ADENOMA SEBACEUM AND TUBEROSE SCLEROSIS OF THE BRAIN *

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MINNEAPOLIS

Adenoma sebaceum is a germ plasm developmental defect of the skin, involving especially the sebaceous glands. Other elements of the skin, however, may be affected, as noted by Balzer,¹ Crocker,² and others, and confirmed by a study of the case herein reported. In the Balzer type of adenoma sebaceum, changes in the sebaceous glands may be slight. The Pringle type is characterized by an enormous hyperplasia of the sebaceous glands. The Hallopeau-Leredde type shows a predominance of the fibroma element; the surface may be verrucose. Mixed types, in which one lesion shows great hyperplasia of the sebaceous glands and a neighboring lesion may show only nonsebaceous changes, are not uncommon.

The germ plasm defect affects not only the skin, but also a number of other organs: the brain, kidney, heart, intestine and liver, and probably other organs. The changes in these organs are analogous to those in the skin, and consist in the formation of embryonal heart muscle tumors in the heart, the formation of a variety of tumors in the kidneys, and the condition in the brain known as tuberoze sclerosis. These visceral changes, in their origin as germ plasm defects, in their microscopic structure, and in their clinical course, show a close relation to adenoma sebaceum and the nevus group of skin affections. They are often termed nevoid or organ nevi, in order to distinguish them from the ordinary birthmark.

Adenoma sebaceum is thus a part of a widely distributed disorder. The signs and symptoms of this disorder are largely dependent on the localization of the lesions. Marked involvement of the heart or kidneys often leads to a fatal result. Slight lesions in the skin with pronounced involvement of the brain or tuberoze sclerosis give idiocy or epilepsy. Extensive lesions in the skin with slight or no involvement of the brain give a normal or nearly normal mentality.

In the heart and kidney, the study of this condition has been limited for the most part to a description of the predominating tumor. In the heart, this is a rhabdomyoma, which may cause death, often during the first few years of life. In the kidney, the predominating tumor has

* From the University of Minnesota Medical School.

1. Balzer: *Arch. de Physiol.* **6**:564, 1885; *ibid.* **7**:93, 1886.

2. Crocker: *Diseases of Skin*, Ed. 3, Philadelphia, P. Blakiston's Son & Co., p. 986.

been either a mixed tumor or a teratoma, or the tumors have been described as fibromas, fibrolipomas, leiomyomas, fibrolipomyomas, angiofibromas, angiosarcomas, and liposarcomas. In the brain, the condition has received more exact study under the term tuberose sclerosis of the brain.

TUBEROSE SCLEROSIS OF THE BRAIN

Tuberose sclerosis of the brain consists essentially of an overgrowth or hyperplasia of the neuroglia, forming tumors or tumor-like growths

Fig. 1.—Adenoma sebaceum: The Pringle type of lesion on the cheeks and chin in the case reported. The larger Balzer type of lesions were removed by fulguration before this photograph was taken. Two padlike nevi are present on the left lower eyelid and forehead.

in the brain cortex and about the ventricles. The growths about the ventricles vary in size from a grain of wheat to a pea. Considerably larger growths are found in the cortex, and may be raised or sunken. Histologically, the findings are characteristic. There is great overgrowth of neuroglia, disorientation or dislocation of nerve cells, and

very large cells which may resemble either neuroglia or ganglion cells. The process is analogous to, and genetically identical with, the adenoma sebaceum lesions of the skin. Depending on the size and location of the tumors or growths, the neurologic and mental symptoms may be absent, or there may be slight mental impairment, idiocy, epilepsy or symptoms of brain tumor.

REPORT OF A CASE

A. C., a man, colored, aged 18, had first shown symptoms of epilepsy when 5 years old. About one month later, numerous small tumors or growths appeared on the face, involving especially the cheeks and nasolabial folds.

Fig. 2.—Back of the neck and shoulders; same case as Figure 1. The extremely numerous, closely set pigmented nevi are not well shown. Many tablike nevi are shown, one over the right shoulder projecting at right angles to the skin.

