RESULTS OF TREATMENT BY SEPTAL DERMOPLASTY (SAUNDERS' OPERATION) IN HEREDITARY HEMORRAGIC TELANGIECTASIA (RENDU OSLER'S DISEASE). A REVIEW OF 12 CASES

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Hereditary telangiectasia of the skin and mucous membranes is always considered a rare disease with an incidence less than that of hereditary purpura haemorrhagica or haemophilia. However, it constitutes a nosological entity which is well defined and easily diagnosed. It is a hereditary vascular dysplasia and consists of cutaneous and mucous telangiectases which bleed easily despite there being no alteration in the coagulating mechanisme of the blood. Telangiectases and angiomata are frequently localised at the level of pituitary mucosa and clinically present with recurrent epistaxis causing anaemia. This has, for a long time, resulted in the disease being considered the realm of rhinologists and haematologists. But, in recent years the implications of the disease have widened and a study of its visceral aspects is of interest to gastro-enterologists, urologists, chest physicians and to surgeons. This familial angiomatosis presents itself as an immature disease.

Although Sutton described telangiectases as early as 1864, it was Babington in 1865 who first recognised "hereditary epistaxis". He reported in "The Lancet" seven cases of recurrent epistaxis which were distributed through four generations of the same family. In 1896, Rendu from Paris, differentiated the disease from other haemorrhagic conditions, in particular from haemophilia. Osler, in 1901, confirmed Rendu's clinical description, emphasising the hereditary characteristics in what he called "familial recurrent epistaxis associated with multiple telangiectases" with absence of any abnormality of haemostasis. So, from this time, "epistaxis-disease" was differentiated from "epistaxis-symptoms". Weber's works, published in "The Lancet" from 1904-1907 circumscribed and completely defined the symptomatology of this condition, usually known as "Rendu-Osler-Weber's disease".

The hereditary nature of this condition is almost always apparent. Genetic studies by numerous workers have shown the disease is transmitted as an autosomal dominant.

The two sexes are equally affected. Wintrobe's work has shown that the frequency of the condition is relatively high in countries of Anglo-Saxon origin, less common in Latin races, rare in Jews and very rare in Negro races (only three cases had been published up to 1957).

Anatomically, Rendu-Osler's disease has characteristic telangiectases with lesions of the skin and mucous membranes. Mucosal telangiectases, always accompanied the cutaneous lesions but, able to exist alone, are very superficial seated just beneath the respiratory epithelium. The nasal distribution is almost

constant. The figures of Mme Blanchet-Capot (Thesis, Paris 1959) show that in 72% of cases, the septum is affected, while in 33% it is the turbinates. The lesions are most frequently situated on the nasal septum at the level of the Little's area or behind it. The inferior and middle turbinates are frequently involved. Lesions may be diffuse, spreeding behind the nasal fossae, rarely as far as the cavum. In the course of our surgical work, we were impressed by the frequency of lesions on the floor of the nose.
The dorsal surface of the tongue is involved in 50% of cases, the hard and soft palate in 27%, the gums in 17%, the mucous membrane of the cheeks in 13% of cases. Lesions of these sites are easily observed when they are present and facilitate diagnosis.
Livingston and Carr (1956) have shown in histological studies the existence of vascular cavities of irregular size and shape. Their wall is very thin, consisting of a single cellular layer of simple tubular epithelium, lacking the elastic and muscular components. The surrounding chorion is formed by thin, loose connective tissue without elastic fibers. The connective tissue which separates the lacunae of blood contains degenerated collagen and elastic fibers in the telangictatic zones.

Thus it is a hereditary disease of the vascular mesenchyme which must be considered a tissue monodysplasia.
Above all, one must emphasize the progressive nature of this telangiectatic dysplasia, which recurs after various attempts of therapy and which makes treatment very difficult. The histological structure, with its cavities of blood, facilitates understanding the frequent failure of different methods of treatment. The pathology of this curious condition continues to be disputed; the commonly hold theory at present is that it is a systemic disease affecting the arterio-venous anastomoses.
Clinically, it is a progressive condition, the symptoms becoming more troublesome as time goes by. It usually begins with occasional epistaxis in late childhood or before puberty, or more rarely after 20 years of ago. The frequency of nose-bleeds varies from patient to patient. Initially minimal, their frequency and their severity gradually increase. After some years, the haemorrhages may occur daily.

The second stage, that of confirmed haemorrhagic angiomatosis, develops after a few years and is recognised by the appearance of cutaneous and mucous telangiectasis. Sometimes, lesions develop gradually and the patient and his family find it difficult to state the date of onset with any accuracy; sometimes, on the contrary there is a rapid development of telangiectatic tissue, which may be manifested by hemorrhages, usually from the nose. Thus, the course of the disease progresses and may be accompanied by increased frequency and severity of epistaxes. These can menace the patient's life and repeated blood transfusions may be required.
The epistaxis may remain isolated or there may be associated bleeding from deep mucous membranes: haematemesis, haemoptysis, intestinal haemorrhage, haematuria-potentially dangerous bleeding which may be heavy and treatment may be very difficult.
So, the patient becomes chronically anaemic and this is characteristic of the third and often terminal period of the condition (Hicquet and Cambrelin); hypochromic anaemia develops, which the patient is unable to control. There

may be less than 3 millions red blood cells with anisochromia and a haemoglobine of less than 6 gr/100 cc of blood and a colour index of less than 1. The serum iron may be lowered to 20—50 γ /100 ml. The various tests to establish the haemostatic properties of the blood are always normal.

The prognosis of Rendu-Osler syndrom must always be guarded and in severe or recurrent forms death from haemorrhages is not infrequent. Does this explain the number of methods of treatment that have been recommended for this condition? Here we shall restrict ourselves to describing different means of therapy used in the nasal manifestations of Rendu-Osler's disease and emphasize, in many instances their inadequacy.

The frequent recurrence make the appraisal of their efficiency very difficult in view of the progressive nature of this telangiectatic dysplasia.

Medical means (vitamins P, K, C, snakes venom, hormonal therapy by ethinyloestradiol, in the male associated with testosterone, and synthetic antihistamines) have only an auxiliary value. Transfusions of whole blood or of packed red cells, sometimes combined with iron therapy, only counteract the consequences of haemorrhages. Local treatment with plugging, compression with gelatin or spongel, plugging with finger-stalls of goldbeaters skin (Wintrobe) and cauterisation by chemical or thermic methods are valuable only in mild forms of the disease. Injections with sclerosants (quinine-urea) is very difficult to perform.

Electro-coagulation, difficult because of the diffuseness of the lesions, is often used but predisposes to a risk of perforation of the nasal septum and of haemorrhage when the scab separates.

Treatment by physical agents is currently popular with most authors and it appears that it often cures or produces prolonged remissions.

The diffuse spread of the angioma on the entire nasal mucosa (septum, floor, turbinates) poses a difficult problem in the distribution of the dose over the whole surface.

Radiotherapy (1500 r in 2 latero-nasal fields) can be effective, or sometimes treatment with radium. This is widely used since Mac Key and Mac Kenty (1927) used a nasal probe containing tubes of radium. Its disadvantage is that it is inadequate in the upper parts of the nasal fossae and it is difficult to repeat due to the risk of an overdose (hence necessitating treating one nostril at a time) and of the frequency of cartilaginous necrosis producing a septal perforation.

Pierquin improved this method, using wires of radioactive gold or iridium in place of radium. They are placed in plastic tube with 3 radioactive wires controlled by a magnifying light.

An interval of two months is allowed between treatment of each nostril. Perquin's technique permits homogeneous irradiation of the nasal fossae.

We have ourselves obtained an almost similar result by placing radium needles in a piece of nylon sponge which is inserted in the nasal fossa to be treated.

In the severe or recurrent forms of Rendu-Osler's disease, the frequent failure of all these techniques has led to the consideration of surgical treatment. Arterial ligation (external carotid artery, anterior ethmoidal artery and even internal maxillary artery) is not without danger and usually has only a small and transitory effect.

Submucous resection of the septum has been advocated. Cervino and Wirth,

in 1948, recommended bilateral resection of the septal mucosa "as a window" possibly associated with ligation of the ethmoïdal arteries. In 1956, Kindler and Tiedmann resected the entire nasal septum.
In October 1959, at the Academy of Ophtalmology and Oto-Rhino-Laryngology of Chicago, Saunders presented the surgical treatment which he had developed for severe forms of the disease. It consisted of the excision of part of the septal mucosa, leaving the perichondrium in place, followed by a skin graft after paralateronasal rhinotomy.
We have been very interested in Saunders' procedure and have used it with slight modifications in 12 cases of Rendu-Osler's disease which had epistaxis severe enough to interfere with social and professional life and to cause severe anaemia. In eleven of the twelve cases, surgical intervention followed failure of others treatments.

The technique was as follows:
— Operation under general anaesthesia with controlled hypotension.
— The nostril is exposed by a low para-latero nasal incision, enabling the alae nasae to be elevated to explore the corresponding nasal fossa (the height of the lesion has surprised us and explains the failure of radiumtherapy).
— Elevation of the septal mucosa, facilitated by an associated local anaesthetic, the perichondrium being left in place.
— Excision as widely as possible of the septal mucosa in its whole height, continued at the base of the septum on the floor of the nasal fossa.
— Haemostasis, usually by compression, sometimes with the aid of an electric bistouri.
Placing the skin-graft: this is of glabrous skin, taken from the thigh. It is a split thickness graft of 0,5—0,6 mm thickness.
— Suture of the graft, which is fixed at the base, at the top and in front by interrupted sutures of chromic catgut or silk 000.
The graft is pushed back posteriorly and applied carefully to the septum. If there is a septal perforation, the graft forms a bridge accross the perforation.
— Lesions of the turbinates, which are often very important, are treated by extensive and deep electro-coagulation.
— At the end of the operation, the nasal fossa must be free from blood.
The nose is packed with gauze impregnated with terramycin and hydrocortisone ointment. The nasal flap is replaced and is sutured in two layers.
— The packing is removed on the eighth day.

Study of our reports shows that Saunders' operation gives very good results in practically every case. Postoperatively, there are often crusts which gradually disappear and usually after several months, the skin graft gradually acquires a mucosal appearence. It does no develop mucosal glands but is moistened by mucus secreted by neighbouring glands.
Only once we have seen a recurrent haemorrhage due to a small granuloma situated at the junction of the graft and the floor of the nasal fossa. This was easily tied off and treated by electro-coagulation.
In another case, operated on over three years ago, the patient has occasional small epistaxis, incomparably smaller than the pre-operative bleeding and she is delighted with the result. Septal perforations, common when the disease

used to be treated by radium or electro-coagulation, do not give problems, the graft forms a bridge across the perforation.
The aesthetic result is good. The scar, in the line of the nasal fold is rapidly almost inconspicious. Surgical intervention of Saunders is not physiological, involving the replacement of mucous membrane by a skin graft (this is its aim since Saunders described the skin by the expression "lining constitutionally able to indure") taken from a zone little affected by the telangiectatic process. We have observed that one is often surprised to see the nature of the graft change progressively, as it acquires, little by little, the characteristics of mucosa.
An important secondary result is frequently recorded in the opposite nasal fossa where we have often observed a diminution of the frequency and the severity of epistaxis, though we do not know why. For this reason, even when the patient requires surgery to the other nasal fossa, is seems desirable to delay the second operation for several months after the first, in order to allow time for spontaneous improvement to take place.
We have stressed that frequently the mere fact of skin grafting transforms the graft into a mucosal-type lining and the nature of the graft seems to be of little importance. If utilisation of a graft of cheek mucosa or of fascia lata were advocated, we think that only two points are of significance for the success of the intervention.
— The ablation as completely as possible of the diseased mucosa, completed by electro-cautery of telangiectases on the turbinates.
— Covering the exposed perichondrium (the perichondrium ensures vascularisation of the graft) by a graft of which the epithelial or connective tissue nature matters little.
A follow-up of our earlier cases for over six years justifies the value of the procedure and our outlook.

RÉSUMÉ

La maladie de Rendu-Osler, télangiectasie hémorragique héréditaire cutanéo-muqueuse, débute habituellement par des épistaxis dont l'importance s'accroît peu à peu. La répétition des hémorragies, leur abondance conduit le malade le plus souvent à un état d'anémie hypochrome parfois très grave nécessitant des transfusions répétées et un traitement local hémostatique.
L'échec et l'insuffisance des différents moyens thérapeutiques utilisés, qu'il s'agisse des traitements médicaux, de l'électro-coagulation, des ligatures artérielles, de la radiothérapie ou de la curiethérapie ou encore de l'utilisation des isotopes tels l'Au 198 ou l'Iridium 192 ont amené Saunders à codifier le traitement chirurgical des formes graves de la maladie de Rendu-Osler par une dermoplastie septale effectuée à l'aide d'une greffe mince de peau après résection de la muqueuse malade.
Nous avons utilisé cette technique dans 12 cas de maladie de Rendu-Osler entraînant des épistaxis graves, perturbant la vie sociale et professionnelle de nos patients et entraînant une anémie importante. 11 fois, l'intervention a été pratiquée après échec des autres thérapeutiques. Les résultats sont bons. Les hémorragies cessent habituellement totalement permettant au malade de reprendre des activités sociales et professionnelles normales.
Les suites immédiates sont souvent marquées par la présence de croûtes

