Birthmarks: Diagnosis and Therapy

A. BERENSTEIN

INN Institute for Neurology and Neurosurgery, New York; USA

I. Introduction

A diversity of complex and often confusing classifications of head and neck vascular lesions may be found in the literature. The majority of these are descriptive, based on clinical appearances and pathological (histologic) features, and are not useful in modern clinical practice. Pretherapeutic pathologic examination is difficult or even hazardous to obtain; significant haemorrhagic complications have been known to occur following biopsies of these lesions. The specimen obtained may not reflect the various components of the lesion, and does not take into consideration the type of flow present.

The most useful classification would be one that could predict the clinical behavior of individual lesions, and lead to the selection of the most appropriate, currently available mode of therapy. At present the best available clinico-pathologic classification is that of Mulliken and Glowacki (1982), which includes tissue culture, histochemical and electron microscopic studies. It enlightens some of the most difficult aspects of these lesions and is based on the separation of vascular lesions into two groups: those with a proliferative and sometimes potentially involutive behavior (haemangiomas); and those without (vascular malformations) which can be further classified according to the morphology of

the abnormal channels present. From our clinical and angiographic experience we have reached a similar type of classification.

II. Postulated Embryogenesis

The embryogenesis of hemangiomas is not well established. Recently, Paula North (North 2000) has postulated that true haemangiomas are metastases of the placenta, a very attractive hypothesis that can explain the biological behavior of haemangiomas.

The mechanism of formation of vascular malformations has been deduced from the work of Woollard in 1922 on the maturation process of the capillary network of the limb bud of the pig. However, the analogy between the development of the limb and that of the head and neck must be reconsidered as several important differences in the embryogenesis of these two regions exist.

The progressive centrifugal development of the limb around a fixed arterial source, requires a constantly growing vascular bed similar to a growing tree.

The various forms of vascular lesions have been considered by some authors to be caused by the arrests occurring at different stages of vascular development. For example, Kaplan, who based his conclusions on the vascular development of the extremities, related the capil-

lary vascular lesions to an early stage 1 (undifferentiated capillary network) abnormality; later in the same stage, the lesion would be a cavernous type haemangioma. An arrest in the second stage (retiform stage) will produce a form of arterio-venous fistula (single hole or true AVM with a nidus).

Finally, at stage 3 (maturation stage) arrest would lead to venous or lymphatic malformations.

The development of the head and neck area involves different and more complex changes (rotations, invaginations, migrations) of the tissues which locally crumple or blossom during the first weeks in utero.

We know from Paget's work (1948) that during normal development of the head and neck, the vasculature undergoes a series of changes in its branching patterns. Regressions and annexations of some arterial sources or territories account for the unique bidirectional flow in every branch of the head and neck area and for the variability in the territories supplied by a given artery.

The relationships between the development of the facial buds and the changes in the arterial tree are difficult to establish. Both the ICA and the VA result from the persistence of several consecutively independent segments during the final maturation of the main head and neck vessels (Berenstein, 1987).

Woolard's work (1922) has shown that in the limb bud of the pig, the veins are located in the periphery of the bud, whereas the arterial system is in the central portion. If one considers the traditional mechanisms evoked to explain the various types of vascular lesions, one can predict that malformations with a predominant arterial component should be located deep within the extremity while venous malformations should be more peripheral. Although this generalization is frequently true it is not constant: patients with Klippel-Trenaunay syndrome often have deep venous malformations of the lower extremities.

In the maxillofacial area, each facial bud can be related to an embryonic vessel. However, during secondary development, bridges that modify the haemodynamic characteristic of their boundaries are established. Due to the nature of the specific modeling of the maxillofacial buds, it may be predicted that the vascular system of adjacent buds will overlap and

eventually compete, leading to the annexations and regressions mentioned above. It becomes then almost impossible to find what could correspond to the initial central or peripheral portion of the maxillofacial buds.

The folds between adjacent buds represent critical areas for capillary maturation, primarily on the venous side. After this has occurred, the arterial system can establish the necessary haemodynamic balance providing the nutritional equilibrium of the final dispositions. Delay in bud fusion produces specific arterial anatomical variation because the usual bridging tissue has been omitted. If the maturation of the capillary network is simultaneously delayed, vascular lesion may be seen in association with the arterial variations without clefts (Berenstein, 1987).

