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BENIGN VASCULAR TUMORS AND VASCULAR MALFORMATIONS IN CHILDHOOD: A RETROSPECTIVE ANALYSIS OF 1127 CASES*

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SUMMARY: Akyüz C, Yarış N, Kutluk MT, Büyükpamukçu M. (Oncology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Benign vascular tumors and vascular malformations in childhood: a retrospective analysis of 1127 cases. Turk J Pediatr 1997; 39: 435-445.

Vascular lesions in childhood are classified as vascular malformations and hemangiomas. Vascular malformations are congenital abnormalities thought to arise from defects during embryological development of vascular tissue. Hemangiomas are benign tumors of vascular endothelium and can spontaneously become involuted in almost all cases.

One thousand one hundred and twenty-seven patients with vascular lesions were followed by the Department of Pediatric Oncology, Hacettepe University, for 19 years. Diagnosis was based mainly on history, clinical condition and follow-up data in 98.2 percent of cases. The distribution of the vascular lesions was as follows: 969 patients had hemangiomas, 120 had lymphatic malformations, 18 had combined vascular malformations, 11 had venous malformations, six had port-wine stain, and three had angiokeratoma. Except for ten cases with Klippel-Trenaunay Weber syndrome, vascular malformations were not accompanied by any syndrome. *Key words: hemangioma, vascular malformation, benign tumors, vascular tumors, vascular birthmarks.*

The issue of whether vascular lesions should be accepted as benign tumors, malformations or hamartomas has been discussed for a long time. Previously all vascular lesions had been mistakenly discussed under the heading of hemangioma and were generally accepted as benign tumors of vascular tissue[1-4]. Mulliken and Glowacki[5] proposed a new classification of vascular lesions on the basis of their histopathological and clinical features. Vascular malformations and hemangiomas are the major categories of this classification (Table I). These authors emphasized that hemangiomas have appeared in the first months of life, showed a rapid postnatal growth and very slow involution. Unlike hemangiomas, vascular malformations may generally be recognized at birth, grow commensurately with the child and never regress[5].

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Table I: Classification of the Vascular Lesions

I) Hemangiomas
II) Vascular malformations
1. Capillary vascular malformations
a) Port-wine stain
b) Angiokeratoma
2. Telangiectasias
3. Venous malformations
4. Lymphatic malformations
5. Combined forms

Hemangiomas are the lesions made up of hyperplasic, mature endothelial cells which are coated by multilaminated basement membrane. Proliferation of the endothelium may be present in the superficial dermis (capillary hemangioma), lower dermis (cavernous hemangioma), both of these layers (mixed hemangioma) or in some other tissue (muscle, liver, larynx, etc.)[5,6]. In contrast, vascular malformations are formed by ectatic, malformed channels lined by flat endothelium adjacent to a thin basement membrane[5,6].

Except in the case of some complications, such as compression or obstruction of important structures, Kasabach-Merritt syndrome and heart failure, it is accepted that the best management of cases with hemangiomas is clinical observation without treatment. Indications for the treatment of vascular malformations are cosmetic or functional[7].

The aim of the present study is to classify the vascular lesions in cases referred to our clinic for nineteen years using history and physical examination without any sophisticated laboratory techniques; to analyze the natural histories, and clinical and epidemiological features of the patients; to discuss treatment modality; and to underline the differential diagnosis of these lesions.

Material and Methods

From December 1971 to December 1990, 1127 cases with vascular lesions were referred to the Pediatric Oncology Unit of Hacettepe University Children's Hospital. Follow-up registrations and photographs of cases were retrospectively investigated. Patients were evaluated with regard to sex, age, complaints and the characteristics of the lesions. Diagnosis was made on the basis of natural history, clinical condition and follow-up data. According to these findings, all patients were classified as hemangioma or vascular malformation.

We accepted the pale-pink macular or telangiectatic lesions present at birth as the first signs of the nascent hemangioma. In later weeks and months, we observed that the lesions became darker in color and simultaneously enlarged.

Lesions which became raised from the skin, have sharp edges, bright red-purple color, and a smooth or rough surface are described as the capillary type. Those of normal skin color or bluish soft masses with a smooth surface are accepted as the cavernous type. When both types of lesions were present together, we classified it as mixed type. We observed that lesions started to fade and diminish in size after a stable phase. They finally disappeared with wrinkles and atrophy, or without leaving any trace on the skin.

