“VICTOR BABES” UNIVERSITY OF MEDICINE AND PHARMACY TIMIȘOARA
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DOCTORAL THESIS

IMAGING DIAGNOSIS, INTERVENTIONAL THERAPEUTICS AND POST-THERAPY MONITORING OF VASCULAR ANOMALIES AT CHILDREN. CLINICAL, HISTOPATHOLOGICAL AND IMAGING CORRELATIONS.

- SYNOPSIS -

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Key words: vascular anomalies, hemangioma, MRI, ultrasound

INTRODUCTION

Vascular anomalies are not only a medical problem, but also an aesthetic one, with the patient developing subsequent psychological sequelae, along with adaptation gaps in society. Vascular anomalies represented by vascular birthmarks were encountered in many famous figures. In 460 B.C., the first vascular anomaly was described: an arterial aneurysm discovered by Hippocrates.

In 1990, during the Amsterdam congress, the foundation was laid for a scientific society covering vascular anomalies. The society itself was established in Denver in 1992 under the name of the International Society for The Study of Vascular Anomalies (ISSVA), and, including at present, its members meet every every 2 years

Vascular anomalies are a problem for parents, doctors and, last but not least, for the patient. Sometimes they can be aggressive by expanding. Hemangiomas are distinct tumors from vascular malformations. The aesthetic aspect is an issue with regard to the integration into society and the development of the individual. Treatments are continuously under research and current interventional procedures may be an alternative in some cases.

The first therapy approached for hemangiomas is with propranolol, but the response of the lesions may vary. There is no standard treatment. The monitoring of the treatment is clinical but also by imaging; therefore, the degree of vascularization of the lesion and its reversion can be assessed.

Imaging methods have also evolved. For diagnosis, the range of investigations is nowadays wider and new clinical methods and techniques are constantly being developed.

Recent data support the histopathological classification of hemangiomas. However, because the molecular classification is non-existent, targeted therapies have not been established.

Tumor vascular abnormalities, especially deep hemangiomas that occur late and which cannot be classified as a diagnosis from a clinical point of view, are a challenge for the radiologist. Choosing the best method for differential diagnosis is difficult, given that the aim is to avoid unnecessary biopsies and the exposure to other invasive diagnostic methods. Confusions in the diagnosis of hemangiomas occur because of the complexity of vascular abnormalities and of their intricacy. In this study, the classification of vascular abnormalities based on clinical, histological and cytological features has been adopted.

The special part contains a statistical analysis of vascular abnormalities over a period of 5 years, but also an analysis based on imaging examinations; in Part Two, we have also conducted an experimental study.

PATIENTS, MATERIAL ȘI METHODS

The study was carried out at The Clinical Emergency Hospital for children “Louis Turcanu”, which serves the Western part of Romania. The study was conducted between 2014-2018 and included 214 patients between one day and 18 years of age, patients who were diagnosed with vascular deficiencies. The first intention examination used for all patients was the ultrasound. The CT investigation was carried out in 18 cases and the MRI was carried out for 57 patients.

Imaging techniques have made a selection of the cases, in some cases conservative treatment and monitoring have been chosen, while others have required biotechnology and complex therapeutic techniques, as well as subsequent imaging monitoring.

Pediatric imaging has unique challenges that are not met in adult examinations. The need for sedation in small children requires a comprehensive and succinct CT and MRI investigating protocol. Additional challenges for pediatric patients include their small size, low signal and inherently low scan resolution. In view of the above, I believe that a suitable algorithm is required for both diagnosis and monitoring, in which to take account of the pathology, the patient's age, and which should contain protocols adapted for the diagnosis and a characterization as comprehensive as possible without prolonging the examination time and, implicitly, the sedation time.

Ultrasound, CT and MRI exams have been included in the diagnostic algorithm of such formations. All the patients included in the study have been subjected to ultrasound, it being a non-invasive method, fast and not expensive. During the ultrasound examination, we have followed the structure of the lesions, the type of vascularization and we have determined the location with respect to superficial or deep planes. In addition, we were able to differentiate lesions with a solid structure from those with a cystic structure.

For trans-spatial lesions, top-of-the-range imaging examinations have been performed. CT investigations provided details about bone structures, calcifications and angiographic details, but a major disadvantage of this method is irradiation and we have tried to select another method, whenever it was possible. MRI is the most sensitive method for the characterization of soft tissues, allowing for a true and fair characterization of these tissues.

The diffusion technique and the calculation of the ADC values allowed for the differentiation of benign and malignant lesions in the research performed.

CONCLUSIONS

The sex ratio (F:M) of vascular abnormalities was in favor of the female sex, it being comparable to the literature data.

The age of presentation at the specialist doctor was less than 1 year in most cases, with a maximum around 6 months, corresponding to the proliferation of child hemangiomas when such tumors exhibit accelerated growth and start alarming parents.

The therapeutic options applied were surgery, medication and interventional in two cases.

The small percentage of patients from rural areas shows poor medical education in this population segment.

Vascular anomalies require a multidisciplinary approach (pediatric surgeon, dermatologist, radiologist, oncologist, anatomical pathologist).

A wide variety of vascular anomalies, including complex syndromes, has been found in the study.

Vascular anomalies are a cosmetic problem leading to psychosocial sequelae of the future adult.

Subcutaneous and deep hemangiomas require imaging in order to differentiate from malignant tumors.

Superficial hemangiomas with clinical atypical presentation require imaging scans.

All hemangiomas leave fibrous scars of tissue after involution.

Infant hemangiomas do not show calcifications, only congenital hemangiomas can.

Hemangiomas have both arterial and venous flow.

Lymphatic anomalies are prone to infiltration and do not respect borders.

Venous anomalies do not produce skin differences and can mimic tumors. They may be frequently associated with calcifications.

Ultrasound is a good method for the diagnosis and monitoring, but is sometimes not sufficient, with limitations in viewing deep planes; it is the method of first intention exploration in most cases of vascular malformations and tumors, but it is limited in cases of far-reaching structures (orbit, brain).

MRI has become the method of choice for the examination of tumors of soft tissues due to its multiplane capacity, to its lack of ionizing radiation and to its contrast between tissues.

The calculus of the apparent coefficient of diffusion plays an important role in differentiating benign and malignant lesions.

EXPERIMENTAL STUDY – APPLICATION OF DWI AND THE DWI CALCULUS ON THE EXPERIMENTAL MODEL

The experiment included in the present work was designed to study the magnetic resonance method of the apparent coefficient of diffusion as a quantitative method of differentiation between tumor angiogenesis versus the hemangioma, a benign tumor.

A value greater than $1.2 \times 10^{-3} mm^2/s$ is an exclusion criterion of tumor angiogenesis.

The experiment was performed by the transplantation on the chorioallantoic membrane of a non-volutive congenital hemangioma. 3 eggs were introduced into the lot examined: two with the transplanted hemangioma

and a developed vascular network, and one egg marked as a control egg, without angiogenetic network.

The DWI is based on the measurement of the Brownian movement of water molecules in a tissue voxel, which movement includes the Brownian extra-, intra-, and trans cellular movement of the individual water molecules. The calculation of the true ADC value is a more accurate way of quantifying the diffusion restriction.

The calculation of the ADC was done manually, by placing the center of the ROI on the vascular network around the transplant.

The quantitative assessment of the ADC mapping is greater than 1.4 in all measurements performed, it being one of the criteria supporting the benign nature of a lesion.

The purpose of this experiment is to demonstrate that the DWI and the calculation of the ADC are achievable on a vascular network such as the one in the described study and correspond to the data in the literature, therefore categorizing such lesion within benign pathologies.

The method is applicable and useful to any patient, including neonates, when space-replacing formations at the level of the soft tissues are to be categorized and differentiated as benign versus malign, and radiographic and ultrasound imaging is insufficient, given their limitations.

OBJECTIVES

Differentiation of hemangioma angiogenesis and tumor angiogenesis

WORKING PROTOCOL

An in vivo experimental study has been performed on the chorioallantoic membrane.

ASSESSMENT OF THE ANGIOGENESIS OF THE EXPERIMENTAL MODEL OF HEMANGIOMA BY MEANS OF MRI

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A value greater than 1.2 x 10-3mm2/s is an exclusion criterion of tumor angiogenesis.

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DISCUSSIONS

A study published in September 2018 concludes that all benign tumors of soft tissues except lipoma have ADC values > 1.275 x $10^{-3}mm^2/s$, while

hemangioma and hollow hemangioma have the highest ADC values. Malignant tumors have ADC < 1.1 x $10^{-3}mm^2/s$.

CONCLUSIONS

The quantitative assessment of the ADC mapping is greater than 1.4 in all measurements performed, it being one of the criteria supporting the benign nature of a lesion.

The purpose of this experiment is to demonstrate that the DWI and the calculation of the ADC are achievable on a vascular network such as the one in the described study and correspond to the data in the literature, therefore categorizing such lesion within benign pathologies.

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