami and Lee, 2017)**.

Angiogenesis begins after three gestational weeks, when the heart begins to beat and blood starts circulating in the capillary plexus. Biomechanical and hemodynamic input induces active vascular remodeling. The capillary plexus is remodeled into a functional structure that includes large-caliber vessels for low-resistance rapid flow and small-caliber capillaries for diffusional flow. This remodeling occurs by the regression, sprouting, splitting, or fusion of preexisting vessels. Endothelial cells in the capillary plexus differentiate into cells with arterial and venous natures **(Suami and Lee, 2017)**. Specification is believed to be related to expression of Efrin B2 in arterial and Ephrin type b receptor 2 (EphB2) in venous endothelium. Lymphatic channels are formed from veins at the six or the seventh gestational week **(Maclellan et al., 2014)**.

Biomechanics and fluid dynamics regulate angiogenesis. Through embryogenesis, high local blood flow produces enlargement of vessel diameters, whereas low blood flow