Observation of experimental lathyrisim in the rat

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Abstract

The clinical manifestations, roentgenologic studies, and histopathologic findings of the central nervous system of rats with induced lathyrisim were described. The question of whether the experimental lathyrisim is due to a primary central nervous system involvement or is entirely secondary to bony abnormality is not conclusively answered by this study. However, the evidence of diffuse widespread vacuolization which is more marked in the cord, medulla, and cerebellum than in the hemisphere, strongly suggests the former etiology.

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OBSERVATION OF EXPERIMENTAL LATHYRISM IN THE RAT

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Human lathyrism resulting from prolonged ingestion of the sweet pea (Lathyrus odoratus) has long been recognized in the Mediterranean area and in India. There have been many reports of observation on experimental lathyrism in rats following the initial works of GEIGER et al. reported in 1932.

Symptoms so far described consist of ataxia, tremor, kyphoscoliosis, spastic paraplegia, degenerative arthritis, exostosis, dissecting aortic aneurysms, and incontinence. The toxic factors of the sweet pea have been identified as \( \beta \)-\((L-1\text{-glutamyl})\) aminoproprionitrile and \( \beta \)-aminonitrile. Neurologic manifestations have been consistently observed, but the mechanism of their production remains still obscure.

The purpose of this study was to observe the microscopic pathologic changes of the central nervous system in the condition and to attempt to reveal the correlation of such changes with the clinical findings.

MATERIAL, METHOD AND RESULT

Twenty albino rats of the Wistar strain weighing an average 40 gms were used. Sex distribution rate was 1: 1. Subjects were divided into two equal groups (10 in each), one for the control and one for the experiment. Animals selected were young, aged 3 weeks, as it was anticipated that changes might be more readily produced in the developing central nervous system. Control animals were maintained on the usual laboratory diet (Rockland complete rat diet). The experimental group was fed with the diet consisted of 70% sweet pea and 30% Rockland diet. Animals were weighed and evaluated carefully at weekly intervals during the 42-day period of study.

Throughout the entire period of 42 days, all control animals exhibited steady growth and weight gain without significant symptoms. Experimental animals, without exception, gained weight at about half the rate of the control animals and developed definite evidence of lathyrism after

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3 weeks. Three rats died during the period of study after developing severe symptoms. Two of these, dying at 30 and 35 days, were eaten by the other rats, so that pathologic findings could not be obtained. A third animal, dying on the 25th day, was found to have pericardial hemorrhage suggesting dissecting aortic aneurysm.

Remaining animals all developed kyphosis, tremor, ataxia, spastic paraplegia and decreased reaction to painful stimuli below the mid dorsal area (Fig. 1). All were incontinent and appeared generally ill. Furthermore, animal 1 developed a large ventral hernia, and 3, 5, and 6 also developed smaller inguinal hernias.

Fig. 1. Experimental rats receiving the 70% sweet pea diet developed, without exception, ataxia, tremor, kyphoscoliosis, spastic paraplegia, incontinence and decreased reactions to painful stimuli within 3 weeks.

All animals were sacrificed on the 42nd day. The accompanying illustrations demonstrate kyphosis of the dorsal spines and hernias (Fig. 2). One animal with severe lathyrisn was returned to the usual laboratory diet on the 42nd day and was observed for another 10 days. There was surprising improvement of the spastic weakness and of reactions to painful stimuli, and diminution of tremor during this period.