On a practical basis, the classical embryonic folds are not helpful in predicting the morphology or channel predominance of maxillofacial vascular lesions. Facial clefts and their various locations may be more helpful since it is possible to relate one artery to every single meridian as described by Tessier (1976). This will be specifically discussed with the Sturge Weber (Berenstein, 1987).

The study of the arterial vasculature of the palatine clefts (Fredericks 1973) shows that the clefts behave like anatomic barriers to vascular development and that their margins are highly vascularized (Ricbourg 1981 unpublished data). If this embryonic abnormality (the cleft) is associated with persistence of the embryonic state of the capillary network, vascular malformations should be found on the margin of the clefts or on the upper and lower corresponding meridian of Tessier (1976).

In the conclusion of her analysis of the palate cleft arterial supply, Fredericks rejected an ischemic phenomena by lack of vessel as a cause of the morphological gap. The author strongly suggested that due to the specific pattern of their blood supply, the existence of the clefts may be due to a "haematogeneous factor". The capillary arrangement of the cleft margins, which can be regarded as a pre-angiomatic state, may illustrate another aspect of the same factor. This "haematogeneous factor" could be responsible for the development of the vascular lesions with or without clefting or its equivalent.

Depending upon its nature, this developmen-

tal vascular disorder may manifest as a lesion which is:

- quiescent
- clinically expressed but reversible
- expressed but stable
- progressive.

The evolution or enlargement of the abnormal nidus will be due to proliferative cellular activity with tumor-like growth (Haemangiomas), or to a haemodynamic process, which increases the flow into the nidus (vascular malformations). Both mechanisms are believed to exist and they lead to the development of lesions with entirely different clinical behavior.

In summary:

1. Maxillofacial vascular lesions may be related to abnormal capillary maturation.
2. Their topography can in part be correlated with the facial buds.
3. Facial clefts constitute important landmarks of the critical areas of the developing maxillo facial area.
4. Vascular lesions with arterial predominance should theoretically occur on the margin of a meridian with no necessary cleft.
5. Venous malformations in the area should bridge two adjacent buds over the meridian.
6. Compartments within vascular lesion may account for the absence of apparent folds or clefts.
7. Neither sites of the disorder which gives rise to a vascular lesion nor the mechanisms responsible for its development are known.

III. General Classification

Clinical Behavior and Treatment Strategy

The classification that we use is similar to that of Mulliken and Glowacki (1982). Under a generic name of vascular anomalies, two types of lesions will be differentiated: vascular malformations and vascular tumors. Complex vascular anomalies will be presented as a separate group, but belong to the vascular malformations.

The predictable difference in clinical behavior in the two major categories of vascular lesions, haemangiomas and vascular malformations, dictate entirely different therapeutic approaches.

The treatment strategy that we propose is based on a ten year experience with vascular malformations and haemangiomas in different

parts of the body. Each territory carries specific therapeutic risks which will affect the choice between conservative management and the search for a complete cure. The understanding of vascular lesions and progress in their treatment is one of the most rapidly changing areas in medicine. Therefore, the possibility that therapeutic techniques may be improved in the future dictates against the use of unnecessary potentially mutilative procedures now.

1. Haemangiomas

Haemangiomas are tumors that enlarge by proliferation of endothelial cells and some (infantile haemangiomas) may involute by progressive cellular death and dropout. At histologic examination, potentially involutive haemangiomas of childhood consist of masses of endothelial cells with or without vascular lumens. The stimulus for involution is unknown. Possible mechanisms include occlusion of the vascular bed by endothelial cellular proliferation or by humoral factors. What we see histologically as the lesion involutes is a lack of thrombosis or infarction. However, there is nothing in the vessels or stroma that would predict involution.

Potentially involutive haemangiomas of childhood have characteristic angiographic features which are similar to other benign tumors. They include mass effect, an organized pattern of arterial supply from adjacent arteries, drainage into dilated superficial veins which empty into normal veins, and parenchymal stains which are often lobulated. Arteriovenous shunting may be present. Non-involutive cavernous haemangioma of adults typically appears as avascular masses on angiography, although, some parenchymal blush and filling of vascular spaces may occur in the late venous phase, if sufficient contrast material is injected. They grow like tumors and should not be considered as vascular malformations.

