

بسم الله الرحمن الرحيم



HOSSAM MAGHRABY



شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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Evaluation of the Use of Sirolimus in Treatment of
Complex Vascular Malformation and Tissue Overgrowth
Syndromes

Thesis

*For Partial Fulfilment of MD Degree
in Pediatric Surgery*

BY

Mohamed Aly Abdelhamid Abdelbaky

M.Sc., M.B, B.CH. Ain Shams University

Under Supervision of

Dr. Hatem Abdelkader Saafan

*Professor of Pediatric Surgery Department
Faculty of Medicine – Ain Shams University*

Dr. Iman Ahmed Ragab

*Professor of Pediatrics Department (Hematology and
Oncology)*

Faculty of Medicine – Ain Shams University

Dr. Amr Abdelhamid Zaky

*Professor of Pediatric Surgery Department
Faculty of Medicine – Ain Shams University*

Dr. Mohammed Said Elsherbeny

*Assistant Professor of Pediatric Surgery Department
Faculty of Medicine – Ain Shams University*

Dr. Mohamed Moussa Dahab

*Assistant Professor of Pediatric Surgery Department
Faculty of Medicine – Ain Shams University*

Faculty of Medicine
Ain Shams University

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
<i>Avf</i>	<i>Arteriovenous Fistula</i>
<i>AVM</i>	<i>Arteriovenous Malformation</i>
<i>AVMs</i>	<i>Arteriovenous Malformations</i>
<i>BRBNS</i>	<i>blue rubber bleb nevus syndrome</i>
<i>CH</i>	<i>Congenital hemangioma</i>
<i>CLOVES</i>	<i>congenital lipomatous overgrowth with vascular, epidermal, and skeletal anomalies</i>
<i>CLM</i>	<i>Capillary Lymphatic Malformation</i>
<i>CM</i>	<i>Capillary Malformation</i>
<i>CT</i>	<i>Computed Tomography</i>
<i>CTA</i>	<i>Computed Tomographic Angiography</i>
<i>CVM</i>	<i>Congenital Vascular Malformation</i>
<i>CVMs</i>	<i>Congenital Vascular Malformations</i>
<i>DIC</i>	<i>Disseminated intravascular coagulopathy</i>
<i>ISSVA</i>	<i>International society for the study of vascular anomalies</i>
<i>KHE</i>	<i>Kaposiform hemangioendothelioma</i>
<i>KTS</i>	<i>Klippel-trenaunay syndrome</i>
<i>LFVM</i>	<i>Low-flow vascular malformations</i>
<i>LIC</i>	<i>Local intravascular coagulation</i>
<i>LM</i>	<i>Lymphatic malformation</i>
<i>LMWH</i>	<i>Low molecular weight heparin</i>
<i>MRA</i>	<i>Magnetic resonance angiography</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>mTOR</i>	<i>Mammalian target of rapamycin</i>
<i>NGS</i>	<i>Next-generation sequencing</i>
<i>NICH</i>	<i>Non-involuting congenital hemangioma</i>
<i>PICH</i>	<i>Partially involuting congenital hemangioma</i>
<i>PI3K</i>	<i>Phosphatidylinositol 3 kinase</i>
<i>PedsQL</i>	<i>Pediatric quality of life</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>PWS</i>	<i>Parkes-weber syndrome</i>
<i>RICH</i>	<i>Rapidly involuting congenital hemangioma</i>
<i>SCORAD Index</i> ...	<i>(‘Severity Scoring of Atopic Dermatitis: The SCORAD Index’, 1993)</i>
<i>US</i>	<i>Ultrasound</i>
<i>VA</i>	<i>Vascular anomaly</i>
<i>VEGF</i>	<i>Vascular endothelial growth factor</i>
<i>VM</i>	<i>Venous malformation</i>

Abstract

BACKGROUND AND OBJECTIVES: Management of complex vascular malformations and overgrowth syndromes is challenging. They usually present at birth and have different complications including bleeding, pain, cosmetic disfigurement and functional impairment. This study was done to determine symptomatic relief and quality of life improvement after sirolimus.

METHODS: The intervention phase included sirolimus administered orally on a continuous dosing schedule at a starting dose of 0.8 mg/m², and its level to be maintained between 4-12 ng/ml. Dose was rounded to the nearest 1mg tablet form.

Assessment of response to sirolimus was done (usually 2 weeks after start of sirolimus) clinically by assessment of clinical improvement of the main complaint of the patient e.g. bleeding, pain, cosmetic disfigurement. Laboratory Improvement of patients labs after start of sirolimus e.g elevation of hemoglobin and Mean cell volume. Arabic translation of pediatric quality of life PedsQL 4.0 was done again 6 months after start of sirolimus. Assessment of safety of sirolimus was done clinically by surveillance for incidence of any complications e.g chest infections, diarrhoea, mucositis. and laboratory assessment after 2 weeks and after every 6 months including blood picture, liver function test (Alanine transferase) , kidney function test (creatinine), fasting lipid profile :cholesterol and triglycerides and sirolimus trough level.

RESULTS: 33patients were enrolled, Age of the patient during start of sirolimus ranged from 5 months to 13 years with median age 3 years. Bleeding stopped in 15 patients (93.8%), cosmetic Disfigurement improved in 21 patients (80%) and perception of pain improved in 8 patients (72.7%). Also, mean pediatric quality of life score rose from 65.18 to 78 after sirolimus. 10 (30%)patients had adverse effects from sirolimus including infections 15.2% ,mucositis 12.1% and diarrhea 1%.

CONCLUSIONS: Patients with complex vascular malformation require multidisciplinary team for diagnosis and management. Symptomatic relief in patients after sirolimus is evident with better quality of life.

KEYWORDS: Sirolimus _Vascular malformation_ Overgrowth syndromes