THREE FATAL CASES OF PELLAGRA, WITH EXAMINATION OF THE SPINAL CORDS.

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I THINK it was Bouchard, in 1864, who first drew attention to the changes in the spinal cord of pellagrous patients, but though Tonnini and Belmondo¹ continued the researches, it was not till Tuczek's masterly treatise appeared in 1893,² that much light was thrown on the pathology of the disease. He had the opportunity of making eight autopsies in Italy, and found in all of them sclerosis of the posterior columns and columns of Goll. In six cases there was also lateral sclerosis, and the lesions were found mostly in the dorsal region, but in one case there was also cervical anterior sclerosis. In 1894, Pierre Marie³ contrasted Tuczek's pellagrous sclerosis with the posterior sclerosis of tabes dorsalis. I was most anxious to confirm, in Egypt, the results already arrived at by Tuczek; but though I had for some years made myself familiar with the clinical and naked-eye pathological appearances of pellagra,⁴ I could not obtain microscopical sections of the cords until I had the good fortune to meet Dr. F. E. Batten, lately Pathologist to the National Hospital for the Paralysed and Epileptic, in London, who most kindly made many sections and furnished me with a report upon them, from which I have freely drawn for this paper—which, so far as I know, is the first contribution to the subject in the English language.

CASE I.—Ahmed, an Egyptian peasant, æt. 50, was admitted to hospital on December 13, 1898, from the Out-Patient Department, suffering from diarrhoea, from which he had suffered for the past four months.

There was a previous history of intermittent fever. On admission he was found to be suffering from pellagra and ankylostomiasis, the chief pellagrous symptoms being some roughness of skin on feet, legs, knees, elbows, hands, and neck, besides patches on both iliac crests and on the sacrum. He said he had had more or less of this eruption for two years, that he first noticed it on the

¹ *Riforma med.*, Roma, 1889, No. 256; "Le alterazioni anatomiche del midollo nella pellagra e loro rapporto coi fatti clinici," Reggio-Emilia, 1890.

² *Klinische und anatomische Studien ueber die Pellagra*, Berlin, 1893.

³ *Semaine med.*, Paris, 1894, p. 17.

⁴ *Brit. Journ. Dermat.*, London, 1898, vol. x. p. 395; *Journ. Tropical Med.*, London, 1898, vol. i. p. 63.

feet and knees, that it disappeared during the summer, and was most evident in the early spring months. In addition he had some early atrophy of the skin on the backs of the hands, and at the front and back of the neck. His tongue was denuded and fissured, and he had some six motions daily with tenesmus and abdominal pain, but no bloody stools. His knee-reflexes were exaggerated, he had pain and tenderness on both sides of all the dorsal vertebræ, he slept badly at night, and his mental condition was distinctly melancholic. Beyond great anæmia, and an enlarged malarial spleen, there was nothing else worthy of notice.

Three days after admission, at noon he suddenly became comatose, with hemiplegia and left-sided facial paralysis; the head turned to the right; no conjugate deviation of the eyes; pupils dilated; conjunctivæ sensitive; breathing not stertorous, but lips blown out at each breath; both knee-jerks obtainable, the left being brisker than the right.

A few hours later it was noted that he had some hiccough and that the abdomen had lost its rigidity and had become flaccid. He died the same night. The post-mortem examination was performed the following morning.

Rigor mortis was present, the body was badly nourished, the pericardium contained two table-spoonfuls of clear yellow serum. The left ventricle of the heart was somewhat hypertrophied, the heart muscle was not fatty, but of a peculiar light chocolate colour, and there was some atheroma of the aorta. Both lungs were extremely œdematous, the liver weighed 1190 grms., and was very pale, but no bilharzia worms were found in the portal vein or in the small vessels of the liver.

The intestines contained 200 ankylostoma worms. The spleen weighed 230 grms., and was soft, with some perisplenitis. The kidneys, bladder, and ureters were normal.

The left temporo-sphenoidal lobe of the brain was bright red in colour on the surface, and very soft in consistence. On cutting into it, it was found that the whole subjacent tissue, as far as the internal capsule, was one huge mass of softened substance, consisting of degenerated brain tissue, and massive clots of dark almost black blood. This softening was about $2 \times 4 \times 2$ in. in size.

The spinal cord was apparently normal to the naked eye, and was kept in Müller's fluid, for Dr. Batten's examination, whose report says:—

"1. *Marchi's method*.—There are scattered all over the section of the cord a few black dots, but these are not limited to any one tract, and no significance can be attached to them.