Conservative treatment is the rule for most patients with involutive haemangiomas. These lesions, which have a strong female predominance (5:1) are present at birth in only approximately 30% of patients. The majority appear in the first three months of life. They typically demonstrate a period of rapid growth (proliferation phase), usually in the first 6 months of life followed by a period of gradual involution

which generally begins at about 12 months of age and is complete by 7 years (Pitangy 1984). Involution can be expected to occur in over 95% of patients (Bowers 1960, Bingham 1979, Blackfield 1957). Unfortunately, it is not possible to predict the 5% of patients in whom involution will not occur. Active therapy to increase the rate of involution is indicated in selected patients including those with functional impairment (orbital, oral, subglottic), complications (haemorrhage, congestive heart failure, hypoprophthromi-nemia; see Kasabach Merritt syndrome) and extremely large lesions. The most effective nonsurgical treatments are:

- systemic corticosteroid therapy and/or
- embolisation.

Corticosteroids should be tried first, but unfortunately are not always effective and may not be well tolerated, especially where long term treatment is required with steroid dependent lesions. Haemangiomas are at least theoretically responsive to radiation therapy, but this modality is not currently considered acceptable due to its long-term side effects (malignancy, regional growth impairment, and scarring). Streptokinase, heparin and aspirin have been used with mixed results. Aminocaproic acid has been used in some patients, but is also not an innocuous drug (Neidhart 1982). In selected patients, embolisation using small particles can be expected to be effective in arresting the proliferation phase and speeding the onset of involution.

2. Vascular Malformations

Vascular malformations are inborn errors of vascular morphogenesis. They may be formed by any combination of abnormal capillary, arterial, venous, or lymphatic channels with or without shunt. Changes in size are secondary to rheologic (haemodynamic) changes. They are neither proliferative nor potentially involutive. They are almost always present at birth, they may expand but they do not have cellular proliferation. At histologic examination, they consist of channel of varying morphology without an endothelial cellular stroma.

A wide spectrum of angiographic appearances exists for the vascular malformations and correlates with the underlying channel abnormalities. The positive angiographic differences include the opacification of channels which do

not normally exist whereas the relevant negative angiographic differences, include the absence of a well defined parenchymatous "tumoral blush" (although some small vessel malformation may show a blush). Lymphangiomas and haemolymphangiomas of the oral regions are considered to be malformations rather than true neoplasms (Batsakis 1979).

Pure lymphatic malformations do not regress spontaneously. They often communicate with adjacent systemic veins and may be combined with venous or arteriovenous malformations (haemolymphangiomas). Haemolymphangiomas may expend acutely, secondarily to infection, haemorrhage or venous thrombosis, and may then incompletely regress (spontaneously or after embolisation), leaving behind some hypertrophic area involved (tongue, floor of the mouth, cheek, lips).

Port wine stain is a vascular malformation and consists of small capillaries, venous or venular channels located within the dermis. Port wine stains are frequently present in the mesodermal dysplastic syndromes and when isolated in the face, may represent a minor expression of Sturge Weber syndrome.

The clinical behavior of vascular malformations varies according to the morphology of the channel abnormalities, their secondary haemodynamic effects and locations. They differ significantly from haemangiomas because of the absence of proliferative and involutive potential. Certain lesions may exist in a dormant state until stimulated to expand by a trigger factor. The majority enlarge gradually in proportion to the growth of the patient. Their effects vary from minor cosmetic blemishes to major deformity or functional impairments. The treatment of these complex lesions requires careful planning by a multidisciplinary team. In general, treatment of vascular malformations in children, should be conservative in the absence of significant functions or life threatening complications. Radiation therapy has no therapeutic role at present, unless all other modalities endovascular, surgical or a combination of these fails.

Incomplete surgical resection should be avoided as it is frequently ineffective, may aggravate the problem, and makes future endovascular therapy difficult or impossible. Mulliken (1982) proposed a rheologic basis for the therapy of vascular malformations which is in

accordance with our current philosophy and embolisation techniques. In adults, the aggressiveness of the therapeutic approach may depend more on the team skills, cultural environment (as it relates to the goal of treatment and possible complications) rather than to the characteristics of the vascular malformations.

