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Hemangiomata

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I. ABSTRACT

HEMANGIOMATA

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The subject of hemangiomata is much more complicated than one realizes when the literature is reviewed. A common impression is that the condition is a congenital lesion of the skin, I.E., a "birthmark", sometimes associated with similar insignificant (?) lesions in some of the internal viscera. On the contrary, there is probably no organ or area in the body which may not be involved and not infrequently death is due directly to the hemangiomata. The lesions are extremely variable in their form: some are immediately recognizable as blood vessel structures while others require extensive microscopic study in order to identify their origin. The two factors: multiplicity of areas involved and the variability of the growth, has given rise to an enormous literature on the subject and a corresponding wide range of terms and synonyms.

Classification

The pathology of all the types of hemangiomata has not been developed. Moreover, good correlations between clinical features and microscopic structure is also lacking for many of the varieties. For this reason, no satisfactory classification has been made. At present, there is not even a satisfactory term for the entire group. In the absence of something better, the group must be designated as "hemangiomata." The term implies a growth which is not readily acceptable since one form is represented by symptomatic disturbances of blood vessels. The division between congenital malformations and new growths is completely confused. The following table is an attempt to summarize and classify the ideas of several authors. It illustrates also the imperfections in our knowledge of these lesions.

Hemangiomata

1. Symptomatic
   a. Secondary angiomatosis (or telangiectasis)
   b. Artificial arteriovenous aneurysms

2. Malformations
   a. Primary angiomatosis (or telangiectasis)
   b. Venous angiomata
   c. Arterial angiomata
   d. Arteriovenous angiomata

3. Neoplasms (angioblastoma)

Pathology and Genesis

Secondary angiomatosis. This group of vascular blood vessel disturbances is associated with some other disease. Among these are: jaundice, pregnancy, blood dyscrasias, syphilis, thyroid and pituitary dysfunction, cardiovascular disease, lead poisoning, inflammatory disease producing perivascular fibrosis or endarteritis and sepsis. There is no area of predilection but the mucous membranes are less apt to be involved. The process may be discrete, local, or there may be a general telangiectatic process over the entire body. The lesions advance with the progress of the primary disease and subside if the patient improves. Very little attention has been paid to this group but its importance is obvious. Treatment of the lesion is unnecessary since it disappears spontaneously with improvement of the systemic condition.

Artificial arteriovenous aneurysms may be considered in connection with the

spontaneous type.

Primary angiomatosis or telangiectasis is the form of hemangiomata which has attracted the most study. For the sake of brevity and also since there is no sharp line of division this type and the venous, arterial and arteriovenous forms may be considered together. The lesions may be single, multiple, localized or diffuse and may involve any tissue or area of the body. In the telangiectatic type, the capillaries are dilated. The endothelium shows no proliferation. The adjacent extravascular tissue usually is normal except for some compression. Various studies of the walls of the vessels have been carried out in the hope of gaining information as to the genesis of the condition. No conclusive results have been obtained. Evidences of atrophy of the various layers is present but no conclusion has been reached as to whether this is a cause or a secondary effect of the dilation.

The dilations of the larger vessels are of three types: arterial, venous and combined. The division is not altogether convincing. Two forms are quite definite: venous and arteriovenous. An enormous variability is present. In general, the lesion consists of a "snarled mass of blood vessels" with multiple communications in the venous and arterial channels. The central mass is made up of blood vessels without any purposeful arrangement. Their luminae are extremely irregular in size and shape. The endothelium usually shows no proliferation (see under neoplastic variety). The structure of the walls of these central vessels apparently has no constant form. Based on the relative amounts of muscle, elastic tissue and collagenous material attempts have been made to classify the structures as veins or arteries. The results are not convincing. It is apparent, however, that these central vessels do show the elements of true larger-sized blood vessels but in an irregular, malformed manner. The elastic and muscle layers are broken and imperfect. There is a marked tendency for secondary changes to occur: calcification and frequently thrombosis. It seems, however, that spontaneous healing by means of these secondary changes occurs, if at all, only uncommonly.

The communications to the arterial and venous systems are multiple. The veins nearly constantly show extensive changes. They are frequently enormously dilated, like sausages, and convoluted. Sometimes sacular deformity is present. The change in the veins is dependent on the arterial force transmitted through the central mass. If the arterial openings are large and the intervening mass is small, the venous change is most marked. In the artificial arteriovenous aneurysms, the most extreme deformity of the veins results because there is no buffering angiomatous mass between the communication. The arterial side of the malformation also suffers. The vessels are dilated, elongated and therefore tortuous. The physical laws governing these changes are not easy to understand. The greatest change again is seen when the arteriovenous channels are widest and with only a few intervening channels. The extreme forms of arterial change are found in the cases of artificial arteriovenous fistulae.

The question arises--what evidence is there to consider these masses of malformed blood vessels as arteries or veins? The histological investigations, as discussed above, are not convincing. However, in case of brain angiomata, the tumor mass has been exposed and actually observed in life without surrounding tissue obstructing the view. In these cases, two types have been seen: one form in which the vessels are full, dark and appearing like a mass of veins and the other form in which the growth is pulsating and arterial blood can be seen inside the vessels.

