COMMUNICATIONS

TELANGIECTATIC GRANULOMA—BOTRYOMYCOSIS

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As these two historically closely associated conditions are rarely met with in ophthalmological literature, a typical case of telangiectatic granuloma of the eyelid may be of interest.

Botryomycosis was first found by Bollinger (1869) in the lung of a horse; 10 years later Rivolta described the frequent botryomycotic tumour in stallions after castration. After that, cases in the skin, muscles, the udders of a mare, the inner organs of horses were described as well as occasional cases in other animals (Torlais). The most recent article on the subject dealt with a case in a pig (Clarenburg and van Heelsbergen, 1933).

The disease is characterized by conglomerates of little globules, measuring 5/100 micr. and resembling a bunch of grapes. The globules consist of a thin capsule, containing numerous cocci, measuring about 1 micron. Under the influence of this botryococcus ascoformans (syn. zoogloea pulmonis equi [Bollinger], dyscomyces equi [Rivolta], micrococcus botryogenes [Rabe], botryococcus ascoformans [Kitt]) tumours develop consisting of a framework of connective tissue filled up by granulation tissue. In the centre of these areas of granulation tissue the conglomerates of botryomycotic globules are found. Often this centre becomes necrotic and melts together, fistulae develop towards the free surface, in the discharge of which the conglomerates of typical globules can be found enabling a clinical diagnosis.
The botryococci freed after rupture of the capsule of the globules, cannot be differentiated from ordinary staphylococci in the smears. As to the possibility of differential diagnosis in cultures opinions differ though all authors agree that at any rate the differences are extremely small. It can only be stated that one has not succeeded up till now in obtaining botryomycotic tumours with ordinary pyogenic staphylococci, as has been reported for the botryococcus. In an inoculation experiment with botryococci, recently performed by Clarenburg and van Heelsbergen, the botryococci proved to be pyogenic (development of abscesses), in the neighbourhood of which a small tumour developed, containing the typical globules.

Telangiectatic granuloma was formerly described under the heading "human botryomycosis" by Poncet and Dor, who first described these little granulomata in man and claimed to have found the typical cocci (1879). Already in 1899, however, Sabrazès and Laubie denied a relation with botryomycosis and created the name telangiectatic granuloma. The staphylococci are chiefly found on the surface and not in the typical arrangement in globules. Nevertheless, recently authors again tend to accept the pathogenetic rôle of staphylococci, expressed in the name granuloma pyogenicum (Hartzell).

Though the histological picture of Poncet and Dor was afterwards corrected by other authors—they claimed to have found sweat-gland elements in these little tumours—the clinical picture they gave was frequently confirmed and now as many as 450 cases have been published.

In spite of the fact that in 75 per cent. of cases these little tumours are reported to arise after an injury, the wound itself is never persistent, as in an ordinary granuloma. Apparently the injury only means here an inoculation with the pathogenic agent. The wound itself and the reactions it gives evidently are of little importance; in 25 per cent. no injury at all is reported.

The telangiectatic granuloma develops as a generally solitary, pediculated, granuloma-like, easily bleeding tumour. It feels rather solid, at least, is not so soft as an ordinary granuloma. It may grow to the size of a pigeon's or chicken's egg in weeks, months or years and, though benign, shows a marked tendency to recurrence if not carefully excised.

It especially develops in the uncovered parts of the skin (9/10 of all cases). 1/3 is found at the fingers, 1/4 at the lips, and mucous membranes of the mouth. The diagnosis is easily missed and a malignant growth suspected. So Luchs of the department of pathology of the Freiburg University states that of 26 cases inspected there, in only one case was the diagnosis of granuloma made clinically. This and its still unclear aetiology, will be the
reason why, e.g., in recent surgical literature, cases of telangiectatic granuloma are still described (Gerbatsch, 1932).

About a year ago I saw a typical case of telangiectatic granuloma of the eyelid (Fig. 1). A boy, aged about 16 years, when cutting wood, got a very superficial injury of the inferior eyelid. After about a week a fleshy tumour developed, a few days later there was some bleeding and the tumour fell off. Shortly after, however, it recurred and increased in size constantly and rapidly, while there was repeated nocturnal bleeding. The boy consulted his physician, who cut off the pediculated tumour, after treating the wound with lapis. This, however, did not put a stop to the process, as soon there was a recurrence with periodic nocturnal haemorrhage and rapid growth. One night, when there was a more profuse haemorrhage than usual, he went to a clinic, where the bleeding was easily controlled by a simple bandage. The next day he was referred to the University Eye Policlinic. The photograph shows the pediculated tumour originating from the inner margin of the inferior eyelid. It most resembled a granuloma. As, however, malignancy could not be excluded the stalk was very carefully removed, so that macroscopically no tumour-tissue was left. There was no visible infiltrative growth in the normal surrounding tissue, to which the tumour was attached only superficially. Up till now (one year later) there has been no recurrence of the growth.

A survey of the tumour shows a framework of connective tissue, especially well developed in the stalk, but very soon disappearing as it radiates in the body of the tumour. Between the strands of connective tissue in the stalk and the part of the body adjacent to it there are dense masses of cells, amidst which numerous small lumina can be detected in many places. The greater—peripheral—part of the tumour, however, shows an astonishing abundance
of smaller and larger vessels with a scarcely visible wall spread in a tissue, almost resembling an embryonal vitreous body (Fig. 2).

A larger magnification shows that the dense masses of cells in the proximal part of the tumour consist chiefly of tissue cells (angio-blasts, fibroblasts, connective tissue cells, and endothelia), while exudation cells (leucocytes, lymphocytes, plasma cells) are met with in a small number only, there being large areas where such cells are only occasionally seen. Here and there a haemorrhage can be traced, which may have been spontaneous or secondary to the trauma of extirpation. Numerous lumina are found in over 3/4 of this part of the tumour, partly as simple holes in the abundant protoplasm of the crowded cells. However, generally they show a lining of endothelial cells, often so abundant that it gives an impression as if they could scarcely find a place, their nuclei bulging in the lumen of the vessels. This part of the tumour is conspicuous for a blastomatous nature (angiosarcoma), but mitoses are found only occasionally.

The numerous vessels in the peripheral part of the tumour never show a distinct fibrous wall, though their lumina may be very considerable, the lining being chiefly endothelial. In many—especially the larger vessels—the endothelia become flatter and look like the endothelia we are familiar with in normal vessels. The tissue in which the vessels are spread is sometimes apparently structureless, generally distinctly fibrillar; mucus reactions were

**Fig. 2.**

Part of tumour practically free from exudation cells.  

a Abundant tissue cells of central part.  
b Ectatic capillaries of peripheral part.
negative. The majority of the cells scattered in the tissue are tissue cells, most authors considering them as angioblasts ("Capillarsprossen"), exudation cells are rare.

The tumour has an epithelial covering, for the greater part resembling that of the skin, only in a small area that of the conjunctiva, without mucous cells however. A few very deep and narrow "crypts" covered by epithelium are seen.

Apart from this "normal histology" of the tumour, certain secondary changes are present; haemorrhages, if from the large subepithelial vessels, sometimes perforating the epithelial covering, illustrating the clinical feature of recurrent haemorrhage; if

![Fig. 3](image-url)

**Fig. 3.**

Globule containing cocci with a distinct capsule, which in this globule is continuous with a streak of homogeneous tissue of the tumour.

in the mass of the tumour itself, sometimes leaving a fibrinous network.

In many places the tumour is superficially ulcerated; here and there is evidence of inflammation in deeper parts of the tumour. Only superficially could I find staphylococci in great numbers, often arranged in globular masses. Here and there a distinct capsule could be traced, which probably must be derived from tissue elements (Fig. 3). Nevertheless, this structure recalls the findings in botryomycosis. Professor de Vries, pathologist in this University, showed me a case of septic endocarditis in which the arrangement of staphylococci in discs (probably globules) was seen, though no capsules could be traced. (Schmelzer describes a similar arrangement in his case of telangiectatic granuloma.)

The epithelium shows pathological changes of secondary importance (atypical stratum corneum, melting together of cells with hole formation), it may be absent.

This is a typical case of telangiectatic granuloma. Other cases
in the region of the eye were reported by Michelson: typical tumour of the skin of the inferior eyelid in a middle-aged woman; Tisseraud: raspberry-like growth of the size of a pea under the eyebrow in a boy 10 years of age; Luchs: tumour developing at a spot where the glasses were rubbing against the skin; Bargeton: broad pediculated tumour of the cornea after injury; Wohl: tumour of the external canthus, X-ray treatment during one year without success, extirpation, definite cure; Wescott: small tumour of the inferior eyelid, noticed during 10 weeks in a boy, aged 9 years; Torlais: pediculated tumour of the free margin of the inferior eyelid, a second case at the canthus internus after an injury; Schreiber: two cases at the margin of the eyelid; Anzilotti's case; Schmelzer's case.

In the lacrimal sac, cases were reported by Wagenmann, Piesbergen and Scheerer only, though tumours in these regions, labelled as granuloma or polyps, are reported "to resemble a haemangioma" in their architecture. And as we know that in the discussions as to the nature of telangiectatic granuloma some authors seriously discussed the possibility of angiomata (Konjetzny, Lucien Picqué, Terrier) it is not unlikely that in these cases we have to deal with telangiectatic granuloma.

The histology of telangiectatic granuloma is not so typical as its clinical picture. French authors especially described cases with a very different histology, and Torlais in his compilatory article even gives a division into nine groups, of which I only mention here group 7: "sarcoïd form with giant cells in ulcerated chalazion." Evidently French authors—among whom is Dr. Pesme of Bordeaux, to whom I am much indebted, as he was so kind as to send me reports of unpublished cases and brought to my knowledge the important article of Dr. Torlais—consider these tumours in a perforated chalazion not as simple granulomata, as we are accustomed to do. In my opinion such a point of view meets with considerable objections, though it might be difficult to make a differential diagnosis on certain parts of such a granuloma histologically only. Clinically, the telangiectatic granuloma is marked by its greater solidity, its tendency to bleeding and recurrence after simple removal. Histologically in telangiectatic granuloma the very thin vessel walls, the large areas showing no sign of exudation or inflammation, the (often partial, "collar-like") epithelial covering; in chalazion granuloma the infiltration of the thicker vessel walls (Fig. 4), and the predominance of exudation cells (plasma cells) generally allow a differential diagnosis.

The similarity of some of these tumours to angiosarcoma should be borne in mind, though it were only to prevent a disastrous mistake in the diagnosis. Some authors pointed out the similarity in histology to multiple tumours of the skin developing in certain
foreign diseases (Carrion's fever-Verrugia Peruviana, caused by a small rod in the red blood corpuscles (Bartonella), angiofibroma cutis circumspectum (Bennecke). Recently Geiger in Vienna reported a remarkable case of multiple granulomata telangiectaticum developing after a fever of doubtful origin.

In a woman, aged 40 years, three days after the onset of an unclear fever multiple telangiectatic granulomata developed, which showed a tendency to bleeding. The histology of the young tumours showed that inflammatory infiltrative processes were primary, the proliferative, ectatic changes leading to the growth of a tumour being secondary only.

Occasionally a rare organism may be found, e.g., in a carefully studied case of granuloma of the conjunctiva the rhinosporium sebeerii was described; other organisms have been found by different authors—Amoebae (Létulle); "Fusarium Ponceti" (Guiart); a streptothrix (Archibald, and spirilla (Ponzin). This was not confirmed by other authors.

It is very remarkable that a great number of authors (including even Darier), follow Hartzell in his statement that the telangiectatic
granuloma develops under the influence of staphylococci (pyogenic granuloma), which again would link the granuloma to the botryomycosis, only in botryomycosis the cocci are found in the centre of the granuloma tissue, while in telangiectatic granuloma they are found superficially only. Geiger, on the other hand, has shown that in his case inflammatory processes were primary. Schmelzer's case of telangiectatic granuloma is remarkable for the appearance of multiple non-pediculated tumours (t.gr. is nearly always solitary) eight days after a cow's kick against the inferior eyelid, which suggests an animal source of infection. Though the cocci found were arranged partly in globules of about the size of a white blood corpuscle, Schmelzer denies the possibility of botryomycosis on account of the facts: primarily that there was no rapid growth in cultures under 37 degrees and no greater pathogenicity for caviae, features attributed to the botryococcus in differentiating against the ordinary staphylococcus. However, in the most recent veterinary publication Clarenburg en van Heelsbergen state, that the bacteriological d.d. against staphylococcus pyogenes aureus is very vague. Secondly, that the cocci were found in the superficial parts of the tumour only, and, therefore, cannot be the pathogenic agent. As mentioned before, Hartzell and Darier accept the pathogenetic rôle of the staphylococcus in the telangiectatic granuloma and especially Geiger, in his case of multiple t. gr., stated that the inflammatory changes were primary in the process of its development.