We classified the red-purple, smooth-surfaced macular lesions which generally become darker and rough with age as port-wine stains. Dark red, hyperkeratotic, warty-like papular lesions with a tendency to bleed were considered to be angiokeratomas. Lesions characterized by venectasia, varicosities, and soft, non-pulsatile spongy masses with a bluish hue are accepted as venous malformations. Soft, immobile, normal skin colored masses ranging from a few centimetres to extremely large dimensions are defined as lymphangiomas. In the natural history of cases with port-wine stains, angiokeratomas or venous and lymphatic malformations, we observed that the lesions were generally present at birth and never showed rapid growth or spontaneous regression.

Diagnosis was made on the basis of clinical condition and natural history in 98.2 percent of patients. Histopathological examination was performed in 104 patients. Ninety-three of these underwent surgical intervention for therapeutic or cosmetic reasons. Diagnosis was confirmed by angiography in 10 patients with venous and combined vascular malformations and by scintigraphy in one patient with hemangioma and two patients with lymphangiectasia.

Results

Of the 5504 cases with benign tumors or malformations and malignant tumors who were referred to our oncology clinic over a period of 19 years, 1127 had vascular lesions. Of these, 158 were considered to be vascular malformations. The remaining 969 cases had hemangiomas (Fig. 1).

There were 673 females and 296 males with hemangiomas (F/M = 2.3). Mature hemangioma lesions were present at birth in 30.7 percent of cases and were recognized in the first month of life in 58.1 percent of cases (Fig. 2). Rapid growth and slow regression phases were determined in hemangioma lesions from the history and clinical follow-up. The lesions of 969 hemangioma cases were located on skin (961 cases), in the liver (4 cases), in the parotid glands (3 cases) and in the larynx (1 case).

Multiple lesions were seen in 24.2 percent of cases with skin hemangiomas. The total number of skin lesions in these 961 cases was 1293, and most were located in the head/neck regions of the patients (Table II). Six hundred and ninety-four (53.7%) of skin hemangiomas were capillary, 243 (18.8%) were cavernous and 356 (27.5%) were mixed type.