The mass of vessels, even when it does not manifest invasive powers, is often diffuse and destructive. The boundaries between it and normal tissue are poorly outlined. This is illustrated in a series of 142 muscular angiomata in which 96 were diffuse, 34 were sharply demarcated and 12 were partially encapsulated. The tissue within and between the blood vessels is, at least in some cases, the substance of the organ in which the mass is imbedded. In cases of brain angiomata, the atrophic nerve cells between the vessels can be identified by proper specific staining.

The masses apparently enlarge. In the series of muscular angiomata, the following tissues became incorporated within the mass.

Nerve	16	Synovium	7
Subcutaneous tissue	10	Arteries	6
Periosteum and bone	9	Skin	3
		Veins	3

The effect on the general circulation is interesting. Cardiac hypertrophy is said to be a necessary result whenever the arteriovenous connection is of large size and of long duration. Cushing and Bailey in 9 cases (brain lesions) did not observe any cardiac hypertrophy but frequent reference is made to it in the literature. Two explanations are offered: first, the shunt causes an apparent increase in blood volume (?) and second, the shunt produced an anemia of certain areas with a reflex increase of minute volume resulting in hypertrophy.

The genesis of this group of malformations is not clearly understood. A minority believe that they represent a neoplastic growth of blood vessels. A greater number feel that the masses are malformations.

Some of the lesions are present at birth (Patterson and Romanus). Two cases are reported in which the tumor was so large that it interfered with labor. In many cases, the masses are present at or shortly after birth. In Kramer's 142 cases, 82 were present at birth. In Jenkins and Delaney's group of muscle angiomas, the age of onset is given as follows:

Decade	Number
1	95
2	67
3	30
4	7
5	4
6	1
7	1
8	1

These figures give the impression that the greater number of cases are congenital. A very definite familial tendency is present. Statistical data apparently is not available but most authors have noted the familial nature of the disease.

Blood vessels develop as solid cords of cells which become canalized into channels and these primitive arteries and veins undergo extensive intercommunications and anastomosis before the adult system of vessels is established, i.e., the changes in the primitive gill arches (arteries) and the inferior vena cava (veins). In the meninges, the primitive mesenchyme is supplies by a system of vessels which when three membranes are formed are reconstructed into 3 separate sets. Failure in this proper rearrangement of the vessels is considered to be the starting point of the hemangiomata. The afferent mass of vessels and vascular buds undergoes many changes. Out of them, in late fetal life or any time during postnatal life, purposeless masses of vessels may be developed. The number and size of the communications with the normal arteries and veins apparently changes from time to time. New communications may be established. The relative size of the arterial inlet and venous outlet governs the size and nature of the mass. Fluctuation in size and in symptoms has been repeatedly observed clinically.

It seems that the division into telangiectatic, venous or arterial varieties merely represents stages or degrees in the nature of the malformation. The terms nevoid, spiderform, cavernous, serpigenous, etc. are purely descriptive of the gross appearance.

While this theory is one of a purely mechanical malformation, there is an element of growth, i.e., neoplasm, also involved. The degree of this growth activity is the basis for the separation of the angioblastic group.

The angioblastic or neoplastic type of hemangioma is a rather mixed group. In the type described above, the presenting feature of the disease is the mechanical error in circulation; in this group, the outstanding characteristic is the growth. There may be no circulatory error. Two general types are described: the hemangiomatous cysts and the proliferative, recurring or metastasizing hemangiomata.

The hemangiomatous cysts are characteristically found in the cerebellum but it is suggested that some cysts of the liver, pancreas and kidney are of the same nature. The cysts are small, rarely over 2 to 3 cm. in diameter. They have a thin wall and usually a xanthochromic content. The typical and identifying characteristic of the cyst is a small nodule on the inner surface which microscopically proves to be a mass of small blood vessels or endothelium. Grossly, there is very little to suggest a hemangiomatous origin. The nodule of vessels rarely shows invasive properties. Although it has been suggested that the cyst is formed by degeneration of the central portions, the general concensus of opinion is that there is a ballooning out of the periphery by the secretion of the cells. The cysts are usually multiple: a single cyst in the brain and other cysts in the liver, pancreas or kidney and frequently an angioma of the retinal vessels (Hippel-Lindau syndrome). Nephromata, sometimes bilateral may also be associated with these cysts.

Only a few (6%) of the cysts of the cerebellum are of this type. Cushing and Bailey in 67 verified cystic tumors of the cerebellum made the following division.

Astrocytomas	49
Hemangiomas	4
Spongioblastomas	2
Medulloblastomas	2
Pineoblastomas	1
Unclassified gliomas	9

The other variety of angioblastic tumor is a composite of that already described: venous or arterial hemangiomata, plus an infiltrative nature (usually designated as hemangioendothelicmata because of the abundance of living cells).

The histologic study shows proliferation of the endothelium to form either many layers of cells within sinuses, or solid masses. In some cases, extensive search for areas retaining channels filled with blood is necessary before the nature of the tumor becomes apparent. The growth of the tumor indicates its neoplastic nature: some spread rapidly by peripheral extension, recur after excision or develop metastasis (Menville and Bloodgood, Rea, Broder's, Vinson and Davis, Pettersson and Romanus). True metastasis is questionable. The distal lesion may be another primary tumor. It is characteristic of the condition to be multiple as, for example, in neurofibromatosis. Such solid hemangiomata may also be found in any organ.

