HEREDITARY HAEMORRHAGIC TELANGIECTASIA (RENDU-OSLER-WEBER DISEASE) IN A CHINESE FAMILY

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Hereditary Haemorrhagic Telangiectasia (H.H.T.) is a rare familial disease in which sporadic bleeding occurs from vascular lesions distributed throughout the body, especially in the skin and mucous membranes.

Sutton (1864) is generally credited to be the first to give a description of the disease. A year later Babington (1865) described a hereditary disease characterised by recurrent epistaxis, which he traced through five generations; but he did not mention the nature of the lesion. Wilson (1869) described a patient with eruptive angiomata on his face, neck and arms and epistaxis and bleeding gums but he did not state whether the disease was hereditary. Rendu (1896) recognized the hereditary nature of the disease; he reported a 52 year-old man who had epistaxis and small angiomata of the skin of the face, neck, thorax and mucous membranes of the mouth; the patient's mother and brother also had epistaxis and his father had melaena. He termed the disease pseudohaemophilia. But the disease was not widely recognized until the publications of Osler (1901) and Weber (1907). The name Hereditary Haemorrhagic Telangiectasia was proposed by Hans (1909). At present Hereditary Haemorrhagic Telangiectasia is widely referred to as Rendu-Osler-Weber Disease.

The disease has been observed in most of the European races and in Jews (Garland and Anning, 1950). It was not recognized in Negroes till 1948 (Schwartz and Armstrong). Reports of its occurance in Asians are scarce; because of this we are reporting its occurence in a Chinese family.

REPORT OF A FAMILY

W.L.P. a 47 year-old Chinese baker presented with epistaxis. He had been having 3 to 5 episodes of epistaxis since the age of 20 years; he found that packing his nasal cavities with cotton wool and manual compression helped to stop the bleeding. He was hospitalised in 1960, 1962 and 1967 for melaena.

Physical examination showed that his height was 64 inches and his weight was 108 lbs. There were multiple telangiectases over the skin and mucous membranes: in the face, ears, neck, hands and feet, arms and legs, trunk, conjunctiva, lips, gums, tongue and oral mucosae (Figs. 1, 2 and 3). In the nose, bleeding was seen in the nasal septum around Little's area. The fundi were normal. He was anaemic and he had slight clubbing of the toes and fingers but there was no cyanosis. The heart was slightly enlarged and there was a soft systolic bruit over the inferior angle of the left scapula. The liver, spleen and kidneys were not palpable but there was no bruit in the abdomen. The nervous system was normal.

Laboratory investigations showed a haemoglobin level of 12.6 Gm.%; the leucocyte count was 7,100/cu. mm. while the platelet count was 115,000/cu. mm. His blood group was 'Group A'. The partial thromboplastin, bleeding and clotting times were normal. The Hess's tourniquet test was normal. X-ray of the chest showed slight cardiomegaly; the lung fields were within normal limits (Fig. 4). There was occult blood in the stools but there was no haematuria. The erythrocyte sedimentation rate was 8 mm./hour. A barium meal examination in 1963 showed multiple gastric ulcers.

Patient's mother had episodic epistaxis since the age of 20 years. She died in China at the age of 55 years following a bout of severe epistaxis. His father had no history of bleeding tendency. Patient is the only child in the family. His father had a son and a daughter with a second wife; both are well. Patient's wife has no telangiectasia; there are 3 sons in the family. The eldest son is 25 years old and he had an episode of epistaxis at the age of 5 years. He had mucular telangiectases over his left ear, face, tongue, left hand and chest (Fig. 5). The second son is 12 years old; he also has telangiectases over his upper lip and hands. The youngest son is 8 years old and telangiectases were found over his lower lip, hands and left foot. The two younger sons had no bleeding episodes. The family tree is shown in Fig. 6.

Patient's epistaxis stopped in the ward with nose packs. He was started on ethinyl oestradial 0.25 mg. and methyl testosterone 5 mg. daily. On

Fig. 1. Propositus: Telangiectases over face, lips, ears and neck.