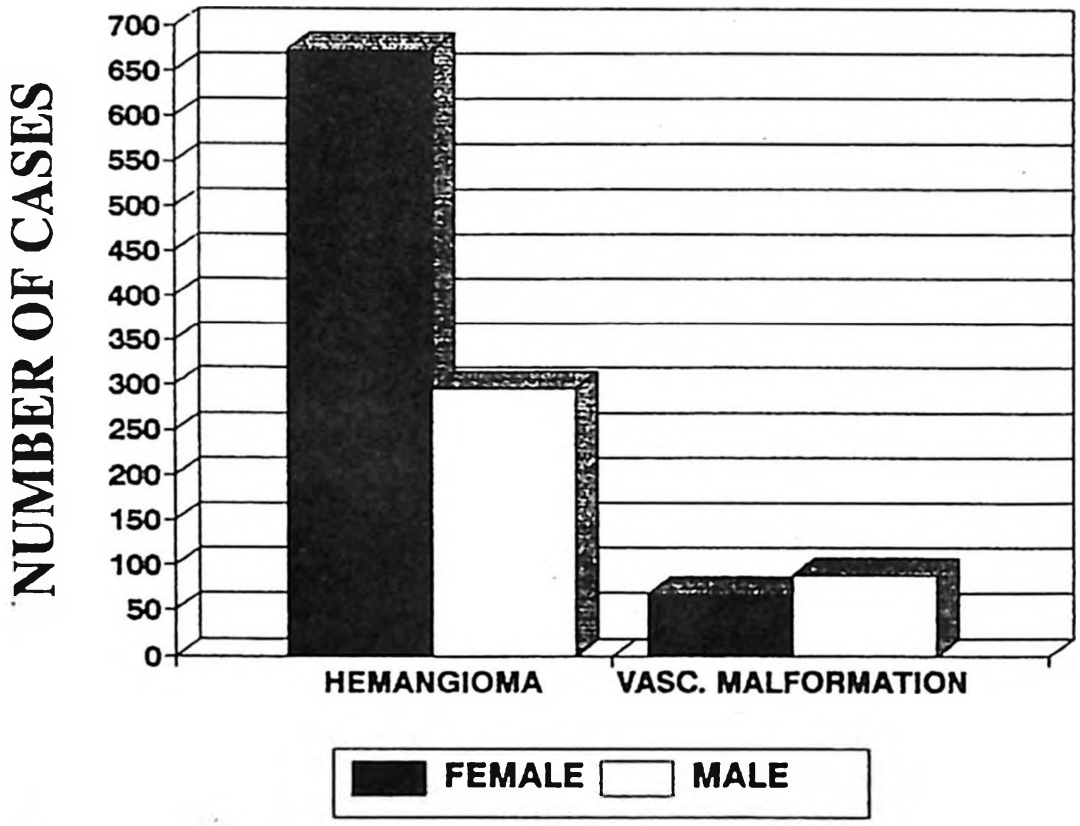

Fig. 1: Sex distribution in 969 hemangioma (female/male = 2.3) and 158 vascular malformation (female/male = 0.8) cases [Vasc. Malformation: Vascular Malformation].

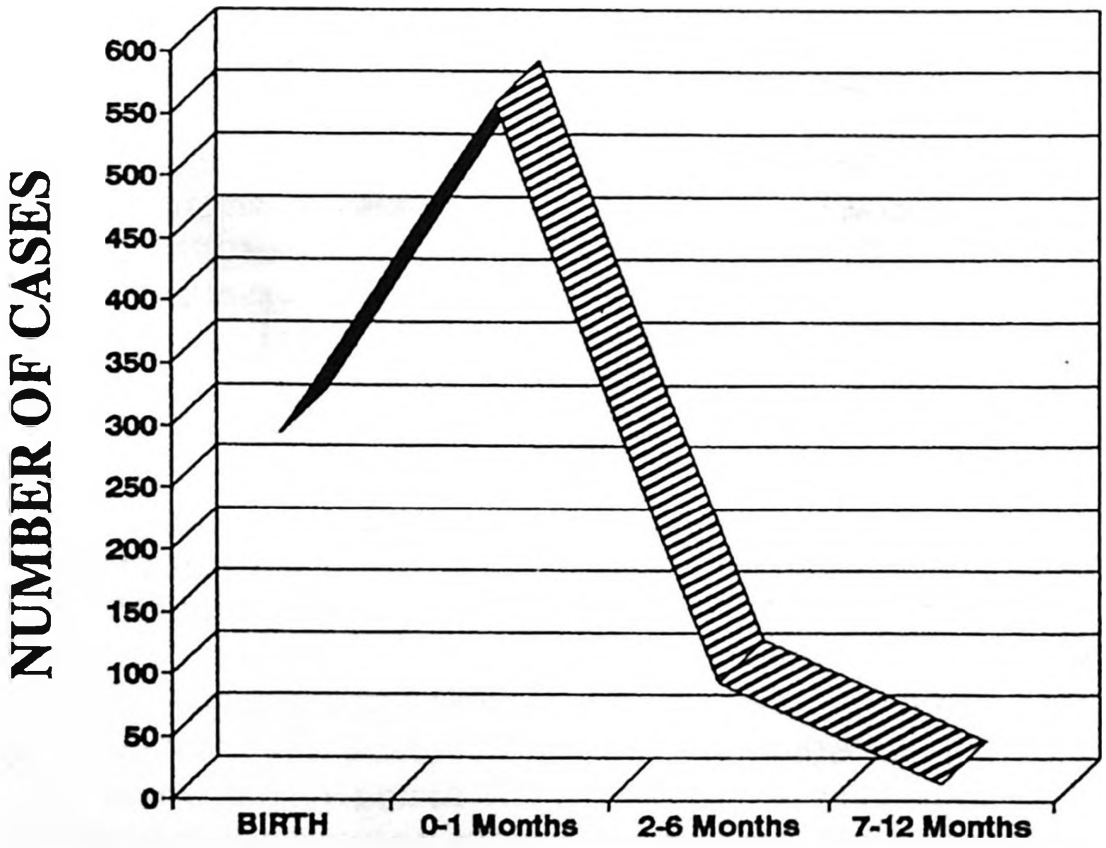

Fig. 2: The distribution of recognition ages of 961 skin hemangiomas.

Table II: Localizations of Hemangioma Lesions

Localization		Number of Cases	%
Skin		961	99.0
	Number of Skin Lesions (*) / %		
Head and neck	788 / 60.9		
Extremity	243 / 18.8		
Trunk	204 / 15.8		
Genital region	38 / 2.9		
Extend over more than one region	20 / 1.6		
Total	1293 / 100.0		
Liver		4	0.4
Parotid gland		3	0.3
Larynx		1	0.3
Total		969	100.0

* Multiple lesions were seen insome of the cases with skin hemangioma.

One hundred and two out of 969 hemangioma cases required treatment because of life-threatening complications. Parents of the 660 patients with small, uncomplicated hemangiomas were informed about the disease and advised to have their cases followed by their local doctors. The remaining 207 cases were followed by our clinic for one to 15 years (median 4.5 years). Ninety-one of these patients showed complete regression, 37 almost complete regression, and 15 approximately 50 percent regression during this period. Complete regression was observed by the age of five in 67.5 percent of cases and by the age of nine in 89.6 percent of cases.

Among the 158 patients diagnosed with vascular malformations, 68 were female and 90 were male (F/M = 0.75). We found that the lesions were present at birth in 70 percent of cases, and appeared between the ages of one to 15 years in the remaining patients (Fig. 3). The distribution of the lesions according to the sub-types of vascular malformations is summarized in Figure 4.

Six cases (4 female and 2 male) of the 158 vascular malformations had port-wine stain. The lesions were present at birth in all six cases and were located on the face in four and distributed over the body in two. In patients whose lesions were located on the face, the lesions were disseminated through the dermatomes of the maxillary branch in two, maxillary and ophthalmic branches in one, and all three branches of the trigeminal nerve in one case. The average follow-up period of these cases was 9.5 years (5-15 years). During this period, none of the lesions involuted and the symptoms of Sturge-Weber syndrome were not observed in any patient.

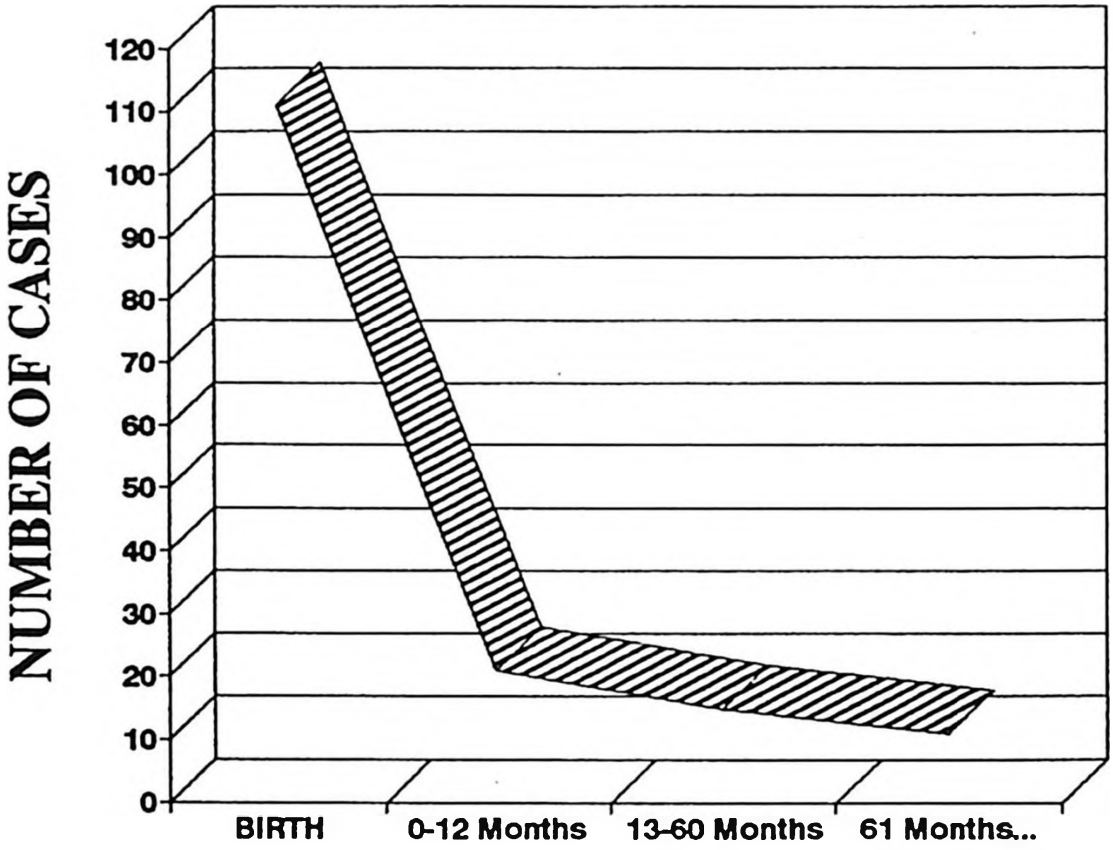

Fig. 3: The distribution of recognition ages of 158 vascular malformatilons.

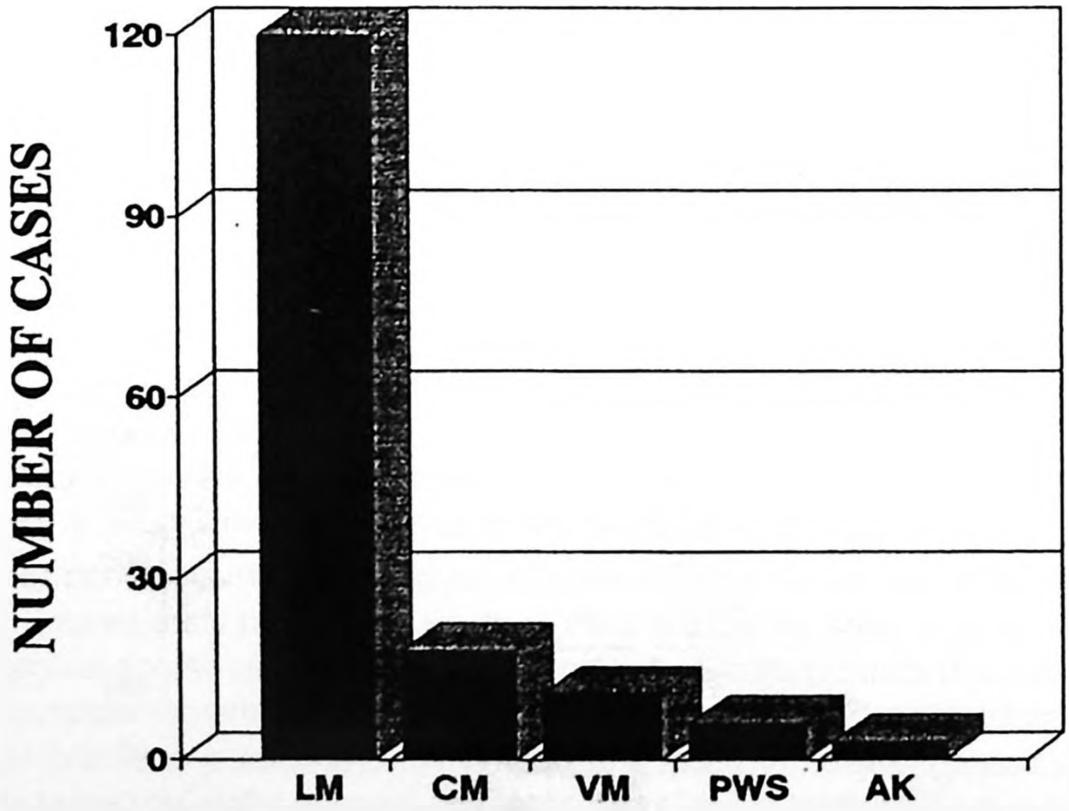

Fig. 4: The distribution of the vascular malformations according to the subtypes [LM: Lymphatic Malformations, CM: Combined Malformations, VM: Venous Malformations, PWS: Port-Wine Stain, AK: Angiokeratoma].

Angiokeratoma, another vascular malformation, was determined in three cases (2 female, 1 male). Lesions, which were recognized at birth, were located in the lower extremities in two patients and the trunk in the third. All the patients suffered from pain and bleeding. Lesions of two patients were surgically excised because of frequent bleeding.

Eleven patients (4 female, 7 male) had venous malformations. The lesions were recognised at birth in nine cases and by five years of age in two cases. These lesions were located in the extremities in eight cases, and widely distributed in the extremities, trunk and face in the remaining three cases. In seven patients, the diagnosis was confirmed by angiography which showed ectatic veins and prolonged pooling of contrast in the venous phase.