Clinico-Pathological Features:

The details of each variety of lesion cannot be given because of the extent of the literature. A few notes and the reference will be given for some of the areas involved.

Breast (Menville and Bloodgood):

3,000 breast tumors, 9 angiomas. Of these, 8 benign and 1 malignant. Clinical diagnosis not easily made. Treatment: radiation; surgery undertaken only in small localized types.

Esophagus (Broder's, Vinson and Davis):

One case in literature: authors report another case (maligment) diagnosed during life on basis of biopsy.

Maxilla (Broderick and Round):

2 cases reported: one died after extraction of a loose, persistently bleeding tooth.

Spleen: (Haines and McIlroy):

1913, 13 cases reported. Reports case of spontaneous rupture of angioma with death due to hemorrhage.

Larynx (Simpson):

In 217 laryngeal tumors, 3 hemangiomata. By 1931, 66 cases reported in literature. Quotes T. H. Sweetser (Laryngoscope 41: 797, Oct. 31) saying that in the adult the angiomata are usually pedunculated and above the cords, whereas in infants they are sessile and below the cords.

Uterus (Dutta, Puscu):

In 1930, 21 cases reported. In the

interval and with the 2 cases in the articles, the total number has risen to 52. All the treated cases recovered excepting one. (Type of treatment not stated). Sudden extreme hemorrhage is a common history.

Vertebrae (Hammes, Alpers and Pancoast):

29 cases in literature (1933). Schmorl Institute, however, reports 10% of 10,000 spines (postmortem) gave some evidence of involvement. The peculiar lack of compression in spite of extensive destruction is commented upon. The roentgenographic features which have been described are parallel, vertical trabeculae of increased density in the bodies of the vertebrae. In Hammes' case, this was absent. Only 4 cases have been cured or improved after operation. Hammes adds another case. Alpers and Pancoast state that in the group, only 11 showed cord compression. None diagnosed before operation. Comments on fluctuation of symptoms. Authors case with compression improved by operation.

Cord (Bucy):

Not common. 1915 only 7 cases, "several" reported since. May be intramedullary, intradural or extradural. Comments on presence of cutaneous hemangiomata in same segment.

Colon (Bancroft):

14 cases found in literature. Present in any part of colon (no mention of small bowel).
Symptoms: melena over long periods often since early life with occasional sudden hemorrhages sometimes fatal. Hemorrhages may occur after operations for other conditions. Surgical treatment poor (because of hemorrhage?). Author cured his case by injection at laparotomy of 1 cc. 40% sodium salicylate solution into main entering vessel.

Bladder and Kidney (Ballenger, Elder, Madden):

16 cases of bladder hemangioma in literature (1st reported in 1851). In Elder quotes Mackay (Brit. J. Surg. 13; 302, '30) saying that 17 cases reported. Total in kidney 18. Main symptom of either is hematuria, often since birth, which is repeated time and again. Pus may be present due to infection of the mass. Madden points out that many "essential hematurias" may be due to telangiectasis in the urinary tract and suggests search for others in exposed parts, such as the nose and skin.

Muscle (Jenkins and Delaney):

Authors analyze 256 cases. (Paper also referred to above at various points).

Duration of symptoms:

0	-	1 yr.	-	24
1	-	5 yr.	-	74
6	-	10 yr.	-	50
11	-	20 yr.	-	36
21	-	30 yr.	-	9
		70 yr.	-	1

Location:

Trunk	84
Upper extremity	64
Lower extremity	107
Not stated	1
Total	256

80% localized to one muscle.

Size: "egg" and "nut" size most common. Range to size up to "child's head.

Skin: over tumor: normal 105 times; blue, 8 times; movable, 55 times; fixed, 6 times.

X-ray:

Negative	10
Phleboliths	14
Calcification	5
Periostitis	3
Soft tissue tumor	2

Note: 19 out of 35 showed some calcification in the tumor.

Results of treatment (radium used only once):

Recovery	198
Recurrence	15
Amputation	3

Sacrifice of tissue and hemorrhage are chief difficulties in surgical treatment. These tumors may be studied by angiography after injection of opaque substance. (Strombeck). Technique given.

Brain:

The literature on the lesions in the brain is very large. The monograph by Cushing and Bailey is the authority on the subject and most of the more recent reports consist of additional case reports.

In general, the signs and symptoms are those of brain tumor. Only a few cases have been diagnosed before operation.

In case of the venous or arterial hemangiomata, epilepsy is a very common symptom. Apparently, a favorite location of the tumor is along the vessels of the motor area; although, as has been suggested, it is possible that more cases with this localization come to operation and hence are observed more frequently. The tumors may occur in other parts of the cerebrum. The epilepsy is followed by a slight or transitory paralysis and the degree of motor involvement seems to progress after each attack. A bruit audible over the mass is a diagnostic point emphasized by Cushing and Bailey. The course is slow. Fluctuation in the severity of symptoms may be present. There is a distinct familial tendency.

