



## MUCORMYCOSIS IN LABORATORY-REARED RODENTS

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## MUCORMYCOSIS IN LABORATORY-REARED RODENTS

During the investigation of multilocular echinococcosis in rodents of various species, the study of tissue-sections revealed five cases of mucormycosis in laboratory-reared animals. These included four northern voles, *Microtus oeconomus inuitus* Merriam and *M. o. operarius* (Nelson),

and one hybrid varying lemming, *Dicrostonyx torquatus rubricatus* (Richardson) x *D. groenlandicus stevensoni* Nelson.

Serial sections of the material preserved in formalin were prepared by the paraffin-embedding method and stained with hematoxylin-eosin.

### Results

*Case 1:* Male northern vole, *M. o. inuitus*, No. 24178, age 22 months; weight 42.4 g; total length 198 mm; died on 27 April 1960. Autopsy showed tumor-like lesions in the duodenum, with adhesions to the colon. One piece each of the colon and duodenum were preserved in formalin.

The wall of the colon was thickened, forming a plate-like tissue 10 mm in diameter and 2.5 mm thick. The lesion consisted of soft, elastic, opaque granulation tissue. Microscopically, about half the circumference of the colon was occupied by granulomatous tissue, which had invaded the mucosa. The focus had little fibrosis, with accumulated lymphoid cells, eosinophils, and epithelioid cells with giant cells. The eosinophils were aggregated as is typical of abscess formation. Giant cells were abundant peripherally. Except peripherally, the lesion had extensive necrosis, within which hyphae were observed, either scattered or in clusters. The hyphae were variable in width, because of inflations and constrictions, measuring from 3 to 5  $\mu$  up to 20 to 30  $\mu$ .

*Case 2:* Female northern vole (subspecies not recorded), No. 29381, age not indicated; died on 16 May 1963, 73 days after experimental infection by *Echinococcus multilocularis*. The liver, subcutaneous tumor, and thoracic organs were preserved. The liver contained no mycotic lesions, and the tumor was a basal-cell carcinoma. The lungs had lesions of purulent bronchopneumonia and pleuritis. One to four foci were found in each pulmonary lobe bilaterally; these measured 1 to 3 mm in diameter, protruded slightly

under the pleura, and were of whitish color with perifocal hemorrhage. The left cardiac and diaphragmatic lobes were adherent.

Microscopically, the pulmonary tissue showed hyperemia and hemorrhage, with widespread necrobiotic to necrotic areas. Macrophages containing hematogenous pigment were abundant perifocally. Numerous hyphae, measuring up to 100  $\mu$  long and 5 to 10  $\mu$  thick, had irregularly invaded the degenerated tissue. Some hyphae showed spherical inflations. Intrafocal blood vessels contained thrombi, which had been invaded by numerous hyphae. Desquamated epithelia containing numerous hyphae were found in bronchioles. Giant cells, macrophages, lymphoid cells, and eosinophiles were present. The hyphae had also invaded the fibrinous exudate on the pleura.

*Case 3:* Male northern vole, *M. o. inuitus*, No. 19956, age 72 days; killed on 8 September 1957. Five intra-abdominal masses were preserved. These were soft and elastic, whitish in color, with a diameter of 1.5 to 4 mm.

Microscopically, the masses were identifiable as lymph nodes; they consisted of more or less spherical, necrotic tissue encapsulated by a thin, fibrous layer, which contained histiocytes. In the necrotic area were irregularly branched, non-septate hyphae; these measured only 1 to 2  $\mu$ , with globular inflations 5 to 10  $\mu$  in diameter. Giant cells, macrophages, and eosinophiles formed a layer between the necrotic tissue and the fibrous layer. Remnants of hyphae were also visible in some giant cells.