"2. *Weigert-Pal method*.—By this method the posterior median columns appear unduly pale as compared with the other columns of the cord. At the level of the second cervical root the change is most marked in the dorsal portion of the posterior median columns, and also in a small triangular area situated just outside the anterior horns, symmetrical on the two sides of the cord, but not visible at the level of the fifth cervical root. At this level the paleness of the posterior median column is noticeable, and the same condition is present in the mid-dorsal region, while at the level of the first lumbar root there is a root degeneration which can be traced down to the third.

"3. *Aniline-blue-black method*.—The vascularity of the grey matter is little if at all in excess of the normal; the cells of the anterior horns appear somewhat swollen but have a distinct nucleus and nucleolus; the cells of Clarke's column are normal. There is an increase of the connective tissue in the posterior median column, and also in the wedge-shaped area above described in the cervical region, the darker staining of the posterior columns is visible in the mid-dorsal region. At the level of the first lumbar the degenerate root stands out with great distinctness, and can be seen on the same side at the level of the third lumbar, which root is evidently degenerate."

It will be noticed that in this case the patient was only three days

in hospital, and that he died not of pellagra but of cerebral hæmorrhage. He had probably been pellagrous for some two years, or there would not have been marked atrophy of the skin nor such distinct evidence of posterior sclerosis.

CASE. 2.—Amina, an Egyptian woman, æt. 33, was admitted to hospital on December 28, 1898, complaining of diarrhœa, general debility, and pain in the lower extremities. She was extremely emaciated, and weighed only 4 stone, 11 lb. The symptoms of pellagra were: slight roughness and atrophy of the skin on the dorsal aspect of the hands and feet, and also on the back, a very denuded tongue, diarrhœa, and motions passed in bed, dementia with persistent muttering, abolished knee-jerks, some sleeplessness, and tenderness on both sides of the spine near the third dorsal, and first, second, and third lumbar vertebræ.

The diarrhœa was somewhat checked in hospital, where her mental condition required bromide and chloral. The temperature was practically normal throughout, but her weight fell persistently to 4 stone, 5 lb., and she died on January 23, 1899, twenty-six days after admission, in the condition called by the Italians "tifo pellagroso."

No ankylostoma eggs were found in the fæces, though she was extremely anæmic. The urine contained a distinct trace of albumin. At the post-mortem examination there was slight atheroma of the aorta; the heart weighed 185 grms.; the lungs were congested and œdematous, but otherwise normal; the liver weighed only 790 grms.; the spleen 140 grms.; the kidneys each weighed 70 grms., and were markedly cirrhotic; the brain weighed 1050 grms., and was very œdematous, while the membranes of the vertex were thickened and opaque.

The spinal cord, when examined in London, showed marked changes.

1. *Marchi's method*.—The paleness of the posterior columns is very noticeable, but under the microscope no recently degenerate fibres can be seen. The cells of the anterior horn are pigmented.

2. *Weigert-Pal method*.—The lack of fibres in the posterior columns is very marked, both sacral and lumbar regions being affected equally. In the mid-dorsal region a pair of normal roots enters the cord, and wedges itself in between the atrophied fibres of the median and external columns; this root can be traced up to the upper cervical region, where again the incoming roots contain more normal fibres. A small wedge-shaped tract is also visible, just outside the anterior horns in the cervical region, in a similar position to that described in Case 1 (Helweg's triangular tract).

3. *Aniline-blue-black method*.—The increase of the connective tissue in the posterior columns is very marked, and distributes itself in exact correspondence with the condition of the roots above described, namely, a pair of roots which has undergone no degeneration in the dorsal region shows no increase of the connective tissue in the area it occupies in the cord. There is no increased vascularity of the cord, the cells of the anterior horn and the nucleus and nucleolus are distinct, the increase of the connective tissue is limited to the posterior columns except in the wedge-shaped tract above described in the cervical region, which appears darker owing to the smallness of the film in this area.

4. *Van Gieson's method*.—There is no evidence of any recent inflammatory action in the grey matter. There is some thickening of the walls of the smaller vessels, especially in the posterior columns, though it is not limited to this region.

The posterior roots of the cervical, dorsal, and lumbar regions were also examined in this case by Marchi, Weigert-Pal, and Stroebe's methods. Marchi's method showed very little recent degeneration, though it was obvious, from the lack of staining, that a very considerable amount of degeneration

had taken place, and this was made evident by staining by the Weigert-Pal method. The greatest amount of destruction seems to have taken place in the dorsal and lumbar regions, and to a lesser extent in the cervical region; the same condition was also shown by the Stroebe stain, a stain which demonstrates the axis cylinders; and only a few axis cylinders could be seen in each root.

This patient died of pellagra and chronic kidney disease, but there was no possibility of knowing for how many years she had suffered from pellagra.

CASE 3.—Hassan Aly, a beggar, æt. 30, was admitted to Kasr-el-Ainy Hospital on January 9, 1898, complaining of diarrhœa. He had suffered for four years from pellagra and ankylostomiasis. He told us that the pellagra eruption came every year about January and left him about June. On admission he had very rough patches on his elbows, forearms, knees, legs, and the dorsal surfaces of his feet and hands. Among other pellagrous symptoms his mental condition was stupid and melancholic; both knee-jerks were exaggerated, and he could only sleep for three hours at night. He had pains on both sides of his spinal cord, from the fourth to the tenth dorsal vertebræ, itching of the skin; and some atrophy of the skin on the backs of the hands, the neck, and the sternum. He was in the habit of living chiefly upon maize, which he bought in the market when he had any money, and then made into bread. He said he had only had diarrhœa for eight days—the number of motions was seventeen on admission, but this yielded to medicine in three weeks' time. His fæces contained eggs of *Uncinaria duodenalis*, *Ascaris lumbricoides*, and *Distomum heterophyes*. He was very emaciated on admission, and his weight fell in consequence of diarrhœa from 109 lb. to 98 lb., and then rose again to 112 lb.

He died of acute pericarditis on March 10, 1898. His temperature was normal in the hospital until three days before he died, when it rose to 102°·5. A post-mortem examination was made the same day by Dr. Symmers, when it was found that the pericardial sac contained a few grms. of purulent fluid. The epicardium was roughened and gritty to the touch, owing to very many minute projections of fibrinous lymph. The endocardium was apparently normal. The right pleura was covered by a thick mass of yellowish lymph, which bound the lung and the pleura together. This semi-membranous layer was about one-sixth of an inch thick. The lungs contained no tubercle, and no bacilli were found microscopically. The small intestines contained ankylostoma worms. The liver weighed 2220 grms.; the spleen was of firm consistence, and weighed 800 grms. He had probably suffered from old malaria, and some doubtful pigment had been found in his blood during life. The spinal cord was kept for examination by Dr. Batten, who reported as follows:—

"1. By the *Marchi method* no degenerate fibres could be seen in any tract or in any region of the cord. The anterior horn cells were pigmented, but not to an extreme degree.

"2. By the *Weigert-Pal method* the cord appeared perfectly normal, and no degeneration could be seen in any region.

"3. By the *aniline-blue-black method* also, the cord appeared normal, the cells of the anterior horn and of Clarke's column were well stained, and the nucleus and the nucleolus were distinct. Some medullated fibres, not only in the posterior but also in the lateral columns, appeared rather pink in colour instead of the usual yellow, and are rather swollen, but apart from this very slight change the cord is normal."

SUMMARY.—In the first case there was some degeneration in the posterior columns, as shown by Pal's method; a degenerate root entered

at the third lumbar, and could be traced up to the dorsal region; the posterior median columns were unduly pale, and the small wedge-shaped tract seen in the upper cervical region, just outside the anterior horn, probably was a well-marked Helweg's triangular tract, and therefore a normal condition.

In the second case, well-marked degeneration of the posterior columns was present, evidently of root origin, as shown by the escape of one pair of roots—the dorsal region. There was an increase of the connective tissue in the area of the affected roots, and some thickening in the wall of the arteries. The posterior roots themselves also showed marked degeneration in their extra-medullary course.

The third case showed practically no change, except possibly some slight alteration in the medullated sheath of certain fibres, as shown by the blue-black method.

Dr. Batten believes, from the examination of these cords, that the sclerosis of the posterior columns is of root origin, and that the increase of the connective tissue in the posterior columns is secondary to the degeneration of the roots. For in Case 1, a single degenerate root can be seen entering at the level of the third lumbar, and can be traced upwards as a distinct degenerate root for a few segments; and again, in Case 2, a normal root is seen in the mid-dorsal region, wedged in between sclerosed roots, and can be traced upwards into the cervical region. That the sclerosis is secondary to the degeneration is shown by the fact that in Case 1, in which there is degeneration of the third lumbar root, the sclerosis at the level of the first lumbar can be seen to be limited to the degenerate root area, and it would be difficult to imagine that the sclerosis was primary in the cord, and limited itself in such a manner.

That the process is essentially a chronic one is shown by the fact that, although the posterior columns are extensively sclerosed, no degeneration can be shown by Marchi's method.