In a few cases, cutaneous hemangiomata on the head or elsewhere have been observed. Levine stated that they occurred in 21 of 30 cases. Sometimes the carotid artery is tortuous and dilated. The other symptoms are those of any brain tumor. The epilepsy, progressive paralysis, slow course, familial history, bruit, cutaneous hemangiomata and the tortuous carotid vessel are the features upon which a preoperative diagnosis might be made. In addition, calcification may be present. The calcification is described as "wavy", "gyriform", "scalloped", "latticed" irregular "doubly-contoured" lines which branch. These marks are due to calcium deposits in the wall.

In case of hemangiomatous cysts, in addition to the general symptoms of cerebellar tumor, there may be a history of familial disease (Lindau, 20%), onset of symptoms in childhood, slow course, and eye signs either preceding or following the onset of cerebellar symptoms. The retinal hemangiomata may or may not be present. In Cushing and Bailey's group in 6 cases rechecked with this point in mind, only one showed the lesion. They believe that the retinal angiomata are manifestations of a generalized nature. For example, acoustic neuromas occur more frequently alone but nevertheless are part of the picture of multiple neurofibromatosis.

Cutaneous hemangiomata are rarely found in this form.

The average age (34 years) of the patients with this type of cerebellar tumor is higher than that for the entire group of cerebellar tumors.

The presence of visceral lesions - cysts in the pancreas, liver or kidneys or hypernephroma - might be of diagnostic value. No case in which these were used in diagnosis apparently has been reported although one case is on record where the cerebellum was explored and a tumor found, after a retinal angioma was discovered.

The treatment of the venous or arterial hemangiomata of the brain has not been very successful. Dandy advises ligation of the entering arteries. Cushing and Bailey feel this is not feasible because of the number and depth of the vessels and the danger of bleeding. They advise no surgery to the tumor itself but suggest decompression and heavy radiation. In case of the cerebellar cystic tumors, removal is advised and especially, removal of the nodule projecting from the wall. If the latter is left behind, the cyst reforms.

Bone (Rea):

290 angiomata, none in bone.
1000 bone tumors, 8 angiomata.

In 1931, in the bone tumors of the Registry, of 15 submitted, 7 were classified as angiomas and 6 as hemangioendotheliomas. Only 2 cases of multiple

bone hemangiomata recorded in literature. Author suggests that the hemangiomata of vertebrae found in such high percentage by some authors are dilated vessels in osteoporotic bone, i.e., secondary ectasias of normal vessels.

Thyroid (Rice):

Author reports first case in American literature. 41 cases reported in Europe. It is said that some of these angiomatous masses are secondary degenerations in thyroid adenomata. In the entire group 5 cases showed metastasis.

Liver (Rea):

Only the proliferative type of vascular masses are considered, i.e., "hemangioendotheliomata." Of these, 20 cases were collected in 1929 by one author; in 1930 another considered only 14 as authentic cases. Inclusion of all angiomatous tumors would raise the total very much since the liver is cited as a frequent site of vascular malformations.

Treatment, General

Discussions of the treatment of hemangiomata in general are surprisingly few in the material reviewed. Some pointed statements, however, can be found. Removal of large and diffuse hemangiomata apparently is a formidable procedure. Some authors recommend surgery only in the small localized types. Biopsy wounds may bleed furiously. The summary of the discussions regarding cranial lesions has already been given.

Apparently radiation is the favorite method of treatment but not satisfactory summary of results was found.

Conclusions

1. Hemangiomata are much more complicated than one may realize. Apparently no organ or area in the body is exempt from involvement. Not infrequently is death directly due to tumor.

2. Classification of various types is not satisfactory. The various forms of lesions may be divided into 3 groups: (1) symptomatic, consisting of the secondary angiomatosis and the various forms of artificial arteriovenous aneurysm; (2) malformations, i.e., primary angiomatosis, venous angioma, arterial angioma and arteriovenous angioma; and (3) neoplastic or angioblastomic types of tumors.

3. Secondary angiomatosis is associated with some other disease, such as jaundice, pregnancy, blood dyscrasia, syphilis, thyroid or pituitary dysfunction, cardiovascular disease, lead poisoning, inflammatory disease producing perivascular fibrosis and sepsis. The lesions may be discrete, localized or there may be a generalized process over the entire body. The lesions subside when the patient recovers from his primary condition. Treatment of the lesion, therefore, is unnecessary.

4. Primary angiomatosis or telangiectasis consists of a dilation of the capillaries. The endothelium shows no proliferation and the adjacent extravascular tissue usually is normal. The lesions may be single, multiple, diffuse and present in any tissue or area of the body.

5. Dilation of the larger vessels is said to be of 3 types: arterial, venous and arteriovenous. The divisions are not altogether convincing. Two types are quire definite, i.e., the venous and arteriovenous. In general, the lesion consists of a "tangled mass of blood vessels" with numerous communications of the venous and arterial channels. The central mass of blood vessels is extremely irregular. Study of the structure of the wall shows irregular and malformed muscles, elastic tissue and collagenous material. The differentiation into veins and arteries on the basis of histological appearance does not appear convincing. Frequently secondary changes occur in the central mass of blood vessels, such as calcification and thrombosis.

6. Communications to the arterial and venous systems are multiple. The

veins leaving the mass show extensive changes, such as dilation and saculation. Changes in the veins are dependent upon the arterial force and the amount of intervening angiomatous channel. When the size of the arterial openings are relatively large and the intervening mass of vessels small, the venous changes are most marked. The extreme form is seen in the artificial arteriovenous fistulae.