IV. Pretherapeutic Evaluation of the Vascular Lesions of the Head and Neck Area

Due to the complexity of these lesions a multidisciplinary approach is necessary to optimize the analysis and treatment strategy by a given team in a specific case. Therefore, the expertise of the various physicians (otolaryngologists, head and neck surgeons, oral surgeons, pediatricians, plastic surgeons, neurosurgeons, ophthalmologists, orthodontists) will help us in determining the clinical, psychological and technical problems or challenges related to the management in a specific instance.

The pretherapeutic evaluation of a vascular lesion of the head and neck must start with a thorough clinical examination of the lesion, the surrounding areas and the rest of the body. The past medical history of the patient and of his family must be noted as well as any triggering factor in the evolution of the lesion. Once this has been established, the differentiation between a haemangioma and a vascular malformation can be made. If it is decided that no treatment should be given, further studies are not usually needed, and a conservative follow-up can be done. Good photographs of the head and neck areas and body should be taken at the initial examination and at subsequent consultations. If treatment is indicated additional evaluations may be made.

Pretherapeutic evaluation will include some noninvasive radiological studies: Chest X-ray, panoramic view of the maxillomandibular area, axial and coronal CT without or with enhancement. Neither plain skull films nor complex motion tomography have proven in our experience to be of any significant value in most solitary vascular lesions of the head and neck. They may be useful to the plastic surgeon for specific needs in presurgical evaluation. MRI has not yet shown any major advantages in the appreciation of bony or soft tissue extension. Intra-venous digital angiography, as in other lesions of the head and neck area, does not provide

enough information to contribute to the decision making process. It reproduces in best of cases information given by a good quality enhanced CT study.

Ultrasound is reserved for cervical and parotid masses, to differentiate the vascular nature of the lesion from other masses (hygroma, branchial cyst or adenopathies). Doppler has not proven to be useful in our experience, although it might demonstrate nonperceptive bruits which would further contraindicate any attempt to biopsy.

With the above information, bony and soft tissue extension, and extension to the orbit or cavernous sinus can be assessed; they represent the key necessary to appreciate the future evolution and technical difficulties in dealing with a deep seated malformation or haemangioma.

Clinical suspicion of angiomatosis from the family history, the examination of the skin or complaints in another territory (digestive system, respiratory system etc.) should probably lead to additional tests. Family examination will be mandatory in some cases (Rendu-Osler-Weber, von Recklinghausen, von Hippel Lindau, Blue Rubber naevi) to appreciate the penetrance of a hereditary angiomatosis.

Finally, specific laboratory tests will be requested with specific attention to coagulation tests (Kasabach Merritt syndrome).

V. Urgent or Emergent Pretherapeutic Evaluations

The pretherapeutic evaluation of vascular lesions is usually not urgent except for subglottic or eyelid haemangiomas, haemorrhagic episodes usually associated to ischemic ulcerations, and dental arcade AVM with bleeding complications. Severe consumption coagulopathies (see Kasabach and Merritt 1940) or heart failure caused by large lesions in neonates or infants will constitute emergency situations. The great majority of vascular lesions of children will be treated conservatively, waiting until complete regression or maxillofacial maturity.

However, appreciation of the secondary consequences of a deeply located dormant lesion and its potential complications (vision, cranial nerves, haemorrhages) following triggering factors, may require complete pretherapeutic evaluation to further establish progno-

sis and eventually consider prophylactic treatment.

Oral cavity lesions with their consequences on the maxillofacial growth represent the best indication of prophylactic treatment; even in the absence of airway or digestive dysfunction, bleeding or cosmetic problem.

More difficult are the lesions in the orbital wall (maxilla, malar, ethmoid, sphenoid region) without visual symptoms which will require pretherapeutic studies probably including selective angiography. Careful attention has to be paid to the school performance of affected children, as it may deteriorate with impairment of the vision, compromises of hearing, or attention, with the onset of a bruit. Children usually do not complain about these changes, therefore proper and direct questioning may be relevant. In this population in particular, but in the adult one as well, appreciation of the psychological consequences of the lesion is sometimes difficult to access.

Pure cosmetic problems represent a difficult therapeutic challenge and whenever possible attempt at complete resolution or cure should be made by combined treatment.

As already mentioned, partial surgery should be avoided.

Asymptomatic pulsatile bruit discovered during clinical examination will invariably lead to pretherapeutic evaluation, to precisely demonstrate the venous channels involved in the drainage of the lesion, and the retrograde congestive consequences that it may induce.

Finally, true port wine stains in the trigeminal territory should only be investigated with CT for diagnostic and prognostic purposes (see below).