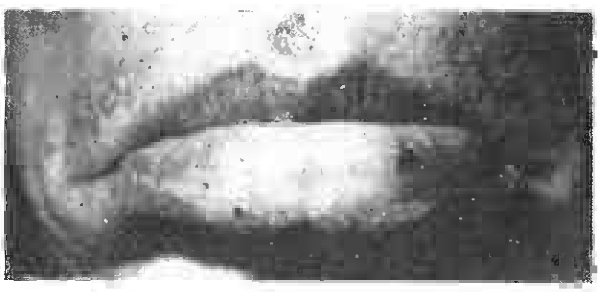

Fig. 2. Propositus: Closer view of the telangiectases over the lips.

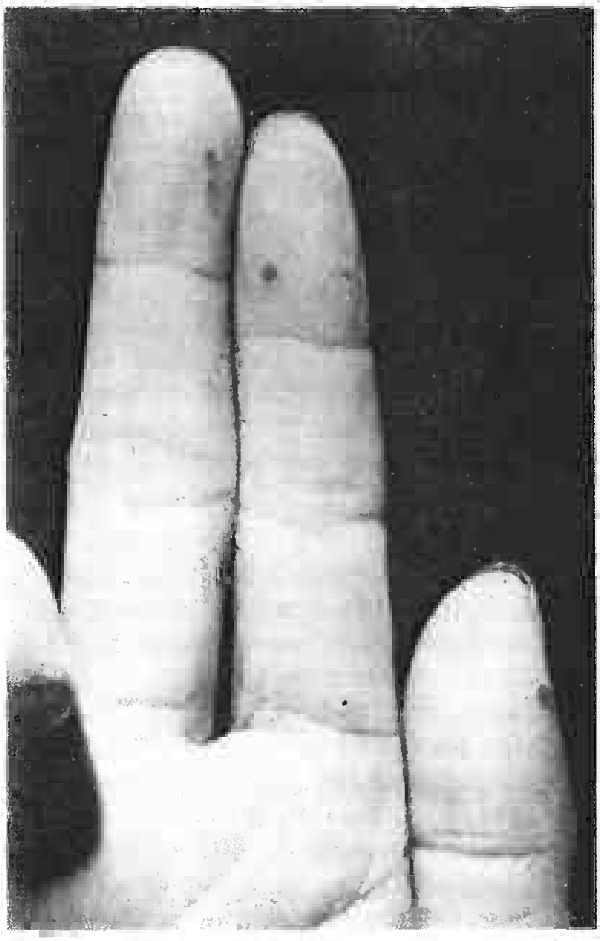

Fig. 3. Propositus: Telangiectases over the fingers.

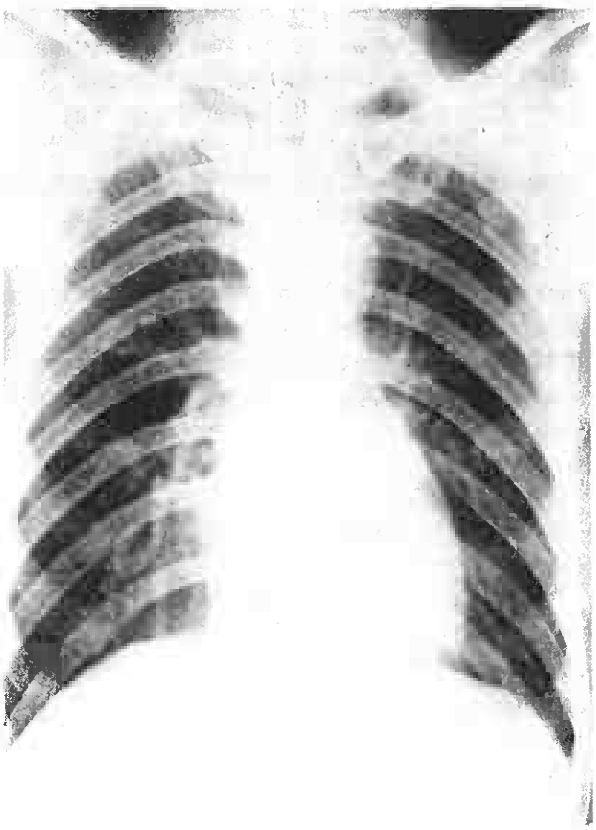

Fig. 4. Propositus: Chest X-ray showing cardiomegaly.

