MULTIPLE HAEMANGIOMATA

Report of a Case

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Haemangiomata* vary in size from the small capillary telangiectasis to a large variety which may be venous, arterial or arteriovenous in type. They may occur in many different sites including bone, muscle, skin, central nervous system, liver and gastrointestinal tract and may be multiple (Ewing, 1942). One particular syndrome consisting of multiple haemangiomata is hereditary haemorrhagic telangiectasia. In this condition small telangiectases occur mainly in the skin and the mucous membranes particularly those of the mouth and nose. Spontaneous haemorrhage, most often nasal, is a prominent feature of the syndrome, as is a strong family history. The condition is also known as the Rendu-Osler-Weber syndrome after those who first drew attention to it (Rendu, 1896; Osler, 1901; Weber, 1907). Haemangiomata of internal organs have been associated as in one of Osler's cases with stomach involvement, in a case described by Schuster (1937) with telangiectasia of the lungs, stomach and duodenum and also in two cases described by Brink (1950), both of whom had telangiectasia of the lungs; one having a frank arteriovenous fistula in one lung and the other presumed diffuse pulmonary lesions, haematuria and an associated haemangioma of the liver; both cases had central cyanosis and clubbing of the fingers.

Although cyanosis in association with multiple haemangiomata might be expected always to be of the central type as in Brink's cases, peripheral cyanosis has also been found, notably by Constam and Brown (1928) whose patient had generalized cutaneous telangiectasia, by McDonough *et al.* (1940) in a patient with haemangiomata in the liver and in the skin of one forearm and Davison *et al.* (1936) in a case of Von Hippel-Lindau's disease.

The occurrence of haemangiomata of the brain

and spinal cord and membranes has frequently been noted (Barnard and Walshe, 1931; Bucy, 1932; Black and Faber, 1935; Claude and Loyez, 1911; Elsberg, 1932; Globus and Doschay, 1929; Lindau, 1926; Richardson, 1938; Wolf and Wilens, 1934; Wyburn-Mason, 1943; and others). In other cases associated cutaneous haemangiomata have been present often in the nerve root area of the segment of central nervous system involved by the more important lesion (Cobb, 1915; Cushing, 1906; Davison, *et al.*, 1936; Hall, 1935; Hugo, 1927; Johnston, 1938; Kaplan, 1935; Sturge, 1879; Weber, 1922; Wyburn-Mason, 1943).

Also vertebral haemangiomata with associated spinal cord compression occur (Bailey and Bucy, 1929; Blackford, 1943; Ghormley and Adson, 1941; Lindquist, 1951; Manning, 1951; Nattrass and Ramage, 1932; Perman, 1926; and others) and are also sometimes associated with cutaneous lesions (Ferber and Lampe, 1942; Foster and Heublein, 1947; Karshner, *et al.*, 1939), but most vertebral haemangiomata must be asymptomatic as Topfer (1928) discovered an incidence of almost 12 per cent. in routine sagittal sections of the vertebral column in 2,154 autopsies. Multiple bony haemangiomata have been observed (Pierson, *et al.*, 1941; Pohle and Clark, 1945). The patient described by the latter authors had also multiple subcutaneous haemangiomata and a presumed cerebral one also.

The present case is unique in having multiple haemangiomata of skin, bones and probably of liver, also involvement of the central nervous system in two or more sites and associated cyanosis of peripheral type with finger clubbing.

Case Report

A woman of 45 years was admitted to the Bristol Royal Infirmary on August 12, 1953, under the care of Dr. A. M. G. Campbell, for investiga-

*In this paper the term Haemangioma is used to mean any kind of tumour consisting primarily of blood vessels and includes the so-called Haemangioblastoma.

FIG. 1.—Showing marked facial cyanosis.

tion with the complaint of constant blueness, numbness and tingling of the hands and legs, weakness of the legs and ataxia. She had all her life noted a tendency for her hands and feet to become blue and numb when cold but this tendency had become more noticeable about two years before her admission to hospital and had gradually become constant and unrelated to the external temperature. The numbness in the feet had spread gradually upwards until its upper level was midway between the knees and ankles. Twelve months prior to admission she had attended the out-patient department when a diagnosis of Raynaud's syndrome had been made; at that time a full neurological examination had revealed completely absent knee and ankle jerks but no other neurological abnormality. During the 12 month period prior to admission she had noted increasing weakness of the legs and ataxia until latterly she was unable to walk unaided. Some swelling of the ankles occurred towards the end of the day and she had become a little dyspnoeic on exertion.

