ANGIOKERATOMA OF THE SCROTUM (FORDYCE)

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Since Fordyce, in 1896, first described a case of angiokeratoma of the scrotum, many authors have reported and discussed about this dermatosis. However the classification and the nomenclature of this skin disease still remain in a state of confusion. Recently I had a chance to see the report of Robinson and Tasker (1946)⁽¹⁴⁾, discussing the nomenclature of this condition, which held my attention considerably.

In this paper I wish to report statistical observation concerning the incidences of this dermatosis among Japanese males, and histopathological studies made in 5 cases of this condition.

STATISTICAL OBSERVATION

It must be first pointed out that this study was made along with the statistical study on angioma senile and same persons were examined in both dermatosis (ref. Studies on Senile Changes in the Skin I. Statistical Observation; Journal of the Keio Medical Society Vol. 28, No. 2, p. 59, 1951).

The statistics was handled by the small sampling method. Totals of persons examined were 1552 males. Their ages varied from 16 to 84 years, divided into seven groups: i.e. the late teen-agers (16-20), persons of the third decade (21-30), of the fourth decade (31-40), of the fifth decade (41-50), of the sixth decade (51-60), of the seventh decade (61-70) and a group of persons over 71 years of age. The number of persons and the incidence of this condition in each group are summarized briefly in Table 1.

Tab. 1. Incidence of ANGIOKERATOMA OF THE SCROTUM

Age	Number of cases examined	Positive cases	Occurrence %	Confidence limit	
				upper limit %	lower limit %
16-20	887	5	0.56	1.47	0.20
21-30	330	5	1.52	3.91	0.54
31-40	97	6	6.19	14.17	2.43
41-50	84	11	13.10	23.65	6.59
51-60	67	9	13.43	25.88	6.28
61-70	63	10	15.87	29.15	5.74
71→	24	4	16.67	40.00	5.40
Totals	1552	50	3.22	4.41	2.24

Angiokeratoma of the scrotum is one of the skin changes which are due largely to age, significant difference being noticed among the incidences of the above mentioned groups ($\chi^2=121.056$, $n=3$, $p<0.001$). Its occurrence is already seen in the late teen-agers, though rather infrequently. As ages advance, its incidence gradually increase and it is especially noticed in males past 40 years of age. The incidence in male over 31 years of age is $\frac{11.94\%}{15.26\% \sim 9.18\%}$ (Occurrence percentage/Confidence limit: upper limit~lower limit). The youngest male seen having this condition was 18 years old.

CLINICAL PICTURE

I had an opportunity to see 50 cases of this dermatosis during the period I was making this statistical observation. Finding nothing particular in the clinical picture of this condition from the reports which were described in details up to this time by many authors, the clinical appearances are briefly summarized as follows.

Angiokeratomas of the scrotum are noted along the course of the veins and capillaries as dark red nodules from the size of a millet grain to that of a pinhead. In the younger lesions the nodules appear bright red just like the senile angiomas and give no signs of warty appearances. This type is usually observed in the younger males, the lesions numbering from 2 to about 7 or 8. As ages advance, the lesions generally increase in number and size and becoming dark or purplish red with warty appearances. As a rule they cause no symptoms.

In regard to the causation of this dermatosis, it has been considered that there is often a history of preceding venous obstruction in the form of varicocele, tumor of the epididymis, hernia, hernioplasty or postoperative trauma of the venous system resulting in venous occlusion⁽¹⁴⁾ or of chronic inflammation in the scrotum such as seen in chronic eczema⁽¹²⁾. In my observed cases no history of the causes leading to this condition was noticed, and furthermore we could find no evidence proving that this dermatosis was related to a preceding history of pernio or of frostbite as in angiokeratoma of Mibelli. But what was interesting was that I noticed its close relation to senile angiomas as summarized in Table 2. Significant difference was shown clearly between the occurrence of this condition in positive cases of senile angiomas and in the negative cases of same ($\chi^2=73.932$, $n=1$, $p<0.001$). The incidence of this condition in positive cases of senile angiomas being $\frac{9.57\%}{13.72\% \sim 6.52\%}$ is much greater than that in negative cases.

Tab. 2. Incidence of ANGIOKERATOMA OF THE SCROTUM
in person with and without ANGIOMA SENILE

Angioma senile	Angiokeratoma of the scrotum	Positive cases	Occurrence %	Confidence limit	
				upper limit	lower limit
Positive cases	418	40	9.57%	13.72%	6.52%
Negative cases	1134	10	0.88%	1.78%	0.42%
Totals	1552	50	3.22%	4.41%	2.24%

HISTOPATHOLOGY

Histopathologic studies were made in 5 biopsy cases of this dermatosis. In each of the cases one small scrotal lesion was examined with the exception that in case 3 four of the tumors were put to examination. Their ages were 35 yrs. (case 1), 41 yrs. (case 2), 51 yrs. (case 3), 67 yrs. (case 4) and 79 yrs. (case 5). The sections were fixed in formalin solution and embedded in paraffin. Staining methods employed are such as hematoxylin and eosin stain, Weigert's stain, elastica-van Gieson's stain, Mallory's stain, Berlin blue iron stain, amyloid reaction with Bennhold's congo red stain, fibrin stain and T. Pap's silver stain.

The chief change in this dermatosis is seen in the epidermis and the upper layer of the dermis. In the papillary layer of the dermis, capillaries are noticed dilated and increased in number. With this histologic changes the capillaries are pushed into the epidermis accompanying the surrounding connective tissue, and as the downward growth of epithelial cells concurrently progresses it forms gradually a kind of cave so that the involved tissues are finally enclosed in the epidermis, connected only through the mouth of this cave with the underlying dermis. Examining a series of specimens, these involved tissues are either seen enclosed entirely in the epidermis or only the thickened epidermis forming a great wall deep in the dermis with no other particular changes can be noticed. Other particular changes noticeable in the epidermis are hypertrophy of the stratum corneum and slight parakeratosis in some cases (cases 2 and 4). Turning our attention to the involved tissues enclosed in the epidermis, we found that the endothelial wall of the capillaries are generally well retained, even in places where the blood vessels are noticed to be greatly enlarged. The collagen fibers surrounding these vessels are also retained. The elastic fiber border, too, is well retained, but in the vicinity of the apex of the cave formed by the thickened epidermis the elastic fibers bordering the extremely enlarged capillaries are diminished or lost. On the other hand, the elastic fibers around the mouth of

this cave are found greatly increased in number. In some cases (cases 2 and 4) the capillary wall is partly injured in the vicinity of the apex of this cave resulting in slight subepithelial and intraepithelial hemorrhages, the blood cells or thrombus being noticed under or within the epidermis. No cellular infiltration was observed in the connective tissue of the involved lesion, but this change consisting of chiefly mononuclear cells was slightly noticeable mostly around the blood vessels in the neighboring upper layer of the dermis. Such a change is not considered a constant or significant feature of this condition.

Studying the histologic picture more minutely, the endothelial cells of the capillary are seen arranged either closely or scatteringly, their nuclears being unequal in sizes. The collagen fibers surrounding the blood vessels especially in the vicinity of the epidermis are found undergoing hyalinization. With this hyalinization the nuclears are noticed usually unequal in sizes, some of them indicating signs of pycnosis, and they are decreased in number almost disappearing in the most distinctly changed place. The elastic fibers do not appear elastic at all, but found as ragged threads suggestive of degeneration. The epithelial cells are seen prominently growing downwards and finally enclosing the involved papillary layer in a form of a cave, but at the apex of this cave the rows of these cells are diminished while at both sides these are seen thickened, in which place the stratum granulosum are seen proliferated to several rows of cells rich in keratohyaline granules. The stratum spinosum is thinned in the vicinity of the apex, cells of which part are diminished and becoming flattened in appearance, their nuclears being unequal in sizes and often indicating signs of pycnosis. The cells of the basal layer which forms the inner wall of the cave are also diminished and flattened with unequal or pycnotic nuclears, and the formation of pigment is almost entirely absent. With T. Pap's silver stain the basal membrane lying under the epidermis is well retained, but where damaged at places the capillaries are noticed injured also.

In summarizing the histologic pictures of this dermatosis found in 5 cases, in which careful studies had been made, it can be said briefly as follows:

The histologic changes characterizing this condition are new formations as well as dilatations of papillary vessels, proliferation and downward growth of epithelial cells finally enclosing the papillary vessels with their surrounding connective tissues in a form of a cave, and hypertrophy of the stratum corneum. The elastic and collagen fibers are, in general, well retained, but indicate somewhat undergoing changes, especially hyalinization in the latter. In the vicinity of

the apex of the thickened epidermis the elastic fibers are found diminished or lost. At times the capillary wall is partly injured resulting in slight subepithelial and interaepithelial hemorrhages. But no evidences of inflammatory reactions are noticeable.

COMMENT

After careful studies, Mibelli reported in 1889 a disease of the skin usually located on the hands and feet chiefly on the dorsal sides of the fingers and toes and characterized by telangiectatic and warty lesions in persons having history of pernio as "angiokeratoma Mibelli". Fordyce, in 1896, regarded his case described as "angiokeratoma of the scrotum" as an atypical case of angiokeratoma Mibelli. In 1925 Hudelo⁽¹⁴⁾ stressed the fact that a definite differentiation must be made between Mibelli's case and Fordyce's case. Later Wile and Belote (1928)⁽²⁵⁾, Traub and Tolmach (1931)⁽²⁰⁾, Robinson and Tasker (1946)⁽¹⁴⁾ and others discussed the same problem. In Japan reports discussing the differences between these two dermatosis were made by Tohyama (1907)⁽¹⁹⁾, T. Itoh (1908)⁽⁷⁾, Sasakawa (1908)⁽¹⁾, Matsumoto (1915)⁽⁹⁾, Sakaguchi and Odaka (1917)⁽¹⁶⁾ and M. Itoh (1924)⁽⁶⁾. Discussions dealing with the classification of this dermatosis may be roughly divided into the following three groups:

1. That angiokeratoma of the scrotum is an atypical case of angiokeratoma Mibelli.
2. That angiokeratoma of the scrotum is an atypical case of angioma senile.
3. That angiokeratoma of the scrotum should be classified as an atypical angiokeratoma differentiating it from angiokeratoma Mibelli.

The authors who may be said to maintain the first view are Fordyce, Traub and Tolmach⁽²⁰⁾, Tohyama⁽¹⁹⁾, T. Itoh⁽⁷⁾, Sasakawa⁽¹⁷⁾, Sakaguchi and Odaka⁽¹⁶⁾ and M. Itoh⁽⁶⁾. They are of the opinion that angiokeratoma of the scrotum and angiokeratoma Mibelli are apparently identical in both their histologic and clinical appearances. Gans (1925)⁽⁴⁾ regards that angiokeratoma Mibelli sometimes appears on the scrotum as Fordyce's type. Wile and Belote⁽²⁵⁾, Weidman⁽²²⁾, Ormsby⁽¹³⁾, Montgomery⁽¹¹⁾ and Robinson & Tasker⁽¹⁴⁾ strongly support the second opinion considering that no essential histologic differences exist between angiokeratoma of the scrotum and angioma senile, both dermatosis presenting the picture of vascular nevus with no histologic signs suggestive of trauma of blood vessels or of subepithelial or intraepithelial hemorrhage or inflammation as found in angiokeratoma of Mibelli. Wertheim (1932)⁽²³⁾ describes in Jadassohn's Handbuch

that angiokeratoma of the scrotum is closely resembled to angioma senile. The third view is maintained by Matsumoto⁽⁹⁾, considering that, though the histologic and clinical appearances of angiokeratoma of the scrotum are identical with those in Mibelli's case, angiokeratoma of the scrotum should be included in the group of atypical angiokeratoma entirely differentiating it from angiokeratoma Mibelli, for the reason that the etiologic factors and location in both cases are clearly different in nature.

According to my observations, this dermatosis, angiokeratoma of the scrotum, could be clearly differentiated from angiokeratoma Mibelli in the following three points; first, angiokeratoma Mibelli occurs in childhood and young adult life, while this dermatosis is closely related to age, especially found in ages over 40 years. In the second place the latter is located on the hands and feet particularly on the dorsa of the fingers and toes, while the former is seen on the scrotum. Thirdly, there is a history of pernio or chilblain in Mibelli's case, while in this condition there are no evidences proving its close relation to pernio or chilblain. On the other hand this dermatosis is markedly resembled to angiokeratoma Mibelli in its clinical and histologic appearances. For instance the histologic picture of case 4 is almost identical to that of angiokeratoma Mibelli, showing dilatations but not new formations of papillary vessels with signs of injured blood vessels resulting in subepithelial and intraepithelial hemorrhage so that the differentiation between the histologic pictures of these two dermatosis could be hardly made. But in the histologic features of other cases the papillary vessels showed pictures of new formations as well as dilatations with no signs suggestive of inflammation.