Lymphatic malformations (120 cases) was the largest group of vascular malformations in our series. Out of 120 cases (51 female, 69 male), 118 were lymphangiomas and two were intestinal lymphangiectasias. In 11 cases with lymphangioma, multiple lesions were observed. The total number of lymphangiomas was 133, and their localizations are shown in Table III. Sixty-

Table III: Localizations of Lymphangioma Lesions

Localization		Number of Lesions (*)	%
Head and neck		61	45.8
Neck	35		
Tongue	8		
Periorbital	4		
Floor of mouth	2		
Other parts	12		
Extremity		29	21.8
Trunk		23	17.3
Axilla		9	6.7
Intestinal mesentery		5	3.7
Mediastinum		3	2.3
Liver		1	0.8
Spleen		1	0.8
Salivary gland		1	0.8
Total		133	100.0

* Multiple lesions were seen in some of the cases with lymphangioma.

nine (51.8%) out of 133 lymphangiomas were of the cystic type. The most prominent complaint (84.7%) of these patients was mass and swelling in various regions of the body. However, 6.7 percent had macroglossia, 3.3 percent had respiratory distress, and 4.9 percent had feeding and/or speech problems.

Lymphangiomas were present since birth in 62 percent of cases and appeared up to the fifth year of age in 90.7 percent. Two cases presented with complaints of abdominal pain, distention and diarrhea; a diagnosis of intestinal lymphangiectasia, which causes malabsorption and protein-losing enteropathy, was confirmed by lymphoscintigraphy and intestinal biopsy. Lymphangiomatous masses in different localizations were excised totally in 50 cases and partially in six cases. Recurrence was observed in 12 and four cases, in totally and partially excised groups, respectively.

There were 18 patients with combined malformations, in which different combinations of lymphatic venous and capillary vascular malformations were present. Five of these patients had capillary and venous malformations eight had capillary and lymphatic malformations, three had venous and lymphatic malformations and two had all three types of malformations in the same localization. The malformations were located on an extremity in 15 patients, on the trunk in one patient, and on both an extremity and the trunk in one patient. Klippel-Trenaunay-Weber syndrome (KTWS) was diagnosed in 10 of these cases in which hypertrophy of the skeleton and soft tissue was present. Venography was performed in three of these 10 patients and occlusion in the proximal branches of the vena femoralis was demonstrated.

Discussion

Benign tumors of vascular endothelium and vascular malformations are the main lesions of vascular tissue in childhood. It has been reported that 21.7 percent of all malformative lesions and all benign tumors in childhood originated from vascular tissue[8].

In the present study, a total of 1127 cases with either hemangioma, lymphangioma, venous malformation, port-wine stain, angiokeratoma or combined vascular malformations were retrospectively evaluated. Hemangioma, a benign tumor of vascular endothelium, is the most frequent tumor in childhood[9, 10]. The number of all patients with benign tumors followed by our department for 19 years was 1175 and 82.5 percent of them were hemangiomas. The incidence of vascular malformations varies with respect to the sub-type of the malformation. The incidence of port-wine stain is approximately 0.3 percent[11] and that of angiokeratoma is extremely small[12, 13]. It has been reported that only five of 3000 new applications to a surgery clinic per year were lymphangiomas[14]. One hundred and eighteen out of 5504 new cases referred to our clinic over 19 years were cases with lymphangiomas.

The diagnosis was based only on the history, clinical condition and follow-up data in 97.9 percent of our cases, on histopathological examinations in 0.9 percent

and on radiological methods in 1.2 percent. Finn et al.[15] stated that hemangiomas and vascular malformations could be clinically diagnosed and distinguished without any histopathological or laboratory examination in 96 percent of cases.

Hemangiomas are more frequent in females than males, but there is no difference between sexes for vascular malformation[5, 9, 14, 15]. In our study, hemangiomas were 2.5 times more frequent in females, while vascular malformations were slightly more predominant in males. In the present study, we observed that hemangiomas generally appeared in the first few weeks of the postnatal period, and showed rapid growth and slow involution phases. In completely regressed hemangioma cases, we saw that regression had occurred in 67.5 percent by the age of five years and in 89.6 percent by the age of nine years. Vascular malformations were generally present at birth, grew proportionally with the child and never involuted. These findings are consistent with the data presented by some authors[5, 15].