In 1940 an Albee bone graft had been done for a lumbar spondylolisthesis. In 1951 a small 'naevus' of the left forehead and a small warty

excrecence on the back of the tongue were excised the former had been present since childhood. Both were histologically capillary haemangiomas. For several years the patient had noticed a small swelling behind the right ear which bled freely if damaged when combing her hair. There was no history of spontaneous bleeding or menorrhagia and no sphincter disturbance.

The patient's three sisters had all suffered with blueness of the hands during the winter months and the eldest had a 'naevus' removed from her forehead as a baby. Otherwise the family history was negative.

On admission the patient presented a generalized cyanosed appearance, the face (Fig. 1), hands (Fig. 2) and feet being deeply blue and the remainder of the skin blotchy. The extremities were sometimes cold and sometimes warm but the temperature made little difference to their colour and the superficial capillaries were slow to fill when emptied by pressure. There was slight oedema of the feet but none elsewhere and no congestion of the neck veins. Several small papillomatous lesions were present on the skin; these were about 3 mm. in length and about 2 to 3 mm. in diameter. One was present behind the right ear, another on the left side of the anterior chest wall, one over each iliac crest anteriorly and two in the posterior part of the natal cleft. A linear operation scar from the third lumbar spine to the sacrum was present and another of similar length over the left tibia (Albee bone graft). There was moderate clubbing of the fingers (Fig. 2). The pulse rate was 80 per min. and the blood pressure 150/100. All the peripheral pulses were easily palpable and full. The heart was normal in size and there were no abnormal sounds or bruits. Apart from scanty fine rales at the lung bases the chest was normal. The liver was palpable, the edge being $2\frac{1}{2}$ in. below the costal margin. It was smooth and not tender and no murmur could be heard over it. The abdomen was otherwise normal.

Neurological examination revealed moderate bilateral papilloedema, slight wasting of the small muscles of both hands and some weakness of grip and diminution of pain sensation in the finger tips. Vibration sense was absent in the right arm as far as the shoulder. The abdominal reflexes were absent in the lower quadrants. All muscles below the knees were weak and a little wasted, especially the dorsiflexors of the feet; there was marked foot drop. Knee and ankle tendon jerks were completely absent and there was depression of all forms of sensation below the knees, the feet being almost completely anaesthetic. The calves were tender on pressure. Plantar reflexes were noted

FIG. 2.—Showing cyanosis of hands and also clubbing of fingers.

FIG. 3.—Oblique X-ray picture of skull showing osteolytic lesion in the right posterior parietal region.

FIG. 4.—X-ray picture of left hip region showing osteolytic lesions of ischium and head of femur (the latter are not clearly seen).

FIG. 5.—Lateral X-ray picture of lumbar spine showing haemangioma of body of third lumbar vertebra.

obtainable. The gait was very ataxic and Rombergism marked. Vibration sensation was absent on the trunk up to the clavicles.

No further abnormalities were found in the central nervous system. In particular there was no bruit to be heard over the skull and no saddle anaesthesia was found to touch and pain.

Investigations

Radiology revealed an irregular osteolytic lesion in the right posterior parietal region (Fig. 3), further osteolytic lesions in the left ischium, left femoral head (Fig. 4) and right tuber-ischium. A lesion of the body of the third lumbar vertebra showed the typical honeycombed appearance of a haemangioma (Fig. 5). X-ray films of cervical and dorsal spine, hands and wrists, chest and long bones, apart from left femur showed no abnormality. Electrocardiogram (standard leads, unipolar limb leads and V leads 1 to 6); no abnormality. Semi-horizontal heart.

Blood: Haemoglobin, 108 per cent. White blood cells, 6,400 per c.mm. with normal film appearances. Wassermann and Kahn tests negative. Serum: Bilirubin, 0.4 mg. per cent.

Alkaline phosphatase: Nine King Armstrong units. Thymol turbidity: Six units. Thymol flocculation: Partial. Colloidal gold precipitation: Four units. No cold agglutinins present. Plasma proteins: Total, 7.9 g. per cent.; albumin, 5.7 g. per cent.; globulin, 2.2 g. per cent. Cerebrospinal fluid: Pressure 200 mm. of water. Queckenstedt normal. Clear fluid. White cells, 0 per c.mm. Protein, 85 mg. per cent. Globulin slightly increased. Wassermann negative. Lange colloidal gold curve 1111100000. Circulation times: Arm to tongue (saccharine), 11 sec. arm to lung (ether), six sec. Visual fields: Normal (Bjerrum screen). Arterial blood oxygen saturation 95 per cent. (femoral artery).

