NORTH AMERICAN BLASTOMYCOSIS IN THE DOG

WITH A REPORT OF SIX CANADIAN CASES

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THE DIAGNOSIS of a systemic mycosis presents a most challenging problem to the small animal practitioner. Perhaps one of the major factors in the apparent lack of clinical diagnosis is the mimicry of fungal diseases for bacterial and viral infections. Diseases due to fungi must always be considered in the differential diagnosis of skin and superficial infections and in systemic disease of unexplained etiology.

North American blastomycosis appears to be the commonest deep mycosis of the dog in North America with approximately 130 cases recorded in veterinary literature. Ramsey and Carter (9) have reviewed all cases up until 1952, 16 in all. Robbins (10) added three more cases in 1953. Ausherman (1), in a most interesting comment, documented his experience with 55 cases, most of which gave serological evidence of infection antemortem. Four cases were added in 1955 by Newberne and others (8) and a single Canadian case has been described by Badame and Peck (2). Menges (7) has recently discussed the clinical signs of North American blastomycosis in 53 dogs.

It is the purpose of this communication to comment on signs seen in North American blastomycosis, to outline steps leading to the diagnosis, and to report on six cases.

CASE REPORTS

Case One

A two-year-old male Doberman was presented with a history of "virus infection" for the past month. A severe cough, noticed at the start of the illness, was still present when the dog was brought for further examination. Generalized superficial adenitis was present and subcutaneous, firm nodules were found on the nose and on the back. The temperature at the time of admission was 103.6° F; during hospitalization this fluctuated between 103° and 105° F. Laboratory examinations revealed a total white count of 24,000; a differential smear showed a marked shift to the left (polymorphs 52%, band cells 36%, lymphocytes 10%, monocytes 1%, and eosinophiles 1%). The blood urea nitrogen was 19 mg per 100 ml blood. Urinalysis was essentially normal. A biopsy of the left inguinal lymph node was performed; the changes seen were considered to be consistent with chronic suppurative lymphadenitis. The subcutaneous nodules on the back formed abscesses on the second day of hospitalization and a culture of the pus demonstrated hemolytic E coli. A diagnosis of lymphadenitis due to generalized infection was made and treatment with tetracyclines was instituted. Some response followed this therapy and the dog was discharged on the eleventh day of hospitalization. One month later the dog was presented again, in extremis. Generalized adenitis, cough,

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cutaneous abscesses, and pyrexia were still present. The total white count was 38,000, polymorphs 26%, band cells 64%, lymphocytes 4%, eosinophiles 6%. Culture from a nasal swab grew Staphylococcus pyogenes. Chest x-ray findings were consistent with pneumonitis, possibly of mycotic origin (Fig 1). The dog died that night. Postmorten diagnosis was systemic disseminated North American blastomycosis, but confirmation by culture of the organism was not obtained.

Case Two

A four-year-old female mongrel was presented with the history of a cough of six months' duration. Its temperature during this time varied between 103° and 104° F. No response was noted to penicillin or tetracyclines. No chest x-rays were taken during this therapy.

Physical examination on admission revealed a normal temperature and no outward signs of illness. Auscultation of the chest, however, demonstrated acute pleuritis and bronchopneumonia of all lobes of the lungs. No other physical signs were noted. Chest x-rays showed peribronchial consolidation of all lobes of the lung with atelectasis of the left diaphragmatic lobe. A diagnosis of bronchopneumonia, possibly mycotic, was made. Hematological examination showed a total white count of 31,000; 32% polymorphs, 58% band cells, and 10% lymphocytes. The blood urea nitrogen was 12 mg per 100 ml blood. Culture of a nose swab produced Bordetella bronchisepticus. The chronic non-responsive cough with pyrexia and radiographic evidence aroused suspicion of mycotic pneumonia. Unfortunately the dog died before cultural confirmation could be made. Postmortem diagnosis was pulmonary North American blastomycosis, with metastasis to the liver, spleen, and left femur. No cultures were made.

Case Three

A four-month-old Boxer puppy was presented with signs of acute bronchopneumonia. The owner, a physician, had been treating the dog with chloramphenicol for one week without any noticeable improvement. The puppy was acutely ill, with a rectal temperature of 104° F and extreme dyspnea. On chest auscultation, moist rales could be heard in all lobes. An x-ray examination of the chest was compatible with a diagnosis of acute bronchopneumonia. Laboratory findings were essentially normal except for a leukocytosis (28,600) and a marked shift to the left (polymorphs 14%, band cells 60%, lymphocytes 26%). Direct examination of swabs from the sputum showed budding, yeast-like cells. Examination of material obtained by bronchoscopic aspiration showed identical organisms (Fig 2). Cultures of these materials produced Bordetella bronchisepticus and Blastomyces dermatitidis. Euthanasia was performed at the owner's request. Postmortem diagnosis was pulmonary North American blastomycosis.

Case Four

This dog, also owned by a physician, was a four-year-old female Labrador Retriever. She was admitted to the hospital for treatment of a chronic ulcer on her left hock. Thirteen days prior to admission the dog had been hunting and had returned from a retrieve with a small puncture wound on the left hock. This had been healing well for four days but then started to discharge a sero-

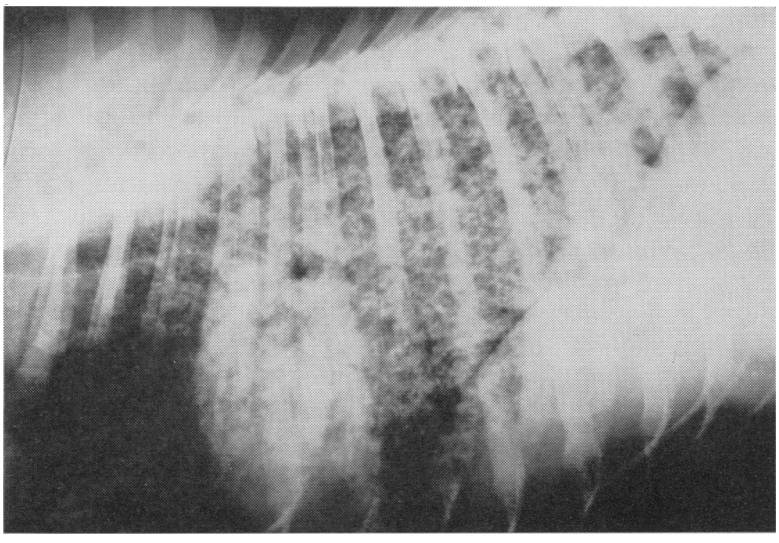

Figure 1. Pulmonary North American blastomycosis. Note the anterior mediastinal mass displacing the trachea dorsally (Anterior mediastinal lymph nodes), and peribronchial calcification.

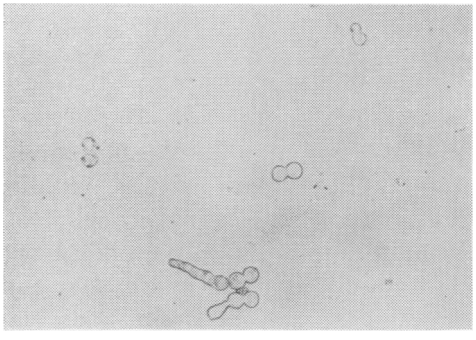

Figure 2. Blastomyces dermatitidis in bronchial exudate obtained by bronchoscopy and cleared in 15% NaOH. Preparation 12 hours old, note the production of pseudohyphae. × 250.

sanguinous exudate. Five days later a prominent nodule had developed at the site and there was slight cellulitis of the leg. Ulceration of the centre of this nodule had occurred and the area was red and shiny. A serosanguinous exudate was noticed. There was no lymphadenitis in the leg.

Smears from the ulcer and exudate showed budding cells with a thick, refractile wall. Cultures revealed Blastomyces dermatitidis, Staphylococcus pyogenes, Streptococcus fecalis, and a hemolytic E coli. Because of the localized nature of the ulcer combined with negative chest x-rays and the absence of regional adenitis, the lesion was removed surgically and a course of potassium iodide given. No recurrence has been noted to this time (24 months following surgery). Histologic diagnosis was cutaneous North American blastomycosis.

Case Five

A seven-month-old female Cocker Spaniel was admitted to the hospital because of a "cold" of two weeks' duration. A sister of the dog had died one month before with a "cold" and then "fits".

The puppy was acutely ill and depressed. The rectal temperature was between 102° and 105° F, respirations 45 per minute, and pulse 112 per minute. Breath sounds were diminished in all lobes and moist rales were heard in both apical lobes. Abdominal pain was elicited on palpation and slight splenomegaly was noted. Cervical adenitis was present and a small fluctuating nodule was palpated in the right lumbar region. A purulent nasal discharge was present.

X-ray films of the chest and abdomen were taken. Acute broncho-pneumonia with some radiation of the process from the left hilum and atelectasis of the left apical lobe was found. Splenomegaly was present but no other abnormalities were seen in the abdomen.

Hematological findings were hemoglobin 9 g per 100 ml, hematocrit 28%, white cell count 18,500 with a differential picture of 82% neutrophiles (all mature) and 18% lymphocytes. The blood urea nitrogen was 65 mg per 100 ml of blood.

The clinical impression was that the puppy had distemper complicated by secondary bacterial infection. The dog was treated with chloramphenicol. On the second day of hospitalization the small abscess in the right lumbar region ruptured and discharged a thick yellow pus. Direct examination of this pus showed organisms which were thought to be Blastomyces dermatitidis (Fig 3); this was subsequently proved on culture. Several other abscesses were found scattered over the cervical region. Euthanasia was performed. The necropsy diagnosis was disseminated North American blastomycosis with metastasis to the bones, spleen, kidneys, and subcutaneous tissue.

Case Six

A six-year-old male Collie was presented because of a sore on the right front paw. This lesion had been present for at least three months and the owner felt that it dated from the time that a cow stepped on the dog's foot. The lesion was purulent and draining although some evidence of spontaneous healing was noticed in its centre. The edges of the lesion were elevated and roughened. Cellulitis was present in the leg and the axillary lymph node was enlarged. When the leg was clipped two other ulcers were found, one on the lateral aspect of the forearm and the other on the medial aspect of the upper arm.

Other physical findings and laboratory studies were not remarkable.

Biopsy of the primary ulcer on the foot and the axillary lymph node showed budding refractile yeast-like organisms when stained with Gridley's stain for fungi (Fig 4). Cultures subsequently revealed the presence of Blastomyces dermatitidis. The two small ulcers on the leg were excised but it was impossible to remove the one on the paw due to its location and size. The dog was placed on potassium iodide intravenously and orally. Healing of the lesion occurred without adverse effects until the twelfth day of hospitalization. At this time the temperature of the dog, which had been below 101° F, rose to 102° F and signs referrable to pneumonia developed. The temperature rose to 104° F during the next two days and cough, nasal discharge, and dyspnea became prominent. Peribronchial consolidation and radiation of infiltration from the hilum of both lungs was seen on the x-ray. The dog died on the eighteenth day of hospitalization. Necropsy revealed North American blastomycosis of the lungs, bone, spleen, and kidneys.

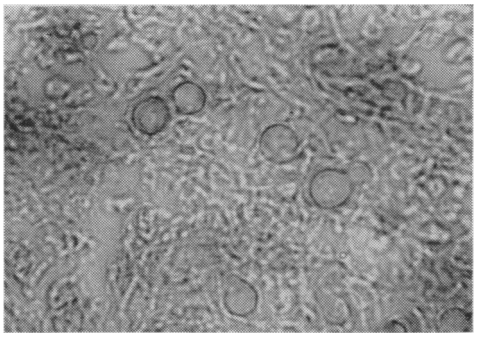

Figure 3. Blastomyces dermatitidis in pus. × 500.

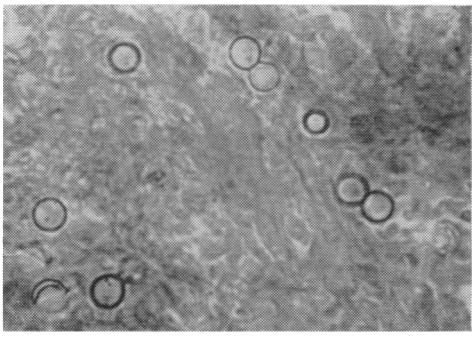

Figure 4. Blastomyces dermatitidis in lymph node biopsy. Gridley's stain. × 500.

Discussion

An analysis of the cases described in the literature is difficult because of variant terminology. Many authors use the term "systemic" to describe some of their cases; most cases of North American blastomycosis will become systemic if the dog does not die during the period of primary pneumonia. From a survey of the literature, however, a general pattern of the disease emerges; pneumonia and skin lesions are the presenting signs in over 85% of all cases.

It would appear then that North American blastomycosis in the dog, as in man, may assume two clinical patterns: primary pneumonitis, which may either have a fatal outcome per se or progress to dissemination, and a primary, usually benign, skin infection.

Pulmonary Blastomycosis

The pneumonitis caused by Blastomyces dermatitidis is usually severe enough to produce clinical signs of respiratory embarrassment. In some cases, however, the disease rapidly disseminates and then the referring signs are subcutaneous abscesses, lameness, or blindness. We feel that "systemic" signs merely represent a late stage of pulmonary involvement and that most of the subcutaneous abscessation and skin lesions arise after pulmonary invasion and not prior to it. Three of our six cases were presented because of pneumonia, and one had a history of a "virus infection" before skin lesions developed. Unfortunately chest x-rays were not made until shortly before the dog died.

The pneumonia seen in this condition is not typical of distemper, bacterial pneumonia, or of so-called "atypical virus pneumonia". The pneumonia seen in blastomycosis is subchronic and does not respond to antibiotic and supportative therapy. X-ray films of the chest confirm this; peribronchial consolidation, mediastinal adenitis, abscessation (usually miliary), and even calcification are seen on chest films.

Hematological examinations are not particularly helpful. Although leukocytosis and a marked shift to the left are present constantly, these findings do not exclude bacterial infection.

With dissemination the clinical picture may become bizarre. Subcutaneous abscesses and lymphadenopathy appear to be fairly constant findings. The

abscesses are multiple and, when aspirated, yield a thin, yellow-gray pus. Blastomyces can be recovered easily from such material. Blindness may also appear during the disseminated form (7, 10). Case 1 represents the full-blown disseminated form. After one month of suffering from a "virus infection" with severe cough, subcutaneous abscesses developed. This was interpreted as bacterial lymphadenitis and the dog died six weeks later, two and one-half months after the start of the disease.

Cutaneous Blastomycosis

In man, cutaneous blastomycosis, in most instances, is probably part of an unrecognized disseminated infection (12, 16). All of the reported cases in dogs, including that of Saunders (11) and our Case 6, probably were a result of dissemination rather than of primary cutaneous inoculation. Case 4 was undoubtedly due to inoculation of Blastomyces dermatitidis into the subcutaneous tissue. The lesion in this case did not resemble the lesions described as part of the disseminated disease. It appeared as a nodule four days after the original injury. This nodule drained a serosanguinous exudate and in five more days ulcerated in the centre. The centre of this ulcer had a raw, red appearance and there was a slight cellulitis of the leg. There were no miliary abscesses around the edges of the ulcer and no tendency for spontaneous healing in the centre of the lesion. Conant (4) has described the cutaneous lesion as a spreading, exuberant, ulcerating granuloma. The edges are elevated and show miliary abscesses. There is a tendency for spontaneous healing and scar formation in the centre of the ulcer. This is the general appearance of the lesion seen in dogs with the disseminated disease and varies markedly from the appearance in Case 4. Five of our six cases do not vary from the reported picture of North American blastomycosis in the dog. The sixth case apparently represents true, primary, benign, cutaneous blastomycosis. It is our contention that superficial abscesses and skin lesions are a late manifestation of the disease which follows primary pulmonary involvement.

The diagnosis cannot really be established until laboratory studies have revealed the presence of the fungus. The methods outlined below are most satisfactory for this purpose.

Skin testing with blastomycin is not a very satisfactory aid to diagnosis since anergy is quite often present in infected dogs. Complement-fixation tests on the patient's serum may, however, prove valuable (1).

Mycologic Diagnosis

Blastomyces dermatitidis, the cause of North American blastomycosis, appears in all types of body material as round, thick-walled, usually single-budding yeast cells. Materials for examination include sputum, bronchial aspirate, pleural fluid, material collected from miliary abscesses found at the base of verrucous lesions, purulent discharges, tissue collected at biopsy, aspirate from subcutaneous abscesses, urine, scrapings from an ulcerous lesion and bone marrow. On culture media incubated at room temperature, this fungus changes from the yeast form and develops branching, septate filaments, forming a primary white

colony. Because this fungus produces a yeast or parasitic form at body temperature and a filamentous or mould form at room temperature it is said to be diphasic. Other pathogenic fungi that are diphasic include Histoplasma capsulatum and Coccidioides immitis.

Direct Examination of Body Material

A direct microscopic examination of body material mounted in a drop of 10–20% sodium hydroxide will reveal characteristic yeast cells. If these are present, a tentative diagnosis is justified. The hydroxide is given 10 minutes to clear the material and then the slide is examined by *reduced* illumination. Blastomyces dermatitidis appears as round, thick-walled usually single-budding yeast cells, having a broad attachment to the parent cell. The normal range in size is from 8–20 microns, but forms as small as 2 and 4 microns have been reported from human infections (5, 13, 14, 15). Also, to add to the difficulty of recognizing Blastomyces dermatitidis in the yeast form as found in tissue, there are a number of reports in the literature describing large forms of Histoplasma capsulatum that may be confused with Blastomyces dermatitidis (3, 13). With these atypical forms in mind it is evident that only by isolating and identifying the fungus in culture can a diagnosis be reliable.

Cultural Identification

The media used for the isolation of Blastomyces dermatitidis are governed by the degree of suspected contamination by bacteria and non-pathogenic fungi.

Sabouraud agar containing 20 units per ml of penicillin, 40 micrograms per ml of streptomycin and 0.5 mg per ml of cycloheximide (hereafter referred to as Sabouraud C.P.S. agar), is commonly used. This medium is incubated at room temperature. Blastomyces dermatitidis first produces a waxy usually moist-looking colony free of aerial mycelium, but soon it produces spike-like masses of hyphae. This is commonly called the prickly stage. Eventually the colony becomes covered with a pure white cottony growth which gradually turns brown with age. A microscopic examination of the white aerial growth shows round or oval conidia ranging in size from 3 to 5 microns in diameter. If the culture is kept about four weeks, chlamydospores having diameter of 8–18 microns will be found with unevenly thickened cell walls. This gives these cells unusual shapes.

Although cycloheximide does not inhibit growth of Blastomyces dermatitidis at 25° C, it has been shown by McDonough et al (6) that 0.4 mg per ml will inhibit some strains at 37° C.

Another good medium for isolation of Blastomyces dermatitidis from contaminated material is Littman oxgall agar. This medium contains streptomycin and crystal violet to inhibit bacteria and ox bile that restricts, but does not prevent, the growth of fungi. The inoculated medium is incubated at room temperature and the growth takes up some of the crystal violet appearing as a bluish gray. It is our practice to transfer suspicious colonies as they appear to Sabouraud agar and make our identification from this medium. On blood agar incubated at 37° C, Blastomyces dermatitidis produces a waxy cerebriform colony which when examined with a low power dissecting microscope looks

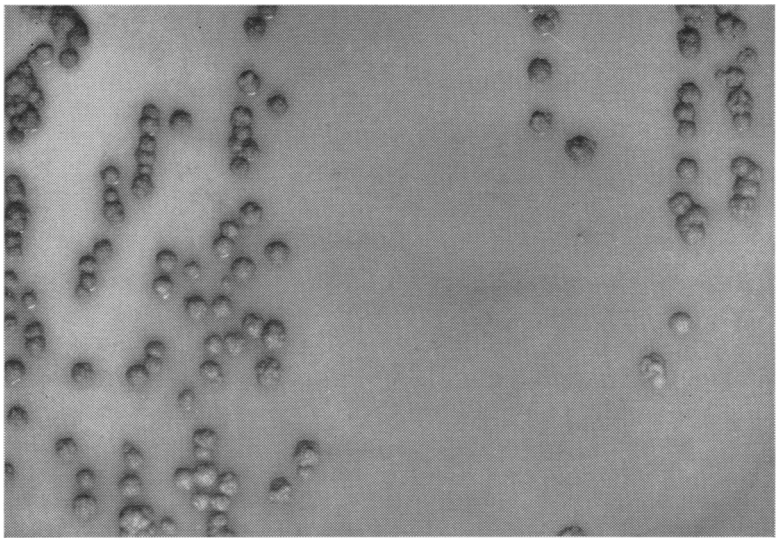

Figure 5. Blastomyces dermatitidis, 10-day-old colonies on blood agar grown at 37° C.

not unlike a drop of apple sauce (Fig 5). If a moist mount is made of some of this growth and examined with a microscope it will be seen to be a mass of budding, thick-walled, yeast cells similar to the form found in tissue. It is always best to verify an isolation by converting it to the other phase ie if the fungus is isolated on a medium incubated at room temperature, inoculate blood agar and incubate at 37° C and check for the characteristic yeast or parasitic form. If the isolation is made on blood agar at 37° C convert growth to the saprophytic form at room temperature.

Summary

Six cases of North American blastomycosis in the dog have been described. Five of these dogs suffered from the disseminated disease and one from a benign, primary skin form. Four dogs were submitted with signs of pneumonitis and two with skin lesions. One of the cases showing the skin lesions died with the disseminated form of the disease shortly after surgery. There is adequate evidence to support the contention that North American blastomycosis in the dog, as in man, is most commonly encountered as a systemic infection and that most skin lesions represent part of this systemic process. The causative agent Blastomyces dermatitidis can be recovered fairly easily from biopsies and most body discharges. The final diagnosis must rest on culture of the organism since the histological picture may be confused with histoplasmosis.

Résumé

L'auteur nous entretient de six cas de blastomycose canine nord-américaine. Cinq des six chiens souffraient de la maladie commune, tandis que le sixième sousfrait d'une forme cutanée primitive de la même affection. Quatre des chiens manifestaient des symptômes de pneumonie, et les deux autres présentaient des lésions sur la peau. Un de ceux qui souffraient de ces lésions mourut de la

maladie commune quelque temps après une intervention chirurgicale. On peut affirmer catégoriquement, avec preuves à l'appui, que la blastomycose canine nord-américaine, tant chez le chien que chez l'homme, se présente, la plupart du temps, sous la forme d'une infection systématique, et que la plupart des lésions cutanées sont des manifestations de cette réaction systématique. L'agent causatif, le Blastomyces dermatitidis peut être recouvré par une biopsie ou dans la plupart des excrétions de l'organisme. Le diagnostic final doit se fonder sur la culture de l'organisme, vu que l'aspect histologique peut être confondu avec l'histoplasmose.

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PERSONAL NEWS

Births

Barlow To Dr and Mrs H Barlow of Edmonton on December 3, 1960—a son, John Peter.

Cotter To Dr and Mrs W Cotter of Hanna Alberta on November 24, 1960—a son, William.

Earnshaw To Dr and Mrs R E Earnshaw of Penticton, BC on August 31, 1960—a son, John Jamieson.

Langford To Dr and Mrs E V Langford of New Westminster, BC on September 20, 1960—a daughter, Kathryn Wendy.

Lantink To Dr and Mrs C J Lantink of Kincardin on January 3, 1961—a daughter, Carla.

Perry To Dr and Mrs D A Perry of Burnaby, BC on October 19, 1960—a daughter, Trenna Grace.

Wood To Dr and Mrs H Wood of Mission, BC on November 1st, 1960—a daughter, Erika Marnie.

Deaths

Blacklock Dr J F Blacklock, Director of Environmental Sanitation for the City of Hamilton, died of pulmonary embolism following surgery on December 23, 1960.

Manchester Dr W R Manchester of Sudbury, Ontario died on January 2, 1961.

Peppin Peggy Peppin, wife of Dr G Peppin of Lethbridge, Alberta died on December 9, 1960.