VI. Angioarchitecture

Our description of angioarchitecture of vascular lesions of the head and neck is based on our experience collected by superselective studies of more than 600 patients over the past 10 years.

The precise angiographic protocol is based on the topography of the lesions. It is necessary to accurately demonstrate the angioarchitecture of the nidus, the feeding arteries and draining veins, the flow characteristics of the lesion and the collateral circulation through the nidus and surrounding healthy tissue; the an-

giographic features which must be analyzed in every case include:

- topography
- nidus angioarchitecture
- secondarily induced high flow
- collateral circulation (arterial and venous)
- iatrogenic changes (surgery, radiation therapy, previous embolisations)
- angiographic changes (evolutive factors)
- arterial ectasias
- mass effect and parenchymal component (haemangiomas, and other vascular tumors)

In practice all of these features may not be defined in each patient but the information obtained represents irreplaceable *in vivo* information that neither direct vision (surgery) nor pathology can give. The capability to identify in specific cases what may correspond to the active portion of the lesion, as opposed to what represents the reversible induced phenomena of surrounding tissues may lead to a limited treatment. The data gathered from the vast quantity of angiographic work has contributed greatly to the understanding and treatment of vascular lesions in the head and neck areas.

Feeding arteries are usually enlarged in the presence of arteriovenous shunting but may be normal in size in the presence of highly vascularized lesions without an arterio venous shunt (as seen in most haemangiomas). Rarely increased size with slow flow circulation will correspond to a normal flow pattern. The classical concept of arterial “steal” and its related symptoms may be difficult to demonstrate; typically the selective angiogram shows preferential flow to the lesion while the feeding arteries to the surrounding tissues are poorly or not visualized. However, the complete examination of the area and the surrounding healthy territories, shows that no vessels are absent. One can demonstrate that the ischemic phenomena noted clinically are not at the level of the arterial “steal” seen at angiography; the venous drainage affects the normal territories by retrograde venous congestion, leading to decreased tissue perfusion and ischemia. By analogy, venous hypertension can explain: the ischemic ulcer of the Klippel Trenaunay disease, the ischemic deficits of the dural AVM draining into the central nervous system venous channels or leptomeningeal vascular malformation in Sturge Weber syndrome, the visual symptoms of “slow flow” dural AVM draining into the

ophthalmic vein, and the usual asymptomatic character of the angiographic "steal" of the entire hemisphere seen in some carotid cavernous fistulas. These lead us to believe that ischemic ulcers in head and neck AVMs represent an excellent indication for arterial embolisation to decrease the strain on the venous system.

Acute (post traumatic) arteriovenous fistulas may create an arterial "steal", however, it has not been our experience that clinically ischemic phenomena were related to arterial deprivation. A different situation exists in the postembolisation trismus which always relates to arterial ischemia induced by embolisation of the normal muscular vascular territory. The same arterial mechanism is involved when ectopic emboli reach the capillary level of a cutaneous territory (distal to the last possible collateral channel) and produce cutaneous necrosis.

Traumatic transformations (iatrogenic or not) typically manifest as evolution in vascular malformations and regression in haemangiomas. The triggering factor behaves differently in these two major categories. But in some other instances endothelial trauma of an arterial feeder to an AVM may stimulate an angiogenetic activity, which will become secondarily active by an angioectatic effect dependent on the type of AVM.

As previously discussed, the precise mechanism involved in the evolution of vascular le-

sions and their reaction to trauma and hormones are not known. Although definitive changes in the architecture of normal nasal mucosa are known to occur with hormonal changes, we have observed no specific angiographic features in the vascular malformation of patients who presented clinically with increased bleeding during their menstrual period. Humoral angiogenetic factors probably play a role in the evolution of certain neoplasm (Folkman 1981) but their role in the evolution of vascular malformations is not at all clear. At this time, we feel that the trigger effect of the hormonal changes on the vascular malformation is a rheologic (angioectatic) one. Trauma clearly plays an important role in the evolution of vascular malformations probably related to non proliferative changes in the endothelium in addition to the development of new shunts, or thrombosis with some impairment in drainage.

Alex Berenstein, M.D.
INN Institute for Neurology
and Neurosurgery
North Division, Endovascular Surgery
170 East End Avenue at 87th Street
New York, 10128 U.S.A.