Miliary Haemangiomata in the Newborn

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The patient to be described was born with hundreds of haemangiomata of the skin and mucous membrane, and died in the fourth week of life in congestive cardiac failure. Necropsy showed multiple haemangiomata throughout the internal organs. We have called this condition miliary haemangiomata of the newborn and have only been able to find four similar cases in the literature (von Falkowski, 1914; Jaffé, 1929; Taylor and Moore, 1933; Snyder and Doan, 1944).

Case Report

A female infant was born at full term, following an uneventful pregnancy. Delivery was normal, birth-weight 3.4 kg. At birth her skin was covered with hundreds of haemangiomata (Fig. 1, 2, and 3). These were present all over the body, on the conjunctivae and on the buccal and vaginal mucous membranes. They varied in size from a few millimetres to 2 centimetres in diameter. The larger ones were raised above the skin surface. All were bright red in colour and all emptied on pressure. When first examined, on the second day of life, the lesions on the lips were bleeding, the liver was enlarged 3 cm. below the costal margin, and the tip of the spleen was just felt. The infant was feeding well from the breast.

Except for slight bleeding from the oral lesions during feeds, the child remained well until the 18th day when bleeding occurred from an angioma on the left buttock. The child was then admitted to hospital, and at this time examination revealed a soft systolic murmur, slight jaundice, and it was apparent that the skin lesions had become more prominent, and were larger. Hb was 16.7 g./100 ml., MCHC 34%, platelets 258,000/c.mm. Occult blood was present in the faeces.

On the 19th day, the baby became increasingly breathless and had difficulty in feeding. Cyanosis appeared on crying and the liver became larger. The pulse rate increased to 160 per minute. A chest x-ray film showed a grossly enlarged heart with pleonaemic lung fields, but no localized shadows were seen. ECG was normal. She was thought to be in cardiac failure and was given digoxin and sedatives. During the next few days there was some improvement, but on the 23rd day

of life the respiration rate steadily increased, and on the following day she stopped breathing and could not be resuscitated.

Family history. The patient was the second child of the family, and the first, a girl aged 19 months, had no haemangiomata of the skin or mucous membranes. The father had no haemangiomata and neither did the paternal grandmother. The paternal grandfather had one lesion on the shoulder, clinically resembling a de Morgan spot (cherry angioma).

The patient's mother had 12 small stellate naevi over the face, hands, and body but none on the mucous membranes. These had become noticeable during

FIG. 1.—Head and neck of patient showing haemangiomata of lips and skin.

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FIG. 2.—Back of patient.

FIG. 3.—Foot of patient.

pregnancy but were still present 6 weeks later. The maternal grandfather had 10 small haemangiomas on the body resembling de Morgan spots. The maternal grandmother had 6 small similar haemangiomas on the skin and a larger one on the upper eyelid. All these members of the family were examined, and there was no

history of a bleeding tendency or skin haemangiomas in the uncles, aunts, and cousins who were not examined.

Necropsy. Examination of the internal organs revealed large numbers of haemangiomas on the alveolar margins and throughout the gastro-intestinal tract. There were 47 lesions in the jejunum, 51 in the ileum, and 2 in the colon. The stomach was clear except for one lesion in the fundus.

The liver was enlarged (200 g.) and had a large number of lesions both on its surface and in its substance. There were many pale pink-yellow areas up to 1.5 cm. in diameter and two larger fluctuant, red areas measuring 3.5×3 cm. in the right lobe. These two lesions were full of blood, and contained a central cavity which was lined by the firm, pink-yellow tissue. They intercommunicated, and drained into an enlarged hepatic vein (Fig. 4). When the liver was cut, the parenchyma was deeply bile-stained.

The pancreas showed three haemangiomas on the anterior surface, the largest being 1 cm. diameter, and lesions were also present on the surface of the thymus.

One haemangioma was present in the larynx at the level of the cricoid cartilage. The lungs showed congestion and a number of small haemangiomas were seen, particularly on the anterior borders. The bladder showed one small lesion above the right ureteric orifice.