Progress

After a short period of rest in bed the oedema of the feet disappeared but returned as soon as she was mobilized. In spite of physiotherapy her walking continued to deteriorate and it was decided to try the effect of a course of radiotherapy to the lesion in the third lumbar vertebra. A course of 3,600 r. in 25 days was given but no improvement occurred and the power in the legs deteriorated still further. Some relief of the cyanosis of the extremities was achieved with the administration of 2-benzyl-imidazoline-hydrochloride ('Priscol'), 25 mg. three times daily. She was discharged home on August 24, 1953 without any substantial alteration in the clinical state and was seen again in the out-patient department on January 7, 1954, when her legs were noted to be weaker than ever, the cutaneous sensory loss in the legs had extended upwards to the mid thighs and there was faecal incontinence. There was also more oedema of the legs but otherwise the physical signs were unchanged. She was seen again as an out-patient on April 8, 1954 when the paralysis of the legs was complete and both arms and shoulder girdle muscles were also very weak. There was congestive heart failure with a grossly enlarged heart, bilateral pleural effusions and ascites. Further progression of her weakness had occurred when she was visited at home in May 1954 and she was bedridden and developing bedsores. She refused further admission to hospital. Shortly after this she developed intense headache and vomiting and died at the beginning of June of pneumonia. Unfortunately no autopsy could be obtained.

Discussion

The patient described was not a typical example of the Rendu-Osler-Weber syndrome because of the absence of the bright red capillary haemangiomas and spontaneous haemorrhages together with

a strong family history which characterize the condition. The lesions removed from the tongue and forehead were, however, histologically haemangiomatous and it is reasonable to assume that the other cutaneous 'papillomatous' lesions were of the same pathology. The vascular nature of the one behind the right ear in this patient was borne out by its frequent bleeding when damaged. The cutaneous lesions found also closely resembled the second type of cutaneous haemangioma described by Osler (1901). Of the bony lesions only that in the body of the third lumbar vertebra showed the typical honeycombed appearance associated with a bony haemangioma, but the others were quite compatible radiologically with this diagnosis, and it is virtually certain therefore that this patient had multiple haemangioma in bones and skin.

Apart from the cutaneous and bony lesions, further haemangioma were no doubt present in the cauda equina and cervical spinal cord; the former giving rise to the progressive lower motor neurone paralysis and sensory loss in the legs with the later sphincter disturbance. This lesion would be in close association with that in the third lumbar vertebra as were the epidural haemangioma with the vertebral ones in the cases reported by Kaplan (1935) and Karshner *et al.* (1939). The cervical cord lesion would explain the progressive sensory loss and weakness of the arms.

The papilloedema and raised cerebrospinal fluid pressure indicated yet another haemangioma within the skull, probably connected with the one seen in the skull X-ray picture, and the enlarged liver with its disordered function tests at a time when there was no venous congestion indicated involvement of that organ also.

The cyanosis shown by our patient was clearly peripheral in type as the arterial oxygen saturation was normal and thus resembled that found by McDonough *et al.* (1940) and Constam and Brown (1928) in their cases. Constam and Brown's case also showed a 'tendency' to clubbing of the fingers. It is to be noted that although there was constant cutaneous cyanosis in our patient, the peripheral pulses were full and easily palpable and the circulation time was about the lower limit of the normal range. It is therefore tempting to postulate that the patient had a general vascular abnormality which allowed stagnation to occur in the superficial capillary bed at the same time permitting an increased flow to the tissues elsewhere. Wilson (1952) has found that clubbing of the fingers is associated with increased local blood flow; also the heart failure in our patient could be explained as due to a longstanding high cardiac output. It is interesting also to note that the cases described by McDonough *et al.* (1940)

and Constam and Brown (1928) both developed heart failure of uncertain aetiology.

Summary

A case is described with multiple haemangioma in skin, bones, liver and various parts of the central nervous system, peripheral cyanosis and clubbing of the fingers with a termination in heart failure.

Reference is made to relevant literature.

The diagnosis and the aetiology of the patient's signs and symptoms are discussed.