**Case 4:** Male northern vole, *M. o. operarius*, No. 32949, age 4 months; died on 1 November 1965, preserved entire. The lungs had many petechial hemorrhages and minute, whitish spots. The spleen was enlarged, with one grayish-white, abscess-like mass, 7 mm in diameter, at the hilus. The hepatic lobes contained many nodular, abscess-like foci, 5 to 20 mm in diameter, and interlobular adhesions. On the anterior mesentery, about 10 nodular foci were found; one measured 13 mm in diameter, and the others were less than 5 mm. The right kidney had petechial hemorrhages, and was adhered to the caudate lobe of the liver.

Microscopically, the large necrotic focus in the liver was surrounded by a thin, fibrous layer. The necrotic area consisted of a homogeneous central portion and a peripheral cellular portion. The latter contained karyorrhectic leukocytes and giant cells, and had been invaded by histiocytes from the fibrous layer. Numerous hyphae showing active, complex branching were present in the focus. In sections, the hyphae were as much as 200  $\mu$  long and 3 to 5  $\mu$  thick,

with many constrictions and spherical inflations; the latter, 7 to 40  $\mu$  in diameter, contained basophilic granules measuring 3 to 5  $\mu$ . The caudate hepatic lobe was adhered to the right kidney by a fibrino-fibrous mass containing numerous hyphae. The kidney, remarkably edematous and hemorrhagic, had multiple focal necrobioses and necroses. Numerous hyphae were demonstrable in the renal tubules, glomeruli, and interstitium. Most of the arteries contained thrombi with abundant hyphae. Interstitial accumulations of degenerated leukocytes were present. At the splenic hilus, the fungal focus invaded the parenchyma, where multiple necroses were noted. Many of the arteries contained thrombi with hyphae. Some rounded foci, corresponding to splenic follicles, contained hyphae and a fibrinous substance. The mesenteric lymph nodes were replaced by necrotic tissue containing numerous hyphae. The thin, peripheral granulomatous layer exhibited an accumulation of histiocytes and giant cells. Some foci were adhered to the duodenum and colon. Early-stage foci were present in the lungs. Thrombi were noted in regressive arterial branch-



FIGURE 1. Case 4, mesenteric lymph node showing active proliferation of hyphae.

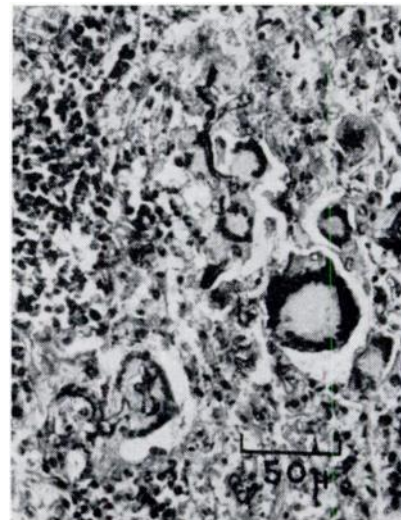


FIGURE 2. Case 4, spleen showing giant cells and hyphae.

es at the center of minute foci. Hyphae were present in thrombi, and had invaded the surrounding pulmonary tissue, which showed an accumulation of eosinophiles and histiocytes.

*Case 5:* Female hybrid varying lemming, No. 31414, 107 g, age 14 months. Killed on 30 December 1964. The liver and two pieces of the small intestine were preserved. A whitish-gray, hard mass with uneven surface, 14 x 13 x 10 mm, was found in the portal area of the liver, embedded in the parenchyma. On the cut surface, the focus appeared to be an aggregation of spherical masses of granulation tissue. Another spherical focus, 7 mm in diameter, was present in the right median lobe, near the gall bladder, and two, 7 mm in diameter, were found in the intestinal wall.

