THE NEURO-ECTODERMAL DYSTROPHIES.

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Of recent years, thanks especially to papers which have appeared in this Journal by MacArthur (1934) and Dixon and Smithers (1935), the important syndrome of acquired epilepsy with multiple subcutaneous nodules produced by cysticercosis or somatic tæniasis has been clearly placed before the profession and especially before those members of it who serve in the Corps. Seen in persons who have served as soldiers or missionaries in India, China or other parts of the globe where infestation with the *Taenia solium* is common, there is a natural tendency to look upon an individual who has been abroad and who has developed symptoms of epilepsy along with palpable nodules under the skin as a probable example of cysticercosis. While it is true that cysticercosis is a relatively common cause of such a syndrome, certain cases of the group known as the neuro-ectodermal dystrophies also require consideration in the differential diagnosis. The differentiation of the two is easy provided that the mere existence of the dystrophies be kept in mind.

As an example, may I cite the history of P.B., aged 35, with nine years’ service in the 1st K.O.S.B.s. In 1919 he was drafted to India, in 1921 to Egypt, in 1922 to Turkey, and returned home for discharge in 1924 being then in perfect health. In December, 1931, he had a series of convulsions of an epileptiform character and continued to have them at intervals of two or three months until 1934 when he was operated upon by Mr. Norman Dott. A wide skull flap was turned down, and some thickening of the membranes noted. On passing a needle into the lateral ventricle it was felt to traverse some firm areas in the brain substance and especially to penetrate a layer of firm tissue before entering the ventricle.

After this operative exploration the fits diminished in number and severity, and are now more of the nature of petit mal.

In 1936 P.B. was admitted for some days to a military hospital, where for the first time the presence of multiple small swellings in the subcutaneous tissues was noted. These swellings had apparently appeared recently and were widely scattered over the surface of the body. Since that time more subcutaneous masses have appeared, and are sometimes slightly tender for a short time afterwards. In no case have the tumours grown to any considerable size. X-ray examination of brain and muscles was negative for calcified cysticerci.
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A tentative diagnosis of cysticercosis was made, and since that time the man has had some twenty subcutaneous swellings excised in the vain hope of qualifying for a pension. On every occasion the swellings have exhibited the clinical appearances of small lipomata, and have been proved to be so on microscopic examination.

This appears to be a classical case of tuberose (potato-like) sclerosis of the brain along with the syndrome of multiple subcutaneous lipomata. The findings at operation of slight meningeal thickening with firm areas of gliosis in the brain are typical as is also the presence of a layer of gliosis around the lateral ventricle. This layer projects into the interior of the ventricle, giving an appearance on section at post-mortem which has been likened to "candle drippings," and may deform the ventricle so seriously as to allow of diagnosis in some cases by ventriculography.

A similar syndrome which might lead to confusion is that of multiple gliomatous tumours on the peripheral nerves, the well-known disease of von Recklinghausen which is not infrequently associated with tuberose gliosis of the central nervous system.

A short summary of this interesting group of diseases might be of interest to those of us who meet with examples of cysticercosis at intervals.

The neuro-ectodermal dystrophies form a group of degenerative lesions which may affect in one or more manifestations one or more of the portions of the nervous system, that is to say, the central nervous system, the peripheral nerves, the autonomic nervous system, and finally the little understood cells in the skin and probably also in other organs which are only gradually becoming recognized as nervous in origin. Any of the types of degeneration, whether gliomatous, fibrolipomatous, angiomatous, or cystic, may affect the skin, the peripheral nerves, the central or the autonomic nervous system, while more rarely, lesions such as cysts or tumours may occur in the internal viscera. Commonly the degeneration occurs in two or more of these situations.

A general outline of the group may best be obtained by a consideration of the main types which have from time to time been described in the literature. Seven groups can be identified.

1. Tuberose sclerosis with mental defect and/or epilepsy. (Bourneville's disease.)
2. Tuberose sclerosis with adenoma sebaceum, a syndrome to which the term "epiloia" is commonly applied.
3. Tuberose sclerosis with von Recklinghausen's type of neurogliomatosis of the peripheral nervous system, along with cutaneous nevi and molluscum fibrosum.
4. Tuberose sclerosis with multiple subcutaneous lipomata.
5. Tuberose sclerosis with congenital xeroderma, ichthyosis or hereditary palmo-plantar keratosis.
6. Angiomatosis of the skin, retina and cerebellum. (Von Hippel-Lindau's disease.)
Cystic degeneration of the central nervous system (syringomyelia) associated with congenital cystic disease of the viscera.

It should be stressed that tuberose sclerosis frequently occurs without peripheral manifestations and that peripheral manifestations are frequent without accompanying tuberose sclerosis. The combination of central and peripheral varieties is, however, sufficiently described to make a connexion between them beyond dispute.

Each of these interesting groups will repay short study.

(1) *Tuberose Sclerosis* (Bourneville's Disease).—This form of cerebral degeneration appears in early childhood and leads to progressive mental defect along with epileptiform seizures in many cases. It may be associated with congenital skin lesions such as ichthyosis, with flat tumours of the retina or fibrolipomatous tumours under the skin of the conjunctiva. The subject of this lesion may be stunted physically, and in one case which has come under my care the dwarfing, which was extreme, was associated with metaphysial bone changes similar to the more severe types of chondrodystrophy.

(2) *Epiloia.*—The syndrome of epiloia consists of central tuberose sclerosis with mental deterioration, epilepsy, etc., along with the development of a peculiar pinkish or red eruption on the cheeks described as "adenoma sebaceum" or Pringle's disease. It is typical of this eruption that it is symmetrically bilateral and has the well-known "butterfly wing" distribution on both cheeks. Little is known of the detailed pathology of the eruption, but the frequency of associated sclerosis of the brain makes it likely that it arises in connexion with nervous structures in the skin.

Flat retinal tumours, also, of course, nervous in origin, are frequently found.

(3) *Tuberose Sclerosis with Von Recklinghausen's Disease.*—Late in last century von Recklinghausen described a syndrome which he called "neurofibromatosis," now perhaps as commonly known as "neurogliomatosis." His cases exhibited multiple tumours upon the peripheral nerves and in the autonomic nervous system, and frequently showed pigmented patches of a nevoid character in the skin or the multiple pedunculated skin tumours called molluscum fibrosum. The correlation between these three features is often so close as to make it likely that both the nevoid patches and the molluscum fibrosum are also of nervous origin. The condition frequently persists throughout life without serious inconvenience to the patient unless an individual glioma grows within a bony canal, as in the optic foramen, causing blindness, on the acoustic nerve within the internal auditory meatus causing the well-known symptoms of a cerebello-pontine angle tumour, or within the spinal canal causing pressure on the cord. In some cases a sarcomatous change may take place in a nodule.

These comparatively common manifestations of von Recklinghausen's disease are well known, but it is not so often recognized that in addition to the skin and peripheral nerves the central nervous system, either the
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The brain or the spinal cord, may be involved by a patchy gliosis, which, when it affects the brain, may be the cause of epileptiform convulsions.

(4) Tuberose Sclerosis with Multiple Subcutaneous Lipomata.—This forms one of the rarest syndromes. Multiple subcutaneous lipomata, making their appearance in adult life, are in themselves uncommon. The tumours bear no relationship to the common solitary lipoma of the outpatient department, for they appear at any time during life, there are many of them, they are frequently a little tender to touch, especially soon after they have appeared, and on excision they often contain a good deal of fibrous tissue as well as fat. In many cases described in the literature the tumours have been symmetrically distributed. Many authors have suggested that this type of lipomatosis was nervous in origin, and that the small fibro-fatty tumours grew upon terminal nerve fibres in the subcutaneous tissues. If this be so the condition has clear relationships to von Recklinghausen’s neurogliomatosis. I have encountered one case of an elderly woman suffering from multiple subcutaneous lipomata and epilepsy where the skin over one lipoma was the site of a capillary haemangioma.

The occasional coexistence of tuberose sclerosis of the central nervous system with multiple subcutaneous lipomata renders the theory of nervous origin even more probable. It is to this group that the case of P. B. which I have described above belongs.

(5) Tuberose Sclerosis with congenital xeroderma, congenital ichthyosis or hereditary palmo-plantar keratosis has been described. Such cases appear to be very rare.

(6) Von Hippel-Lindau’s Disease.—The impression is gaining ground that capillary angiomata of the skin, may, like the nevoid areas of neurogliomatosis, bear some relationship to the nervous system and may arise in connection with nervous structures in the skin or under nervous influences. Cases may, for instance, be met with where an angioma is strictly limited to the distribution of a given sensory nerve.

The syndrome of von Hippel-Lindau consists of the development of angiomatous cysts of the central nervous system, more commonly in the cerebellum, in an individual exhibiting cutaneous angiomatosis. Angiomatous tumours of the retina may also be present.

(7) The relationship of cystic disease of the various internal organs and of the spinal cord to the group of neuro-ectodermal dystrophies is still slender. On the one hand, however, congenital cystic disease of the kidney, pancreas, liver, or lung has been described along with some of the above well recognized types of neuro-ectodermal degenerations, while on the other, cases are on record of coexistence of cystic disease of these organs with the typical appearances of syringomyelia in the spinal cord. It is possible that, were these lesions more carefully sought for, the coexistence might prove to be more common than is at present suggested, and that a closer study of the two conditions might lead to a wider knowledge of the pathology of both.
The following references will be found of value for those who wish to study the subject in more detail.

My thanks are due to Mr. Norman Dott for permission to make use of his operative findings in the case here described.

REFERENCES.


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