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BIBLIOGRAPHY

- BAILEY, P., and BUCY, P. C. (1929), *J. Amer. med. Ass.*, **92**, 1728.
 BARNARD, W. G., and WALSH, F. M. R. (1931), *J. Path. Bact.*, **34**, 385.
 BLACK, W. C., and FABER, H. K. (1935), *J. Amer. med. Ass.*, **104**, 1889.
 BLACKFORD, L. M. (1943), *Ibid.*, **123**, 444.
 BRINK, A. J. (1950), *Quart. J. Med.*, **19**, 239.
 BUCY, P. C. (1932), *Surg. Clin. N. Amer.*, **12**, 1323.
 CLAUDE, M. H., and LOYEZ, M. (1911), *Rev. Neurol.*, **22**, 361.
 COBB, S. (1915), *Ann. Surg.*, **62**, 641.
 CONSTAM, G. R., and BROWN, G. E. (1928), *Med. Clin. N. Amer.*, **11**, 1543.
 CUSHING, H. (1906), *J. Amer. med. Ass.*, **47**, 178.
 DAVISON, C., BROCK, S., and DYKE, C. G. (1936), *Bull. Neurol. Inst., N.Y.*, **5**, 72.
 ELSBERG, C. A. (1932), 'The Diagnosis and Surgical Treatment of Tumours of the Spinal Cord,' 9th Congress, Societe Internationale de Chirurgie, Madrid.
 EWING, J. (1942), 'Neoplastic Diseases,' Saunders, 4th edn., pp. 249-261.
 FERBER, L., and LAMPE, I. (1942), *Arch. Neurol. Psych.*, **47**, 19.
 FOSTER, L., and HEUBLEIN, G. W. (1947), *Amer. J. Roent.*, **57**, 556.
 GHORMLEY, R. K., and ADSON, A. W. (1941), *J. Bone Jt. Surg. (N.S.)*, **23**, 887.
 GLOBUS, J. H., and DOSCHAY, L. J. (1929), *Surg. Gynec. Obstet.*, **48**, 345.
 HALL, G. S. (1935), *J. Neurol. Psych.*, **15**, 305.
 HUGO, H. J. (1927), *J. med. Ass., Sth. Afr.*, **1**, 534.
 JOHNSTON, L. M. (1938), *J. Amer. med. Ass.*, **110**, 119.
 KAPLAN, A. (1935), *J. Mt. Sinai Hosp.*, **2**, 64.
 KARSHNER, R. G., RAND, C. W., and REEVES, D. L. (1939), *Arch. Surg.*, **39**, 942.
 LINDAU, A. (1926), *Acta Path. et Microbiol., Scand., Supp.* **1**.
 LINDQUIST, I. (1951), *Acta Radiologica*, **35**, 400.
 MANNING, H. J. (1951), *Radiology*, **56**, 58.
 McDONOUGH, F. E., DRY, T. J., and ROTH, G. M. (1940), *Proc. Staff Meetings Mayo Clinic*, **15**, 593.
 NATTRASS, F. J., and RAMAGE, D. (1932), *J. Neurol. Psych.*, **12**, 231.
 OSLER, W. (1901), *Bull. Johns Hopkins Hosp.*, **12**, 333.
 PERMAN, E. (1926), *Acta Chir. Scand.*, **61**, 91.
 PIERSON, J. W., FARBER, G., and HOWARD, J. E. (1941), *J. Amer. med. Ass.*, **116**, 2145.
 POHLE, E. A., and CLARK, E. A. (1945), *Urol. Cut. Rev.*, **49**, 283.
 RENDU, M. (1896), *Gaz. des Hopitaux*, **69**, 1322.
 RICHARDSON, J. C. (1938), *Brain*, **61**, 17.
 SCHUSTER, N. H. (1937), *J. Path. Bact.*, **44**, 29.
 STURGE, W. A. (1879), *Trans. Clin. Soc., Lond.*, **12**, 162.
 TOPFER, D. (1928), *Frankf. Zeits. f. Path.*, **36**, 337.
 WEBER, F. P. (1907), *Lancet*, **ii**, 160.
 WEBER, F. P. (1922), *J. Neurol. Psych.*, **3**, 134.
 WILSON, G. M. (1952), *Quart. J. Med.*, **21**, 201.
 WOLF, A., and WILENS, S. L. (1934), *Amer. J. Path.*, **10**, 545.
 WYBURN-MASON, R. (1943), 'The Vascular Abnormalities and Tumours of the Spinal Cord and its Membranes,' Kimpton, pp. 96-183.