A large haemangioma ($1.5 \times 1 \times 1$ cm.) was present in the right cerebellar hemisphere. No haemangiomas were detected in the heart and great vessels, spleen, lymph nodes, bone-marrow (femur, vertebrae, and sternum), kidneys, endocrine glands, cerebrum, spinal cord, and meninges.

FIG. 4.—Cut surface of liver showing the large communicating haemangioma and many smaller ones.

FIG. 5.—Photomicrograph of haemangioma of skin. (H. and E. $\times 540$.)

The heart (44 g.) showed gross right atrial and right ventricular dilatation and hypertrophy.

Histological findings. The histological picture was one of interconnecting cavernous spaces lined by a single layer of flattened endothelium, supported on a loose fibrous stroma. This was seen typically in the lesions of

the skin and alveolar margin (Fig. 5). In some tissues there were minor variations in this pattern.

In the liver were seen a number of different histological pictures which probably represented stages in the development of the condition. First was a small circumscribed area in which there was proliferation of vascular tissue and of bile canaliculi. Many bile thrombi could be seen

FIG. 6a, b, c.—Photomicrographs of three different haemangiomas in the liver, showing the three distinct pictures described in the text. (H. and E. $\times 351$.)

in the surrounding liver tissue (Fig. 6a). In the next stage, the proliferation was more marked and much less well circumscribed. At the edge of the lesion the liver cells were surrounded and cut off into small islands (Fig. 6b). In the final stage, there was no normal liver in the involved area which consisted of a complex of interconnecting cavernous spaces between which ran many bile canaliculi (Fig. 6c). Throughout the liver many areas of extramedullary haematopoiesis were to be seen.

In the three isolated pancreatic lesions the central part was composed of cavernous haemangioma, but around the periphery islands of pancreatic cells were seen surrounded by the proliferating vascular tissue in much the same way as was seen in the liver. There was also proliferation of pancreatic ducts but no 'islet' tissue was seen in these abnormal areas. In the intestinal tract the angiomata lay in the mucosal layer and involved the intestinal villi, some of which were completely replaced by thin-walled cavernous spaces. In the larynx they occurred between the cartilage and epithelium, and in the lung the lesions were seen only in the interlobar septa. The para-aortic lymph nodes, though macroscopically normal, showed thin-walled, ill-defined angiomata.

The lesion in the cerebellum was mainly confined to the spaces of Virchow-Robin, but in places the substance of the cerebellum itself was invaded by angiomatous tissue.

The bones, muscles, kidneys, spleen, spinal cord, cerebrum, thyroid, adrenals, pituitary, ovaries, and uterus were normal.

Discussion

The unique feature of this case is the presence at birth of a very large number of haemangiomata scattered over the skin, mucous membranes, and throughout many internal organs. Four published cases appear to resemble ours. von Falkowski (1914) reported a 2-month-old baby boy with multiple angiomata of the skin, gums, liver, and spleen who had breathlessness and paroxysmal tachycardia. A baby girl was described by Jaffé (1929), in whom a tumour mass was present on the neck and about 100 haemangiomata were scattered over the skin. At necropsy haemangiomata were also present in intestinal tract, lungs, spleen, meninges, thyroid, and bones. Death occurred at the age of 9 months, from streptococcal meningitis. Taylor and Moore (1933) described a 3-month-old girl with many pin-head and pea-sized raised haemangiomata scattered over the skin surface and a large haemangioma over the labia and perianal region: the infant died at 5 months after aspiration of milk, but was apparently anaemic from blood loss. Haemangiomata were present in the liver and lungs. The case reported by Snyder and Doan (1944) also had haemangiomata over the skin, mucous mem-

branes, intestinal tract, mesentery, liver, pancreas, and trachea. The coloured photograph accompanying their paper shows that the skin lesions were very similar to our case, except that, in addition, there was a huge angioma involving most of the front of the chest. Two patients have had similar skin lesions which have shown spontaneous disappearance (Fischler, 1960; D. G. Vulliamy, 1965, personal communication) but as there was no necropsy the internal organs could not be studied.