Therapeutic intervention for hemargiomas should be considered only in rare cases, because the majority of lesions undergo spontaneous involution. Approximately 10-20 percent of hemangioma lesions cause problems, such as bleeding, infections, compression or obstruction[7, 9, 10, 16]. Only 10.5 percent of our cases with hemangiomas required treatment. The remaining 867 cases were followed-up by our clinic or by their local doctors.

The risk factors and management of vascular malformations vary according to sub-type[7, 16, 17]. Cases with port-wine stain should be treated because of cosmetic and psychological problems[18]. The lesions can be camouflaged by cosmetic creams. Laser has been used to treat port-wine stains for over 15 years. Good or excellent response to dye laser treatment can be expected in 60-90 percent of patients[16, 18, 19]. We did not use any treatment modality in our patients with port-wine stain. Treatment of angiokeratomas is usually symptomatic. Electrocoagulation, cryotherapy, laser therapy and surgical excision have been recommended for control of the symptoms[12, 13, 17]. Two of our cases with angiokeratomas underwent surgical treatment because of frequent bleeding. Therapy for venous malformations is usually undertaken for cosmetic and functional reasons. Radiotherapy, electrocoagulation, sclerotherapy, and compression therapy can be used, but usually venous malformations cannot be treated successfully[7, 17]. In the present study, compression therapy with elastic bandage was used in patients with venous malformations on their extremities. The recommended treatment for lymphangiomas is surgical excision. Total excision of these lesions should be carried out if it is possible, but it is not always feasible due to certain anatomical relationships[7, 17, 20, 21]. Heether et al.[22] stated that patients whose lesions were partially excised had remained free of complication and rarely required re-operation. Other modalities such as sclerotherapy and radiotherapy have been proposed for the treatment of

lymphangiomas but the results of these methods were not satisfactory[7, 20, 23]. In our series, 56 of 118 patients with lymphangiomas underwent surgical treatment. Lesions were totally excised in 42.3 percent of cases and partially in five percent. Recurrence rate was found to be 28.6 percent. Six of 16 recurrent lymphangioma cases required re-operation.

Sturge-Weber syndrome is described as the port-wine stain located on the face, ipsilateral vascular malformation in the leptomeninges, and choroid plexus of the eye[24]. This syndrome was seen in 11 percent of port-wine stain cases whose lesions were located in the head/neck region and 29 percent of cases with port-wine stain on the dermatomes of the trigeminal nerve[25]. We had four cases with a port-wine stain on the dermatomes of the trigeminal nerve, but none of these cases was defined as having Sturge-Weber syndrome, possibly because of the low number of port-wine stain cases.

KTWS is characterized by large capillary malformations, varicose veins, lymphatic malformations and skeletal-soft tissue hypertrophy[1, 24]. Capillary malformations on the skin have previously been incorrectly termed hemangiomas[25]. Servelle[26] showed an elongation of the extremity in 86 percent of 786 cases with KTWS, atrophy in 10 percent, varicosity in 36 percent, and capillary malformation in 32 percent of the cases. In the same study, it was reported that the findings of KTWS were seen on the lower extremities in 79.6 percent of cases, upper extremities in 13 percent, both upper extremities in 3.2 percent both lower extremities in 1.9 percent, and all extremities in 2.3 percent[26]. Elongation of the extremity was present in 20 percent, atrophy in 10 percent, varicosity in 40 percent, and capillary malformation in 70 percent of the 10 KTWS cases in our series. Findings were present in the lower extremity in eight, upper extremity in one, and upper and lower extremities together in one case.

Servelle[26] showed some malformations such as agenesis, hypoplasia, and fenestration in veins and the perivenous sheath. Such malformations were defined as the causes of KTWS by Servelle[26], but Baskerville[27] regarded them as the components rather than the causes of KTWS. In three of the 10 KTWS cases in the present study, occlusion in the veins was shown by venography.

It is important to evaluate a vascular lesion present in childhood, whether it is a vascular tumor or a vascular malformation. A capillary hemangioma can easily be underestimated as a port-wine stain and the cavernous type as a lymphangioma. The correct diagnosis can be made with a careful history, physical examination and clinical follow-up. Because over 90 percent of hemangiomas regress, the current accepted management remains careful observation and the education of parents. Families must be properly enlightened in order to alleviate any anxiety and prevent some unnecessary interventions.

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