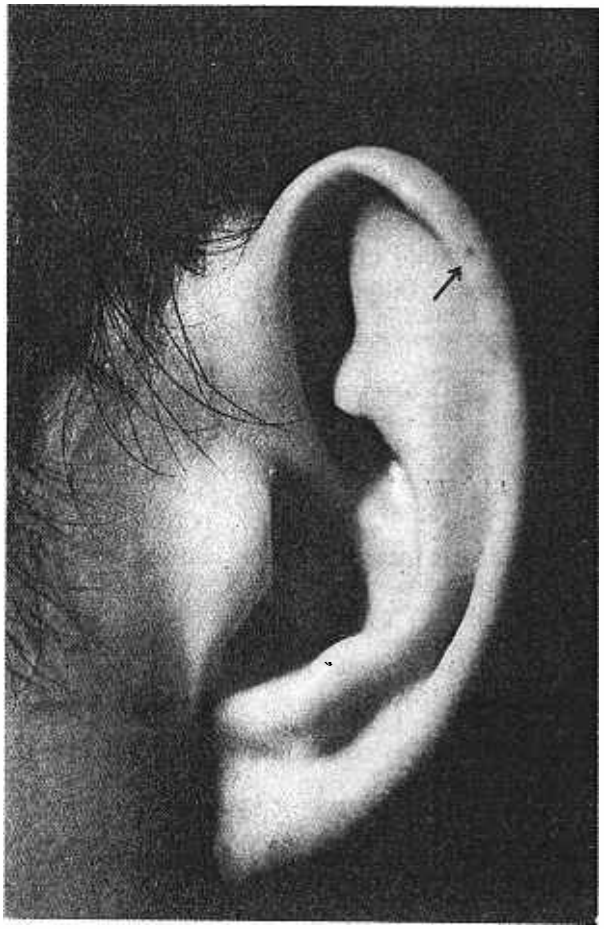

Fig. 5. The eldest son: Telangiectasia over the left ear.

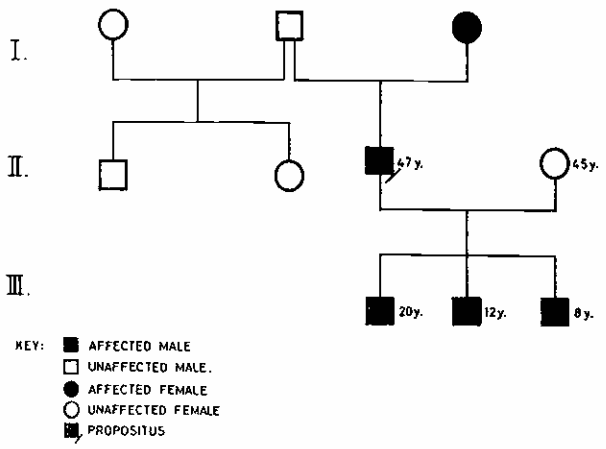

Fig. 6. Family tree of the patient: 5 members over 5 generations are affected. The number besides each symbol indicates age in years at which physical examination was done; those symbol without numbers denote absence of examination.

this regime his epistaxis had improved both in frequency and severity. He developed cholestatic jaundice and methyl testosterone was replaced with intramuscular injection of testosterone propionate 100 mg. weekly. He has been on this regime for 6 months.

DISCUSSION

An inspection of the family tree of our patient (Fig. 6) shows that H.H.T. is transmitted as an autosomal dominant disease. Its dominant trait with a high degree of penetration is well established; both sexes are affected equally (Garland and Anning, 1950). Sporadic cases have been attributed to atavistic skipping (Fitz-Hugh, 1923).

Osler (1907) described 3 types of skin and mucosal lesions: macules, spiders and nodules. Macules are the earliest lesions while spiders and nodules develop later on. The lesions are usually not visible at birth but become evident during the second to the fifth decades of life. But exceptions occur: Snyder and Doan (1944) reported a case of a baby in whom the disease was evident at birth and was fatal in 3 months.