In the cases of Jaffé (1929), Taylor and Moore (1933), and Snyder and Doan (1944), in addition to the scattered haemangiomata, there was one very large lesion, and Taylor and Moore discuss the possibility in their case that this was a primary tumour, with multiple secondaries. In our case, the histological picture, particularly in the internal organs, showed some features that were difficult to interpret. There appeared to be some invasion and destruction of the normal tissue. However, the cells and cavernous spaces which they formed were regular and orderly in their size, shape, and staining; no mitotic figures were seen and the over-all picture did not suggest a malignant condition.

The heredity aspects of our case require assessment. The mother had a few stellate naevi first noted during her pregnancy, and both her parents had a few de Morgan spots (cherry angiomas). These are both very common conditions and would not justify a diagnosis of hereditary telangiectasia in the maternal side of the family. The father and paternal grandmother had no vascular lesions, and there was only one de Morgan spot on the paternal grandfather. There is, therefore, no evidence of an inherited tendency.

Snyder and Doan (1944) thought that their case was an example of the homozygous form of hereditary telangiectasia (Rendu-Osler disease) which is normally inherited as a dominant. Sommacal (1957), in reviewing the four cases similar to ours and another seven infants with multiple haemangiomata, thought that there was no proof that heredity was involved in the aetiology of the condition. In view of these conflicting opinions, and the widespread acceptance of those of Snyder and Doan, the evidence these authors present must be examined critically. The father and mother of their patient had eight and three small telangiectatic foci, respectively; there were none on mucous membranes. The maternal grandfather suffered from epistaxis as a child and had 15 lesions on the skin, but none on mucous membranes. The paternal grandmother had 12 typical telangiectatic tufts on the skin but none on mucous membranes. A paternal uncle was said to be a 'bleeder', having

experienced a near fatal haemorrhage from an unspecified site at birth. The latter sounds most unlike a case of hereditary telangiectasia, the scarcity of lesions and particularly their absence on mucous membranes, together with a negative history of bleeding must make the diagnosis of the other members of the family uncertain. Without better evidence that both sides of Snyder and Doan's case had hereditary telangiectasia we must agree with Sommacal that there is no evidence of a hereditary basis for this syndrome.

The jaundice which developed in our case was presumably due to intrahepatic damage and loss of liver tissue. The cause of the heart failure from which the infant died is of interest. In 1953 Levick and Rubie first recognized heart failure in early infancy due to a multinodular haemangio-endothelioma of the liver. These authors concluded that the heart failure was due to arteriovenous shunts, and these were in fact demonstrated in another case by Le Tan Vinh, Obaldia, Canlorbe, and Lelong (1959). Since 1953 a number of similar cases have been reported (Winters, Robinson, and Bates, 1954; Crocker and Cleland, 1957; Clatworthy, Boles, and Newton, 1960), including one which also had several angiomas of the skin (Desbaillets, 1963). More recently, Cooper and Bolande (1965) have demonstrated the presence of arteriovenous shunts, by post-mortem angiography, in haemangiomata of the head and neck, and also in the mesentery and small bowel. Another case has been described, where neonatal death from heart failure was due to a large cavernous haemangioma of the left thigh (Cohen and Sinclair, 1963). The same mechanism presumably caused the heart failure in our patient, and it is interesting to note that the case similar to ours described by von Falkowski (1914) died with breathlessness and paroxysmal tachycardia, and at necropsy enlargement of both ventricles was found.

Summary

A female baby born with hundreds of haemangiomata of the skin and mucous membranes is described.

Death from heart failure occurred in the fourth week of life, and at necropsy haemangiomata were found throughout the intestinal tract, in the liver,

pancreas, larynx, lungs, bladder, lymph nodes, and cerebellum.

Although invasion of surrounding tissue was apparent in the liver and pancreas, the histological features were not those of malignant disease.

The hereditary aspects of this case and those of four similar published cases are discussed and it is concluded that there is no evidence of an inherited basis for this condition.

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Addendum

Since submitting this paper, a brother to our patient has been born, and he does not have a single cutaneous haemangioma.