In this study the statistical observation was made without differentiating angiokeratomas of the scrotum from angiomas of the scrotum, and it must be emphasized that the histologic features were studied on tissues taken at random from small scrotal tumors regardless of whether they were angiokeratomas or angiomas from persons of each decade as aforementioned, and that all of the tumors showed the same characteristic histologic picture of angiokeratoma, as previously described. Thirdly, this condition was noticed closely related to angioma senile, and occurred mostly in angioma senile positive cases. Referring to the reported literature of this dermatosis, angioma is said to occur on the scrotum (Dohi)⁽³⁾; Weidman has the opinion that there is nothing fundamentally different in the pathologic pictures of the angiomas of the scrotum and angiokeratoma of the scrotum; Montgomery⁽¹¹⁾, in the discussion of Schweitzer's case⁽¹⁸⁾, states his belief that when lesions of senile ectasia occur on the scrotum, they tend to multiply

and there may be some hyperplasia of the epidermis; Sakaguchi and Odaka⁽¹⁶⁾, reported that angiokeratoma of the scrotum in its early stage appear as simple telangiectasia showing histologic changes of only dilatation of the papillary vessels with no signs of hypertrophy of both stratum corneum and stratum spinosum, or inflammation, but in the next stage the papillary vessels are greatly dilated, the growth of epithelial cells are seen progressing and finally enclosing the vessels like a cave and hypertrophy of the stratum corneum are noticeable.

From these observations and discussions concerning this dermatosis, it is reasonable to consider, to my belief, that this condition occurs on the scrotum just as in the same way angioma senile develops on the trunk or other parts of the body without noticeable etiologic factors, but the fully developed lesions of this condition closely resemble with angiokeratoma of Mibelli in their clinical and histologic appearances. Moreover interesting fact is that this condition refers largely to age, already seen in the late teen-agers, gradually increasing as ages advance, and particularly occurring past 40 years of age.

Consequently, as formerly regarded it does not seem unrational to consider this dermatosis as an atypical case of angioma senile or as an atypical case of angiokeratoma Mibelli, but when pointing out the apparent differences between these two dermatosis in their etiologic factors and locations, it is rather reasonable to differentiate this dermatosis from both of these two skin diseases and classify this condition, according to my opinion, under skin changes due largely to age or the so-called senile changes.

SUMMARY

I observed statistically the incidents of angiokeratoma of the scrotum in 1552 males over 16 years of age, and had chances to study 50 cases clinically. Furthermore the histopathology of this condition was studied in 5 cases. From these observations it was summarized as follows:

1) Angiokeratoma of the scrotum is one of the skin changes due largely to age. Its occurrence is already seen in the late teen-agers, though rather infrequently. As ages advance, its incidence gradually increases, and especially over 40 years of age.

2) The incidence in male over 31 years of age is $\frac{11.94\%}{15.26\% \sim 9.18\%}$ (Occurrence percentage/Confidence limit: upper limit~lower limit).

3) Angiokeratoma of the scrotum is greatly related to angioma senile, and it is seen in $\frac{9.57\%}{13.72\% \sim 6.52\%}$ of angioma senile positive cases.

4) The histologic changes characterizing this condition are new formations as well as dilatations of papillary vessels, proliferation and downward growth of epithelial cells finally enclosing the papillary vessels with their surrounding connective tissues like a cave, and hypertrophy of the stratum corneum. The elastic and collagen fibers are, in general, well retained, but indicate somewhat undergoing changes, particularly hyalinization in the latter. In the vicinity of the apex of the thickened epidermis (cave) the elastic fibers are noticed diminished or lost. At times the capillary walls are partly injured resulting in slight sub-epithelial and intraepithelial hemorrhages. But no evidences of inflammatory reactions are noticed.

5) In my opinion, angiokeratoma of the scrotum should be differentiated from both angiokeratoma Mibelli and angioma senile, and classified under skin changes due largely to age or the so-called senile changes.

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Angiokeratoma of the Scrotum
(Fordyce)

Case 1. 35 yrs.
Hematoxylin and Eosin
(high power)

Case 1. 35 yrs.
Weigert's Stain

Case 4. 67 yrs.
Hematoxylin and Eosin