Epileptic attacks and new lesions on the skin had continued to appear since that time. He had four brothers and four sisters. No one in his family was similarly affected.

The numerous small tumors or growths on the cheeks, chin and forehead were red or yellowish-red in color. About the nasolabial sulci, the tumors

Fig. 3.—Balzer type of lesion: Photomicrograph $\times 25$; from the right nasolabial fold. Alterations in the hair follicles in the case reported are shown.

Fig. 4.—Pringle type of lesion: Photomicrograph $\times 25$; from left cheek. Changes in the sebaceous glands in the case reported are shown.

included some that were larger and pale, showing no tinge of red. Most of the lesions were discrete, although some were confluent, forming patches like those seen in lichen planus. Over the face, there were many unusually large comedones. On the left lower eyelid and on the forehead, there were two soft pigmented, padlike nevi. Over the back of the neck and shoulders, there were hundreds of closely set, small pigmented nevi, with many projecting tablike nevi—*nevus pendulum*. On the right arm, there was a large patch of vitiligo, which was thought by the father to be due to a maternal prenatal craving for ice cream. Two quite large pigmented nevi were present on the abdomen. There were no subjective symptoms from the skin lesions. The mental condition was fair. He had been unable to continue in school beyond the sixth grade. The epileptic attacks had been moderately severe. Many of the larger lesions on the face were removed by fulguration, with excellent results.

MICROSCOPIC STUDY

One of the pale, rather large lesions, at the right nasolabial sulcus, was removed with the scissors, and found to conform to the Balzer type of lesion. The hair follicles were altered as regards size and shape, some were rudimentary, and some showed a high grade of degeneration. Changes in the sebaceous glands were slight. The hair follicles were surrounded by connective tissue, resembling a rather richly cellular fibroma.

One of the red lesions from the middle of the cheek was removed by the cutaneous punch. This was a typical Pringle type of lesion. There was massive hyperplasia of the sebaceous glands. Most of the sebaceous glands appeared to be simply hypertrophied or enlarged, the structure resembling normal sebaceous glands. At some points, the sebaceous cells were arranged in short bands or ribbons, did not resemble normal sebaceous glands, and were apparently true adenomas.

SUMMARY

1. Adenoma sebaceum is a germ plasm developmental defect of the skin, involving especially the sebaceous glands.
2. There are three types of adenoma sebaceum. The Pringle type consists of red lesions showing an enormous hyperplasia of the sebaceous glands. In the Balzer type, the lesions are pale, and show alterations mainly in the hair follicles. In the Hallopeau-Leredde type, the surface may be verrucose, and, microscopically, it shows a predominance of the fibroma element. Mixed types are not uncommon.
3. Adenoma sebaceum belongs to the nevus, nevoid or organ nevi group of disorders.
4. The brain and visceral organs, such as the heart and kidney, are often involved in a genetically identical and histologically similar process.

5. Adenoma sebaceum is thus part of a widely distributed disorder, nevoid in character, which may involve the brain and important visceral organs, and is characterized by an overgrowth of certain tissues, the formation of true tumors, and, in the visceral organs, may end in malignant tumor formation.

6. The involvement of the brain or tuberosc sclerosis consists essentially of overgrowth of neuroglia, disorientation or dislocation of nerve cells and the presence of characteristic large cells. The tumors are found in the brain cortex and about the ventricles.³

3. In addition to the references given, the following will be of interest:

Freund: Berl. klin. Wchnschr. **12**:274, 1918.

Schuster: Dermat. Centralbl. **17**:2, 1914.

Fischer: Arch. f. Dermat. u. Syph. **134**:93, 1921.

Hauser: Berl. klin. Wchnschr. **12**:278, 1918.

Shelmire, J. B.: Adenoma Sebaceum, J. A. M. A. **71**:963 (Sept. 21) 1918.

Crutchfield, E. D.: Adenoma Sebaceum Associated with Teratoma of Kidney, Arch. Dermat. & Syph. **2**:368 (Sept.) 1920.