CASES REPORTS

	Age at time of operation	Sex	Other members of the family affected by the disease	Age at the beginning of the disease	Former treatments	Surgical intervention	Follow-up and results
Case 1	54	M	Mother died from epistaxis	44	1954: Röntgentherapy 5000 r. 1961: 3 tubes of radium in the right nostril: 7,2 M.C.D.	1/29/1964 Saunders' operation on the right side.	May 1970. Nice graft. No further bleeding. All is right.
Case 2	67	F	Maternal grand-mother - A cousin.	36	1953: Radiotherapy 5000 r.	2/5/1964 Saunders' operation on the right side.	No further bleeding. Crusting in the early months, this gradually disappearing.
Case 3	65	M		Always nose bleeds.	1948: Repeated cauterisations. 1953: 3 tubes of radium in the left nostril. 1954: Cauterisation. 1965: Anaemia blood transfusions on 7 occasions.	3/31/1964 Saunders' operation on the left side.	One year and four years later; no further bleeding. The graft is good. Slight crusting.
Case 4	40	M		26	On four occasions, radium tubes inserted in his nose.	12/8/67 Saunders' operation on the left side.	August 1968. Nosebleeds requiring a second intervention: granuloma at the junction of the graft and the floor of the nasal fossa coagulation. May 1970. No further bleeding.
Case 5	65	M	Both parents A brother A sister	Since childhood.	Since 1949: Repeated cauterisation. 1953: 3 tubes of radium in the left nasal cavity. 1954: Repeated cauterisations. 1962: Bleeding so heavy that 7 blood transfusions are required.	11/25/1965 Saunders' intervention on the left side.	One year later. Excellent result. Good craft. No crusting. No further bleeding. Mucosal appearance of the graft.
Case 6	60	M	Mother; an uncle a brother; the eldest son.	Since infancy.	Blood transfusions. 1958: Radiumtherapy.	4/13/1967 Saunders' operation on the left side. 5/11/1967 Saunders' operation on the right side.	January 1970. No further bleeding. The patient is well.
Case 7	61	F	A brother.	Since puberty.	1961: 4 tubes of radium in the two nostrils.	4/3/1967 Saunders' operation on the left side.	1970. A few crusts. A few very small haemorrages occasionally. The patient is satisfied.
Case 8	65	F	Father.	Early childhood		9/10/1968 Saunders' intervention on the right side. 9/5/1969 Saunders' intervention on the left side.	May 1970. The patient is well. No further bleeding.
Case 9	73	F	A sister.	Since childhood.	1966: Tubes of radium in the nose. Numerous cauterisations.	10/2/1969 Saunders' intervention on the left side. 3/12/1970 Saunders' intervention on the right side.	July 1970. No further bleeding on either side.
Case 10	56	F	The father. An uncle. A grand-mother. 2 cousins. 1.child.	18	Frequent transfusions but for one year badly tolerated (presence of cytotoxic antibodies and antithrom-bocytic antibodies).	12/2/1969 Saunders' operation on the right side.	June 1970. The patient is delighted.
Case 11	45	M	Father; a daughter 16 years old.	12	Frequent cauterisations.	1/30/1970 Saunders' intervention on the left side.	June 1970. Excellent condition. No further bleeding.
Case 12	48	M	A brother. All his second cousins.	25	Radium on four occasions 1957, 1959; 1960, 1961.	3/16/1970 Saunders' operation on the left side.	June 1970. All is well.

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qui disparaissent peu à peu et après quelques mois, la greffe prend habituellement un aspect muqueux. Une seule fois, nous avons eu une petite récidive hémorragique due à un petit granulome siègeant à la jonction entre la greffe et le plancher de la fosse nasale, récidive d'ailleurs facilement jugulée par une électro-coagulation. Les perforations septales habituelles si le malade a été traité auparavant par curiethérapie ne sont pas génantes. Les résultats esthétiques sont bons, la cicatrice est rapidement presque inapparente. Nous croyons sage de ne réaliser l'intervention qu'un côté après l'autre en deux temps séparés par quelques mois. Nos cas les plus anciens ont un recul de plus de 6 ans, ce qui prouve la valeur du procédé.

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