Microscopically, the lesions consisted of granulomatous tissue with extensive necrotic areas. The latter were composed of dense collagenous fibers and accumulated cells; the cells had a shadowy or "ghost" appearance. The peripheral connective tissue exhibited active vascularization, with accumulations of histiocytes and leukocytes. Some foci of degenerated leukocytes contained a few hyphae, which were polymorphic, branched, and non-septate, ranging up to 40  $\mu$  long and 3 to 5  $\mu$  thick. The diaphragm was adhered to the liver. In the intestinal lesions, the granulomatous lesions had largely destroyed the jejunal wall; the characteristics of these foci were similar to those in the liver. Hyphae were rarely observed in these lesions.

### Discussion

Mucormycosis, or phycomycosis, appears to be one of the rarest of the mycoses (Ainsworth, C. C., and Austwick, P. K. C., 1959, *Fungal Diseases of Animals*. Commonw. Agric. Bur., Farnham Royal; Smith, J. M. B., and Austwick, P. K. C., 1967, *Fungal Diseases of Rats and Mice*. In Cotchin, E. F., and Roe, F. J., *Pathology of Laboratory Rats and Mice*. Blackwell, Oxford and Edinburgh; Schiefer, B., 1967, *Pathomorphologie der Systemmykosen des Tieres*. In Bieling, R., Kathe, J., Köhler, W., and Mayr, A., *Infektionskrankheiten und Ihre Erreger*, 6: 77-87. G. Fischer, Jena). The pathogenic mucoraceous fungi are assigned to three genera, viz., *Absidia*, *Mucor*, and *Rhizopus*, the members of which produce similar pathologic changes in man and other mammals. Mucormycosis is characterized by the formation of granulomata or abscesses, in which accumulation of eosinophiles is remarkable. The lesions are found in the liver, lymph nodes, and other organs, and, occasionally, disseminated infections are found (Christiansen, M., and Nielsen, N., 1929, *Virchow's Arch.* 273: 829-863; Momberg-Jørgensen, H. C., 1950, *Am. J. Vet. Res.* 11: 334-338). Schiefer (op. cit.) pointed out that the diagnostic characters of the mucoraceous fungi in tissue sections include

width of the hyphae (up to 20  $\mu$ ), lack of septae, and irregular branching.

All but one (case 4) of the cases described here had mycotic lesions of restricted distribution, mainly in the abdominal cavity. The location of the foci indicates that the liver, mesenteric lymph nodes, and intestine are the most favorable sites for localization of the organism. Therefore, the most probable route of infection appears to be by way of the digestive tract. The disseminated infection seen in case 4 involved recent hemorrhagic and necrotizing lesions of the lungs and kidney, with lesions of longer duration in the spleen, liver, and mesenteric lymph nodes. Consequently, the pulmonary and renal foci were presumably of hematogenous origin. In the northern voles, the foci consisted mainly of a peripheral, granulomatous layer and an extensive, centrally necrotic area containing abundant hyphae and masses of necrotic cells. Such foci evidently began as abscesses. In contrast, in the varying lemming the hyphae were scarce, probably because of the vigorous, fibroma-like fibrosis. This infection was perhaps chronic, but a host-specific difference in the tissue reaction cannot be excluded.

A few spontaneous cases of mucormycosis in rodents and lagomorphs have

been reported; Symeonidis and Emmons (1955, Arch. Path. 60: 251-258) found subcutaneous lesions in mice; Bell and Elmes (1965, J. Path. Bact. 89: 307-317) reported chronic renal and pulmonary infections in rats; and Herrmann (1964, Z. Versuchstierk. 4: 57-67) found foci in the ileum, colon, and liver of a rabbit. Smith and Austwick (op. cit.) considered rats and mice to be resistant to phycomycosis, both naturally and experimentally. They stated that the few spontaneous infections were generally contracted

under conditions of increased susceptibility brought about by the administration of drugs, exposure to radiations or by other agents. In man, a relationship between mucormycosis and diabetes may exist (Gregory, J. E., Golden, A., and Haymaker, W., 1943, Bull. Johns Hopkins Hosp. 73: 405-419). The cases described here are the first to be recorded in wild rodents. Their becoming infected may be in some way related to environmental factors by which they were affected in captivity.

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