The brain and cord were removed from the sacrifice animals and fixed in 10% formalin. Six experimental subjects showed the marked angulation of the cord in the lower dorsal region, but compression of the cord could
Fig. 2. Roentgenologic studies of the sacrifice rats on the 42nd day of the experiment. A is the roentgenogram of a control animal. B, C and D are roentgenograms of the experimental group and these demonstrate marked kyphoscoliosis of dorsal spines associated with ventral or inguinal hernia.
Fig. 3. Histopathological findings of the central nervous system of rats with induced lathyrism. Diffuse widespread vacuolization were most marked in the cord and diminished in ascending sections. A, B, C, D, E sections were stained with the Weil's myelin stain and A', B', C', D', E' with the Thionin technique for cellular structures. A, A' sections were made from the cord below the angulation, B, B' at the site of angulation and C, C' from above the angulation. D, D' sections were made from the cerebellum and E, E' from the hemisphere.
not be confirmed on gross examination. Sections were made below, at, and above the angulation of the cord. Additional sections were made to include medulla, cerebellum, midbrain and hemispheres. Sections were stained with Weil's myelin stain technique and with the Thionin technique for cellular structures.

Examination of these sections revealed large pericellular clear areas (Vacuolization). Similar spaces were seen separating fibers in the long tracts. These were distributed throughout, but were more marked in the cord, medulla and cerebellum than in the hemispheres. Furthermore, these were most marked in the cord and diminished in ascending sections (Fig. 3). These were more markedly demonstrated in the Weil-stained sections. There was no demyelinization or evidence of neuronal structural change noticed to indicate structural damage due to kyphosis of the cord in this study. Vacuolization did not appear to involve cortico-spinal or other tracts in a differential manner. These pathological findings were not found in the control animals.

**DISCUSSION**

Degeneration of the lateral columns in human lathyrism was present in two reported human cases in literature\(^6\). The clinical picture of lathyrism in rats and human beings is not identical. Nevertheless, there are many points of similarity between the roentgenologic characteristics of lathyrism scoliosis in rats and idiopathic scoliosis in human beings.

Human idiopathic scoliosis is believed to be related to defective protein metabolism. However, lathyrism scoliosis was not prevented, nor the onset of symptoms delayed, in rats receiving 10% casein with a sweet pea diet. This would suggest that altered protein metabolism is not the primary change in rat lathyrism\(^7\).

**GEIGER, LEWIS, et. al**\(^8\)\(^9\), as regards the cause of rat lathyrism, described the spastic paralysis observed in their experimental animals and suggested that it might be due to cord compression at the site of the kyphosis rather than to a primary neurologic lesion. On the contrary, **VI-VANCO and GIMENEZ**\(^10\) thought that the origin was neurotoxic according to their experiment in which extensive laminectomy performed prior to inducing lathyrism in rats failed to prevent paraplegia, but did effect recovery on returning the affected rats to a normal diet. A similar fact was observed in this experiment, as noted before.

It is obvious that the clinical picture of rat lathyrism shows not only spastic paraplegia but specific symptoms of the central nervous system.
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involvement such as ataxia, tremor, and restlessness.

PONESTI, et al. tried to demonstrate the histopathological changes of the central nervous system related to the clinical toxic symptoms in lathyri­
nized rats, but no definite microscopic changes were obtained except some local destruction of the cord at the site of the kyphosis in the rats with paraplegia.

Whereas, as described above, diffuse, widespread pericellular vacu­
olization in the cord, medulla, cerebellum, and less in the hemisphere, was observed in this study. These microscopic findings could be con­
sidered as the toxic changes of the central nervous system related to the clinical manifestation, namely the spastic paralysis of rat lathyrism. Furthermore, the recovery from the clinical symptoms by returning the affected rats to a normal diet is more easily explained as a diffuse reversible involvement of the central nervous system rather than as a simple mechanical destruction of the cord secondary to kyphosis.

CONCLUSION

The clinical manifestations, roentgenologic studies, and histopatho­
logic findings of the central nervous system of rats with induced lathyrism were described.

The question of whether the experimental lathyrism is due to a pri­
mary central nervous system involvement or is entirely secondary to bony abnormality is not conclusively answered by this study. However, the evidence of diffuse widespread vacuolization which is more marked in the cord, medulla, and cerebellum than in the hemisphere, strongly suggests the former etiology.

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REFERENCES


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In addition to the lathyrysm-inducing factor from L. Odoratus, several other studies on lathyrysm have been conducted. Here are some notable references: