Insulin-producing Islet Cell Tumor in an Ectopic Pancreas of a Red Fox (Vulpes vulpes)

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Source: Journal of Wildlife Diseases, 20(1) : 70-72

Published By: Wildlife Disease Association

URL: https://doi.org/10.7589/0090-3558-20.1.70

A thick cross-striated cuticle, coelomyarian musculature and very large lateral chords which protruded into the pseudocoelom. The chords were divided into sublaterals and contained a prominent excretory canal. Fragments of larvae were teased from formalin fixed tissue. In lateral view (Fig. 4) the mouth of the larva was surrounded by two large, round, bilobed lips. A long buccal cavity, approximately 80 μm long, extended from the mouth to the esophagus. The larvae had characteristics of Spirurida and were identified as *Gendrespirura* sp. (Chabaud, 1958, Ann. Parasitol. Hum. Comp. 33: 445–508; Chabaud, 1975, CIH Keys to the Nematode Parasites of Vertebrates, No. 3, Pt. 2, Commonwealth Agricultural Bureaux, Farnham Royal, Slough, England, 30 pp.). Representative specimens have been deposited in the U.S. National Parasite Collection, Beltsville, Maryland 20705, USA (Accession No. 77695).

There are several reports of *Gendrespirura* (published as *Habronema*) *hamospiculata* in scaly anteaters (Baylis, 1931, Ann. Mag. Nat. Hist. 8: 191–194; Hsu, 1932, Peking Nat. Hist. Bull. 7: 99–115; Baylis, 1936, Ann. Mag. Nat. Hist. 17: 257–272; Vuylsteke, 1956, Rev. Zool. Bot. Afr. 53: 441–447; Le Van Hoa, 1962, Mission (de Witte) (1946–1949) Explor. Parc. Nat. Upemba, 65: 3–58; Rasheed, 1965, J. Helminthol. 39: 349–362; Myers and Kuntz, 1969, Can. J. Zool. 47: 419–421; Kamara, 1975, Bull. Anim. Health Prod. Afr. 23: 265–268). All but the last two reports were from African anteaters. Since fourth stage larvae of *Gendrespirua* have not been described from Asian anteaters it remains undetermined if the species in this case is *G. hamospiculata*. The polypoid lesion due to this parasite has not been described in any of these reports.

Journal of Wildlife Diseases, 20(1), 1984, pp. 70–72

Insulin-producing Islet Cell Tumor in an Ectopic Pancreas of a Red Fox (*Vulpes vulpes*)

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In May 1981, a young female red fox, exhibiting convulsions and salivation, was killed and examined at necropsy. It was in a good state of nutrition. One-fourth of the tail was missing, but the wound seemed to have healed without complications. The lungs were congested. The liver was swollen and showed a few lesions from ascarid larvae. The adrenal glands were hypertrophic. The kidneys were red in color. The pancreas appeared normal. In the mesentery, attached to the colon, a tumor, measuring approximately 3 × 3 × 3 cm and resembling a lymph node, was seen. No other tumors were observed.

No bacteria were demonstrated in the brain, the liver or the tumor by cultivation on blood agar and Conradi-Drigalski agar plates. Examination for Aujeszky's disease using tissue culture was negative. So was examination for organophosphorus insecticides using pralidoxime-induced reactivation of brain cholinesterases, and for canine distemper and toxoplasmosis using smears stained with hematoxylin and Shorr's differential stain.

Received for publication 18 January 1983.

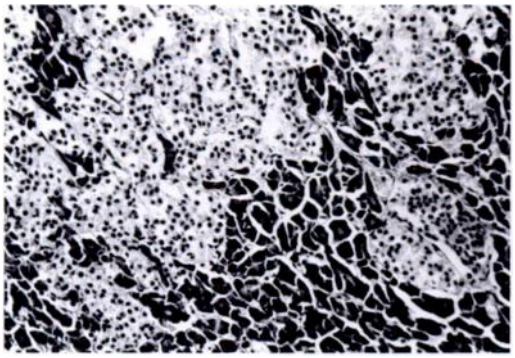

FIGURE 1. Fox pancreas. Exocrine tissue and normal islets of Langerhans in lower right field. Islet hyperplasia left and at top (Hematoxylin-Giemsa ×250).

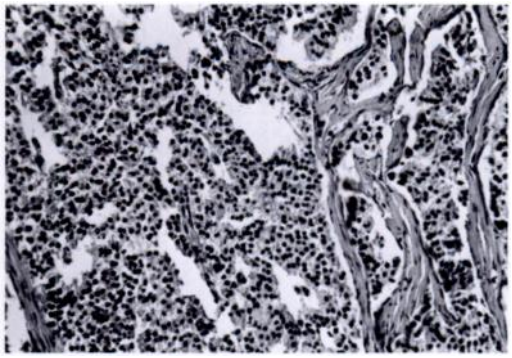

FIGURE 2. Fox islet cell tumor. Uniform cells in trabecular and alveolar arrangement (Hematoxylin-Giemsa ×250).

The tumor was fixed in formalin and embedded in paraffin and sections were cut and stained with hematoxylin and Giemsa. Microscopically a narrow rim of pancreatic tissue with normal islets and islet-cell hyperplasia (Fig. 1) was seen bordering a mass of tissue consisting of light, polygonal cells with small uniform nuclei, and arranged in trabecular and alveolar structures. Focally a tendency to formation of cylindrical cells was seen. The stroma was sparse. The appearance suggested a diagnosis of islet cell tumor. No histological evidence of malignancy was seen, nor was any lymphatic tissue present (Fig. 2). The liver and the kidneys were congested and focal infiltrations of plasma cells and lymphocytes were seen in the kidneys.

Immunohistochemical examination of de-paraffinized sections was performed by indirect immunocytochemical methods (Sternberger, 1979, Immunocytochemistry, 2nd Ed., John Wiley & Sons, New York, pp. 104–169) using the following antisera: guinea-pig anti-insulin (Kommunehospitalet, 8000 Aarhus C, Denmark), rabbit anti-glucagon K 5553 (NOVO, Research Institute, 2850 Bagsværd, Denmark), rabbit anti-somatostatin (Ferring, AB Box 30561, Malmö, Sweden), rabbit anti-pancreatic-polypeptide (Eli Lilly and Company, 307 East McCarty Street, Indianapolis, Indiana 46285, USA), and link antibodies and the PAP-complex (Dakopatts A/S, P.O. 1404, 2200 Copenhagen N., Denmark). The tests disclosed the presence of insulin in the normal islet cells with dilutions of the reagent up to 1:160,000 (Fig. 3). The tumor cells gave a positive reaction with dilutions up to 1:40,000 (Fig. 4). Immunoreactive glucagon (A-cells) and somatostatin cells (D-cells) were present in the normal islets of Langerhans, but not in the tumor cells. Immunoreactive pancreatic polypeptide cells (PP-cells) were seen neither in nor outside the tumor tissue. The specificity of the four primary antibodies was checked by absorption tests in control sections of dog pancreases, whereby it was shown that addition of the homologous hormone antigen to the antisera would inhibit the reaction only within the cell type concerned, and by identification of the four individual cell types in alternating thin sections for electron-microscopy and thick sections for immunocytochemistry. Furthermore it was shown that the secondary antibodies and the 3-amino-9-ethylcarbazol used to detect the primary antibodies did not react non-specifically in the sections, and that the sections contained no endogenous peroxidase after

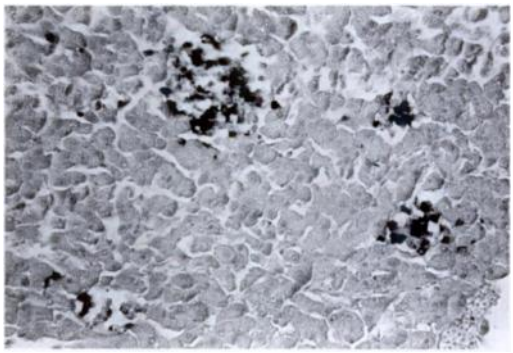

FIGURE 3. Fox pancreas with normal islets showing heavy insulin immunoreactivity (Anti-insulin-peroxidase 1:6,400 ×250).

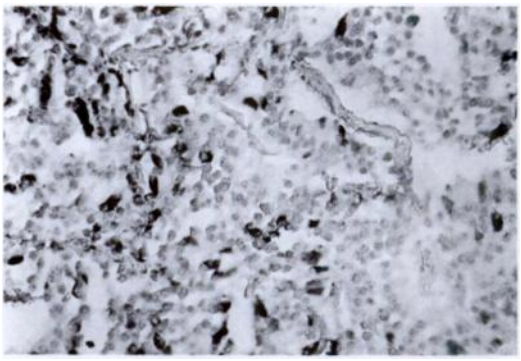

FIGURE 4. Fox insulinoma. Scattered insulin-positive cells (Anti-insulin-peroxidase 1:6,400 ×250).

washing in H_2O_2 prior to the application of antibodies.

In dogs tumors of the pancreas usually occur in animals older than 5 yr. Accessory, ectopic pancreatic tissue is seen occasionally, for instance in the wall of the gall bladder and in the caudal part of the great mesentery (Siegel, 1977, Endocrine Diseases of the Dog, Lea and Febiger, Philadelphia, Pennsylvania, pp. 97–145).

In the present case, no tumors were seen in the pancreas. The tumor formation in the mesentery showed normal pancreatic islet tissue in addition to tumor tissue. The histological features of the tumor were fully compatible with a diagnosis of islet cell tumor and the presence of specific immunoreactive insulin classifies it as an insulinoma. Although the insulin content in the tumor cells was less than in the cells of the regular islets, the total amount of insulin secreted by the tumor could fully explain the clinical signs observed in the fox.

The tumor is believed to have developed from ectopic embryonic pancreatic tissue originating from the dorsal anlage, rather than to represent a metastasis from the pancreas. This is also in accordance with the absence of PP-cells and the presence of A-cells in the normal pancreatic islet tissue surrounding the tumor (Bencosme et al., 1955, Endocrinology, Williams and Wilkins Company, Baltimore, Maryland, pp. 588–593).

This is the only case of a tumor that was seen in 873 red foxes in Denmark which were examined at necropsy from 1969 through 1982.