7. The arteries leading up to the malformation also suffer. The vessels become dilated, elongated and tortuous. Again the greatest changes are seen when the arteriovenous channels are widest and there are only a few intervening channels.

8. In the cases of brain angiomata, the tumor masses can be observed at operation without surrounding tissue obstructing the view. In these cases, 2 types of tumors are present; those which are dark and appear like masses of veins and those in which the growth is pulsating and arterial blood can be seen inside the vessels.

9. The central tangled mass of blood vessels usually does not manifest any invasive power. It is diffuse and compresses the adjacent structures. The intervening tissue is usually the substance of the organ in which the mass is imbedded.

10. Boundaries between the mass and normal tissue are usually poorly outlined. Of 142 muscular angiomas, 96 were diffuse, 34 were sharply demarcated, and 12 were partially encapsulated.

11. The masses enlarge as they become older. In a group of muscular angiomata, the nerves, subcutaneous tissue, periosteum, bone, synovial cavities, arteries, skin and veins may become secondarily incorporated within the mass.

12. It is said that the heart undergoes secondary hypertrophy whenever the arteriovenous channels are of large size and of long duration. Two explanations are offered: (1) the shunt produces an anemia of certain parts with a reflex increase of minute volume resulting in hypertrophy.

13. The genesis of this group of malformations is not clearly understood. The minority believe that they represent a neoplastic growth of blood vessels. A greater number of authors feel that the masses are congenital malformations.

14. Some of the lesions are present at birth and sometimes obstruct labor. In one group of 142 cases, 82 were said to be present at birth. In a group of 256 cases, 95 came on during the first decade, 67 during the second, 30 during the third and only 14 during the remaining decades.

15. From the embryological standpoing, it appears that the central mass of blood vessels is the result of a misplaced embryonic vascular bud. Various communications with the veins and arteries are established either during embryonic life or at a subsequent time and even after the tumor is developed new openings may be formed and these changes produce fluctuation in size and therefore also in the symptoms.

16. The angioblastic or neoplastic form of hemangioma is mixed group. It includes cysts of a hemangiomatous origin and also the various forms of cavernous or solid hemangiomata showing either proliferation, metastasis or tendency to invade and recur. (Hemangioendotheliomata).

17. The hemangiomatous cysts are characteristically found in the cerebellum but it is suggested that some of the cysts of the liver, pancreas and kidney associated with the cerebellar tumor are of the same nature.

18. The cysts are small, have a thin wall and contain a xanthochromatic fluid. The typical and identifying character of the cysts is a small nodule on the inner surface which is made up of small blood vessels or an endothelial mass. These cysts form about 6% of the various cysts found in the cerebellum.

19. The other variety of angioblastic tumor shows a histological character of blood vessels in which the epithelium is rapidly growing,

either producing solid masses of else infiltrating the adjacent tissue and in some cases even producing metastases. The true nature of these metastases is questioned. It is suggested that the distant lesions are other primary tumors.

20. In 3,000 breast tumors, 9 were found to be angiomas and one of these was malignant. The clinical diagnosis is difficult to make before operation.

21. Only 2 cases in the esophagus are reported, one being malignant.

22. Two interesting cases are reported involving the maxilla. One of these had a tooth extracted because of persistent bleeding. Following the extraction, the patient expired in spite of various radical procedures to stop the bleeding.

23. Thirteen cases have been reported involving the spleen. Some of these died suddenly following spontaneous rupture.

24. In 217 laryngeal tumors, 3 were hemangiomas. In 1921, 65 cases were found in the literature. It is said that in the adult the angiomas are usually pedunculated and above the cords, whereas in infants they are sessile and below the cords.

25. Fifty-two cases of angiomatas have been reported involving the uterus. Sudden extreme hemorrhage is a common symptom.

26. Twenty-nine cases involving the vertebra have been reported; although from anatomical studies of the spine, it is said that as many as 10% of 10,000 cases show some evidence of involvement. Possibly these represent ectasias of vessels due to osteoporosis of the bone. Involvement of the vertebra may be very extensive without producing compression. The roentgenographic features are described as parallel, vertical trabeculae of increased density in the bodies of the vertebra. In this group of cases, only 11 showed cord compression.

27. Hemangiomata involving the cord are not common. In 1915, there were 7 cases on record but it is said that several cases have been reported since. They may be intramedullary, intradural or extradural. Here, as also in cases of brain tumors, cutaneous hemangiomata have been observed in the same segment.

28. One author collected 14 cases of the lesion involving the colon. Any part may be involved. Symptoms consist of melena over a long period of time, often beginning in early life and frequently showing sudden severe hemorrhages. Some of these hemorrhages have been fatal. One case of hemangioma of the sigmoid is reported which was markedly improved following the injection of 1 cc. of 40% sodium salicylate solution into the vein exposed at laparotomy.

29. Sixteen cases of bladder hemangioma and 17 cases of the same type of lesion involving the kidney have been reported. Hematuria is often present since birth and is repeated time and again. One author points out that many of the so-called essential hematuria probably are due to telantiectasis in the urinary tract and he suggests that search be made for other hemangiomatas in exposed parts of the body, such as the nose and skin.

30. A large group of the tumors involving muscle have been collected. In a total of 256 cases reported, 84 of these involved the trunk, 64 the upper extremity, 107 the lower extremity. It is interesting to note that in this group, 19 out of 55 showed some calcification in the tumor on the x-ray film. Results of treatment of this group show that 198 recovered, 15 had recurrences and 3 necessitated amputation. Radium was used only once in this group. These tumors in the extremities may be studied by x-ray after injection of opaque substances.

31. An enormous literature has accumulated on the various forms of hemangiomas of the brain. Signs and symptoms which are said to be of value in making the preoperative diagnosis are as follows: epilepsy, paralysis progressing after each attack of epilepsy, slow course, familial history, cutaneous hemangiomata, bruit over the skull and tortuous carotid vessels. In addition,

x-ray of the skull may show a peculiar wavy, doubly contoured line within the tumor which apparently are due to calcium deposits in the walls of the tangled mass of blood vessels.

32. In case of hemangiomatous cysts of the cerebellum, the preoperative diagnosis is difficult to make. One of the most important diagnostic signs is the presence of angiomata in the retina. In addition, the history of a familial disease, onset of symptoms in early life with a slow course may be of value. In one group of 6 cases, only 1 showed the angioma in the retina. Cutaneous lesions are rarely found in this form. Average age in which the patient presented themselves for examinations was 34 years in one series. The peculiar association of cerebellar cysts, retinal angiomas, cysts of the pancreas, liver, kidneys and frequently with bilateral nephroma has been designated as the Hippel-Lindau syndrome or disease.

33. In the bone sarcoma Registry, there have been (1931) 15 angiomatous tumors presented. Of these 2 were doubtful, 7 were classified as angiomata and 6 as "hemangioendotheliomata."

34. In the American literature only one case of hemangioendothelioma of the thyroid has been reported. In European literature (1931) there were 41 cases. Some of these angiomatous masses may be degenerations in thyroid adenomata.

35. With the exception of the tumors in the brain, very little discussion of treatment was found in the material reviewed. Several authors, however, point out that the large and diffuse hemangiomas are dangerous to attack surgically. Bleeding may be furious even from a biopsy incision. Apparently, radiation is the favored method of treatment.

36. In case of brain tumors, the venous or arterial angiomas of the cerebrum when found at operation are best left alone and treated subsequently by radiation. One author advises tying off the arteries.

37. In case of the cerebellar cyst, surgical removal is advised; particularly excision of the small nodule of blood vessels which is secreting the fluid is necessary or otherwise the cysts recur.

38. Of particular interest are the cases reported in the various papers reviewed, or persistent, obscure bleeding, such as hematuria, melena or nosebleed due to a hiddan hemangioma. Of interest also are the cases showing sudden profuse hemorrhage into the body cavities or to the exterior, some of which have proven fatal.

II. CASE REPORT

FATAL, MULTIPLE HEMANGIOMATA

Case is of white male, 36 years of age, admitted to University Hospitals 8-1-33 and expired 9-9-33 (38 days).

"Stroke" in Infancy. Father: three "strokes"

History prior to onset of present symptoms without significance. Laborer; last regular employment was as gasoline station attendant. Had had measles. Left-sided paresis and "stiffness" present since infancy. At age of 2, operation upon left Tendo Achilles for correction of talipes equinus. Father and mother both living, have "arteriosclerosis." Father has had three "strokes." Maternal grandfather died of "kidney disease."

Hemorrhoids; Hematuria for 10 years

Past Complaints: Far-sighted; extensive dental caries, occasional belching of gas, hemorrhoids, occasional hematuria over a period of about 10 years. Had seen blood in urine at various times. Thought it was brought on by colds and by eating heavy meat meals. No other urinary symptoms.

Progressive Neuritic Pains; Weight loss

Onset February 1933, 7 months before death. While at work, observed [illegible] perspiration. About March 1, suddenly developed neuritic type of pain in left lateral and anterior chest.

Pain came in attacks of about 30-minute duration and progressively became worse and more frequent. No relation to depth of breathing or to exertion.

March 15th, Same type of transitory, radiating pain began in interscapular region. Through April and May, the pain more severe and spread to shoulder areas. Forced to stop working. Early part of June, pain developed in arms and arms felt "hot." Head became flexed upon chest and neck stiff.

June 15th, physician called who made diagnosis of acute rheumatic fever. Night sweats developed; became so profuse that three changes of night clothes became necessary. Rapid increase in severity of pain. Relieved by sitting up. Finally, could not stay in bed at all and spent most of time sitting in chair and leaning over table. Last part of July, observed edema of feet and thought that he also had difficulty in controlling his legs. (This last was not observed in the subsequent examination). No pain in legs. Through total period lost 25 pounds.

Admitted - Neuritic Pain

8-1-33 - Large, obese bodily construction. Weight 235 lbs. Left arm and leg spastic and smaller than right extremity. Complains of marked pain in upper part of body and protects arms and shoulders from all contacts. Light touch feels to him like a scratch. No pain on pressure or movement. Kyphosis, scoliosis and stiffness of spine present. Slight edema of feet and ankles. Remainder of examination negative.

Hematuria

Laboratory: Urine (9 catheterized samples) trace or 1+ albumen (in 6 specimens). On two occasions, a few red blood cells seen. Hemoglobin 72% (Sahli), erythrocytes 4,000,000, leucocytes 14,750, with a normal differential count. Blood sugar 99 mgms; blood calcium 12.3 mems.

Multiple Bone Tumors

Numerous roentgenographic studies done. Cervical and thoracic spine show marked hypertrophic arthritis with scoliosis and kyphosis. Considered to be secondary to the muscular paresis. Decalcification of bones present but no evidence of tumor.

Skull: large defect in right parietal area, characteristic of metastatic tumor. Thorax: multiple erosions of ribs on both sides, both posteriorly and anteriorly. These tumors project into pleural cavity and have the appearance of endothelioma of the pleura. Marked destruction of ribs however interpreted as an indication of origin within bone itself. Parenchyma of lung and mediastinum normal. Pelvis and upper ends of femora: multiple osteoclastic tumors involving all the bones but particularly left ileum. This bone almost completely destroyed. Both femora showed similar tumors. Shafts of bones show periosteal proliferation but no erosions. Both kidneys, after intravenous neo-skiodan injection, appear normal.

Consultations: Surgical, urological and ophthalmological consultants added nothing further of note. Neurologist found only the residual evidences of the old spastic hemiplegia.

Course: Course characterized by severe pain in areas previously described. Some days, as much as a grain of morphine sulphate (divided doses) in combination with other sedatives necessary. No new developments until the terminal event.

Sudden Death

Suddenly developed shock-like state with low blood pressure, cold and clammy skin, and thready, rapid pulse. In addition, there was dyspnea and cyanosis. Examination showed complete flatness over entire right chest. Died 15 hours after onset of these symptoms.

The clinical diagnoses were varied. The roentgenologist favored the diagnosis of Ewing's multiple endothelioma of bone in spite of the atypical appearance of the lesions. Other diagnoses which were considered were: multiple myeloma, endothelioma (carcinoma) of the pleura and metastases from an occult parenchymal tumor. A biopsy of the rib tumors was to be done but was prevented by the patient's sudden death.

Autopsy

Autopsy

No Special External Marks

The body is that of a 36 year old, white, male measuring 187 cm. in length and weighing about 230 pounds. The development is of the large muscular type and the body is obese. Rigor is just developing; no jaundice; cyanosis present over face, neck and fingers. The feet and ankles show moderate edema. The abdominal fat measures 30 mm.

No excess fluid present in the Peritoneal Cavity. The surfaces are smooth, glistening and not adherent. The right half of the diaphragm is at the 6th rib and a fluid wave can be palpated through it.

Hemorrhage into Pleura

The mediastinum is displaced to the left side. The left pleural cavity contains no excess fluid and no adhesions. The right pleural cavity contains from 3000 to 4000 cc. of fluid blood. Numerous rounded and oval tumors project into both cavities. The pleura over these masses with one exception is unbroken and smooth. On the convexity of a tumor over the right 6th rib, there is a perforation covered by a small (1 cm.) mass of blood dot. No other defect in the visceral or parietal pleura can be found and therefore this tear into this tumor is interpreted as the source of the hemorrhage into the pleural space. The various rib tumors produced round, oval or spindle-shaped dilations of the bones, ranging in size up to 9x5x5 cm. The growths extend more to the pleural than to the external side of the rib as though following the line of least resistance. The bone in several tumors is completely eroded; in the smaller ones, there is a simple excavation within the medulla. The pericardial sac is normal. No excess fluid or tumors seen.

Cardiac Hypertrophy

The heart weighs 525 grams. Definite hypertrophy of the left ventricle without any dilation. The musculature shows no softening, infarction or fibrosis. The mural endocardium smooth. The valves are well formed, show no evidence of recent or old endocarditis. The root of the aorta has a few atheromatous patches. The coronaries are soft and patent throughout.

No Tumors in Lungs

The right lung weighs 500 grams, left 550. There is some edema in both bases and considerable atelectasis on both sides, particularly in the right lower lobe where there is about 90% collapse of the parenchyma. These areas are bluish in color, soft and flabby. No induration or nodules to indicate bronchopheumonia. No tumors seen within the lung parenchyma.

Visceral Tumors

The spleen weighs 410 grams, is enlarged by the presence of several tumors. One of these tumor masses measures 6.5 cm. in diameter, being approximately round; in addition, there are from 8 to 10 other smaller tumors ranging in size down to about 1 cm. All of these tumors are red, hemorrhagic in appearance and fairly well circumscribed.

The Liver weighs 2850 grams, projects below the costal margin for a distance of about 10 cm. The liver substance itself is somewhat pale and slightly yellowish in color. The liver markings are well retained. The periportal spaces show no fibrosis. Ducts are not dilated. The liver is cut in thin serial sections and 4 very small tumors are found. None of these are larger than 1 cm. in diameter. In the hilus of the liver, there is a tumor mass somewhat lobulated in form, measuring about 5 cm. in diameter. On cross section, there appears to be tumors very much like the others found, hemorrhagic, very little stroma present. The interior of the tumor appears to be composed of blood clot. Along the edges of some of the nodules, a whitish soft stroma can be seen.

The Gall-bladder has a thin wall. The lumen contains no stones. The ducts are patent, not dilated or fibrosed.

Gastro-intestinal Tract: The esophagus, stomach and duodenum show no ulcers or polyps. No tumors. Through the small bowel the mucosa appears normal. There are no tumors found. The colon likewise shows no change.

The Pancreas shows no fibrosis, cysts or tumors.

The Adrenals are well developed and appear rather plump. There are numerous cortical adenomas seen on both sides. No tumors.

Negative (?) Urinary Tract

The Kidneys together weigh 540 grams. The capsules strip easily. No pitting of surface. The cortices and pyramids are well separated. Each kidney is carefully cut in thin sections. There is no evidence of tumor on either side. The pelves appear normal. No papillomas present. The ureters are not dilated. No cause for bleeding identified.

The Bladder has a thin wall. No trabeculation or diverticulae, polyps or tumors. No cystitis.

The prostate shows no hypertrophy, prostatitis or tumors. The seminal vesicles are thin walled and show no fibrosis or infection.

The Aorta shows a few atheromatous plaques in the dorsal area.

Massive Bone Tumors

Bones: The ribs are as described above. In the sternal end of the right clavicle, a small, yellowish nodule about 1 cm. in diameter is found in the medulla of the bone. This nodule is not hemorrhagic but composed of a soft, somewhat gelatinous, yellowish-white material. The spine is not examined except superficially. A chronic hypertrophic arthritis with scoliosis and kyphosis is observed. Both iliae are extensively invaded by tumor. The tumor projects inward into the pelvis and forms masses in each concavity of the ilium. The muscles and fascia overlying this area is stretched out over the tumor. The tumor is fairly well encapsulated. About 300 grams of tumor mass is removed on each side, and more was left behind. This tumor shows yellowish-white areas of stroma but the bulk of the tumor is infiltrated with blood. The ilium on each side is extensively destroyed. The periphery, portion of the posterior part and portions of the rami of the pubis and ischium remain after the tumor is removed. The lower sacrum is involved by tumor which has the general characteristic similar to that described in the ilium. The femora and other bones are not opened.

Head

Examination not permitted.

Summary of Microscopic Findings:

In all the various biopsies of the different tumors, the structure is that of a hemangioma. Large blood sinuses can be seen lined with endothelium and usually filled with blood. There is a varying degree of stroma and endothelium in the different tumors. It also varies within the same tumor mass. Some areas are composed almost entirely of endothelial cells with very little stroma and very little sinus space. On the other hand, there are areas with a well developed stroma that shows the collagen reaction with van Giesen's stain, lined by endothelium and containing blood. These areas have the appearance of a benign hemangioma. The major portions of all the tumor masses examined fail however to give the reaction with van Giesen's stain. They do take the blue stain of the azocarmine. No elastic fibers can be demonstrated within the tumor by means of elastic tissue stain.

Diagnoses

1. Malignant hemangioma, possibly arising in multiple foci.
2. Rupture of hemangioma of pleura.
3. Hemothorax.
4. Cardiac hypertrophy.
5. Pulmonary edema.
6. Pulmonary collapse.
7. Cortical adenomas of adrenals.
8. Tumors involved (at autopsy) clavicles, ribs, liver, spleen, pelvic girdles, sacrum and (clinically) both femora and skull.

Questions

Was the "stroke" at the age of 2 a vascular accident in a cerebral hemangioma?

Were kidney or bladder lesions overlooked at autopsy?

III. ANNOUNCEMENTS

1. DR. WALTER P. GARDNER

Announces the opening of his new office for the practice of Neurology and Psychiatry

at

1054 Lowry Medical Arts Building
St. Paul, Minnesota

Office Hours:
2 to 5 P.M. Tel. CEdar 1393
and by appointment.

2. O. SAMUEL RANDALL, M.D.

Formerly associated with
Minnesota University Cancer Institute

Announces the opening of Offices

1305 Medical Arts Building - -
Fort Worth, Texas

Practice limited to
General Surgery
with Special Reference
to Tumors and Cancer

3. MARCH MEETINGS

There was only one meeting in March, the first (No. 17). Today we resume the series with (No. 18) and, barring unforeseen circumstances the meetings will continue through the spring quarter with the usual summer vacation.

4. CLINIC COMMENTS

The Clinics offered March 26 and 27, through the agency of the Extension Division, to practicing physicians in Minnesota were attended by 130 practitioners. Half the clinics were concerned with malignancy - half with subjects of a more varied nature. All except 14 physicians were from outside the larger cities - only one came from outside the state. A surprising number of recent graduates were present. The audience was exceptional in many ways - It was critical, it was attentive, and it was appreciative. They liked the half-hour time limits (not too long if boring - not long enough if good); they liked the absence of "baby talk"; they liked our attitude toward them; they did not like our soft-spoken teachers (many could not hear certain clinicians); they did not like our amphitheater; they did not like the idea of going home without a promise of more clinics in the fall. Needless to say, those who arranged the meetings appreciate your cooperation and interest.

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5. IN APPRECIATION

I had to put this last, as I find it most difficult to adequately express my appreciation of your kindness to me during and following the fatal illness of Mrs. O'Brien. I wish that I could thank each and every one of you personally, but it would be just as difficult. Although I thought I knew - I never realized the number of good people in this world. I am deeply conscious of a lifetime obligation to you all and I am especially proud to be numbered a humble member of this organization.

Faithfully yours,

William A. O'Brien