Schmelzer's case faintly reminds us of the first and only case of human botryomycosis in the region of the eye described by Faber and ten Siethoff in 1898. The history of this case of botryomycosis is briefly as follows:

A farmer consulted Faber. He said that four months ago his upper eyelid had been swollen. A tumour developed, that perforated and disappeared but at the same time there appeared a number of nodules in the region of the canthus externus and in the superior eyelid. Inspection showed that the conjunctiva palpebrae was swollen and reddened, there was papillary hypertrophy. These inflammatory signs, however, quickly receded on treatment with nitrate of silver. Besides his there was a number of greyish nodules, measuring from 0.5 to 3 mm. in diameter, which, as the conjunctival swelling diminished during the treatment, came more clearly into view. The larger ones perforated; there developed a small fistula, through which a slender probe could be introduced, leading into a small cavity. Faber diagnosed actinomycosis and sent material to ten Siethoff who was able to exclude the possibility of actinomycosis, but found peculiar conglomerates of spherical bodies resembling a bunch of grapes. On pressure
the thin capsule of the globular bodies burst and numerous cocci, not distinguishable from staphylococci appeared. Consequently he made the diagnosis of botryomycosis of the eyelid.

The similarity to botryomycosis of the conjunctiva in horses is striking when the description is considered of the only case I could find in the literature:—

Knapp describes a case in the conjunctiva of a horse, in which under the signs of inflammation small nodules developed in the conjunctiva. The diagnosis was confirmed microscopically. The secretion of the eye infected the surrounding skin and the lacrimal gland. The author mentions another case of conjunctival infection in horses.

As I could hardly believe the observation of ten Siethoff to be false, I looked for another case of human botryomycosis in the non-ophthalmological literature. I found the following cases:—

The closely investigated case of Kayser and Gryns, resembling a case of "Madura-foot." In the discharge from the fistulae they found little bodies, like grains of sand, consisting of conglomerates of globules and surrounded by a thick mass of white blood corpuscles, so that they were difficult to recognize. Under the microscope these conglomerates were freed from the exudation cells by means of a needle. Size of conglomerates 0.500 mm., of globules 8-200 micron., of cocci 0.6-0.8 micron.

Recently a similar case was published by Martinowa of Stalingrad.

Masson found the typical yellow grains containing the globular bodies in the discharge of bone fistulae in a war-wound and classified this inflammation as being of botryomycotic origin.

Stolz mentions four cases of osteomyelitis, in which the typical colonies could be found in the discharge from the fistulae and the granulation tissue as solid little grains of sulphur-yellow colour, resembling actinomyces.

Further cases I could not find, possibly because few are interested in this peculiar behaviour of staphylococci. The typical globules are not found by our common method of examining a discharge, for then the globules are ruptured and the cocci liberated; in cultures staphylococci develop, resembling the ordinary staphylococcus pyogenes aureus. We may conclude that probably either a special variety of staphylococcus or a special reactive condition of the human tissue may give rise in man to an arrangement of cocci in globules, similar to that found in animals in cases of botryomycosis. In contradiction to the statement of recent authors we must conclude, therefore that—though the published cases are very few in number—the possibility of botryomycosis in man has to be accepted. This botryomycosis is histologically and clinically a clearly defined disease.
Summary

Botryomycosis, chiefly met with in horses and apparently only occasionally occurring in man, is characterized by a chronic inflammatory development of granulation tissue and fistulae, causing tumours or swellings of the affected organ under the influence either of a special variety of staphylococcus or of a special reactive condition of the human tissue. Only one case of the eyelid is described. A few cases in other regions could be found in the literature.

Telangiectatic granuloma is clinically, a rather sharply marked off, not uncommon variety of granuloma in man. The aetiology is not sufficiently clear. A personal case of the eyelid is described, and cases from the literature collected.

LITERATURE

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