The commonest presenting symptoms is epistaxis: as is seen in our patient, his mother and his eldest son. Epistaxis may be mild or severe or even fatal as was the case in our patient's mother. In 83 cases described by Dolowitz (1953), 68 (81.9%) had recurrent epistaxis. Cappon (1945) reported that one of his patients lost 1½ pints of blood from epistaxis in less than 2 hours.

Like the father of the patient reported by Rendu (1896), our patient also had 3 episodes of melaena. Thirteen per cent of patients with H.H.T. have melaena or haematemesis; 6% have duodenal ulcer. In those with a gastrointestinal bleeding, 85% have telangiectasia of the lips while in those who have telangiectasia of the lips the incidence of duodenal ulcer rose to 19% (Smith, Bartholomew and Cain, 1963).

It is likely that our patient had pulmonary arterio-venous fistulae as he had clubbing, cardiomegaly and a bruit over his left scapula, although the chest X-ray was negative and no pulmonary angiogram was carried out. The presence of pulmonary arteri-venous fistula in H.H.T. was first recognized by Whitaker (1947). Pulmonary arterio-venous fistula occurs in about 5% of patients with H.H.T. (Bergqvist, Hessen and Hey, 1962). Mayer, Glantz and Brest (1962) stated that out of 220 patients with pulmonary arterio-venous fistulae, 78 (35%) had telangiectasia. Complications include rupture of the fistula causing haemoptysis and haemorthorax; endarteritis with multiple abscesses and cerebral embolism with thrombosis or brain abscess (Dine, Claggett and Bonebraker, 1967). Alexander and Harrington (1955) reported cerebral symptoms in 27% of patients with pulmonary arterio-venous fistulae; while brain abscess

occurred in 9 out of 170 cases (Hodgson and Kaye, 1963).

Patient was the only child in his family: this is not surprising as Goodman, Gresham and Roberts (1967) reported that there was a higher incidence of miscarriage and there was relative infertility in H.H.T.

Vischer (1951) postulated that the gene for H.H.T. may be coupled with the gene for the blood group "O"; patients with the blood group "AO" and "BO" can suffer from the disease. Our patient's blood group is "A": this apparently supports the above postulation. The relationship between H.H.T. and Willebrand syndrome has been described by Quick (1967).

Treatment of H.H.T. is symptomatic and consists mainly in checking bleeding and combating anaemia. Packing of the nose is still the most common procedure to stop epistaxis. Other measures that are sometimes successful include a rubber bag inflated to act as a pressure tampon, application of haemostatic agents such as oxidised cellulose gauze to the bleeding sites, cauterisation by electric or chemical agents and X-ray therapy.

In 1952, Koch, Escher and Lewis made the important observation that oestrogens reduce the haemorrhagic tendency in H.H.T. They observed that in their first case, a 44 year-old woman, epistaxis occurred during the 5 days before onset of menstruation and stopped with the onset of menstruation. Our patient has benefited from oestrogen therapy. There are surprisingly few reports on the use of oestrogen in H.H.T. (Harrison, 1956; Shapiro, 1953).

Pulmonary arterio-venous fistulae may be excised surgically. Hodgson and Kaye (1963) advise excision for patients with cyanosis and polycythaemia, for those who have haemoptysis and for those whose lesions appear to increase in size. Unfortunately the lung lesion may be multiple.

The treatment of gastrointestinal bleeding in H.H.T. is unpredictable. Following gastrectomy, patient continued to ooze to death in the cases reported by Ratnoff (1960) and Williams and Brick (1955). Successful gastrectomy was reported by Condon, Tanner and Cowper (1967) in a woman with hepatic artery aneurysm, H.H.T. and gastric and duodenal ulcers while Everett (1967) reported that subtotal resection of the small intestine was successful in stopping bleeding due to telangiectases of the small gut.

SUMMARY AND CONCLUSION

A Chinese family suffering from Hereditary Haemorrhagic Telangiectasis (Rendu-Osler-Weber Disease) is described. Five members in 3 generations are affected. The disease is transmitted as an autosomal dominant trait.

The beneficial effect of oestrogen in diminishing haemorrhage especially epistaxis is described.

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