Serratia marcescens septicaemia in the dog

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ABSTRACT

A non-pigmented strain of Serratia marcescens was isolated ante-mortem and at post-mortem from the blood of six dogs under intensive medical care. Clinical, bacteriological and pathological evidence confirmed death to be associated with septicaemia from this Gram-negative organism.

INTRODUCTION

Serratia marcescens has been known to exist in both pigmented and non-pigmented varieties (Breed, Murray & Smith, 1957). The organism is usually considered to be a saprophyte whose natural habitat includes soil, water, sewage and food (Breed & Murray, 1957; Gaughran, 1969; Wilson & Miles, 1959). The pathogenic nature of Serratia spp. for animals was first recorded in 1903 by Bertarelli. More recent reports have incriminated this organism as a cause of mastitis (Barnum, Thackery & Fish, 1958) and abortion in cattle (Quintiliani & Gifford, 1969) and subcutaneous abscesses in reptiles (Boam et al., 1970).

Serratia marcescens, particularly the non-pigmented strains, has assumed importance as a nosocomial pathogen for man (Clayton & Von Graevenitz, 1966; Dodson, 1968; Ewing, Johnson & Davis, 1962; Magnuson & Elston, 1966; Smith & Reynolds, 1970; Wilfert, Barrett & Kass, 1968; Williams et al., 1971). It has become a frequent cause of serious infection in hospitalized patients, especially associated with intravenous fluid infusion therapy (Wilfert, Barrett & Kass, 1968).

Death attributable to fulminating Serratia marcescens septicaemia occurred in six dogs under intensive care on intravenous fluid therapy via indwelling jugular catheters. The animals were suffering from a range of debilitating diseases. Three were under post-operative management, while the other three were medical cases.
Case Reports

Case 1
On 8 November 1970 a 7-year-old male Labrador Retriever was presented to The Animal Medical Center in a state of septic shock. The animal had been operated on 7 days previously for the removal of a splenic haemangiosarcoma. Post-operative therapy had included a litre of Lactated Ringer's solution and 250 cc of blood via jugular catheter. Penicillin/streptomycin was administered for 3 days postoperatively, and tetracycline was prescribed on discharge for 5 days.

At presentation the dog was in a state of collapse, having a temperature of 105°F, marked tachycardia and a rapid, thready pulse. A blood culture and routine blood count were taken. Abdominal paracentesis and radiographs did not reveal fluid or evidence of peritonitis. Haematological evaluation revealed a marked leucocytosis; white blood cell count was 59.5 x 10^3/mm^3 with prominent neutrophilia and shift to left. There was mild anaemia marked by dehydration. Packed cell volume was 33%, total plasma protein (TPP) was 8.3 gm%, and blood urea nitrogen (BUN) was 17.8 mg%. The blood culture was positive in 12 hr, *Serratia marcescens* was identified and sensitivity testing was done. The dog was treated intravenously with gentamicin and fluid therapy. The condition deteriorated, however, and death occurred 5 days following re-admission.

Case 2
A 9-year-old male Italian Greyhound was presented on 23 February 1971 with an acute haemorrhagic gastroenteritis. Therapy had included intestinal antibiotics, astringents and anticholinergics; intravenous fluids including Lactated Ringer's and dextrose saline solutions were also given for 3 days. The dog's condition improved, but on the 6th day pain and lameness developed in the right leg and there was pyrexia (temp. 104°F). *Serratia marcescens* was isolated from the venous blood and urine at this stage. Over the next 4 days the dog's condition deteriorated. A repeat blood culture remained positive despite antibiotic therapy. Stupor, circling with nystagmus, and severe right-sided weakness developed. Death was marked by decerebrate seizures.

Case 3
Enlargement of the spleen was diagnosed in a 14-year-old male Miniature Pinscher on 10 April 1971. The diagnosis was based on radiographic evidence and a haemogram that revealed a responsive anaemia, PCV 36%, low platelet count (54,000/mm^3), and leucocytosis (20.6 x 10^3/mm^3). A splenectomy was performed on 11 April 1971. Post-surgical treatment included Lactated Ringer's and dextrose saline solutions administered via jugular catheter and penicillin/streptomycin. Eight days post-operatively the animal developed a fever (temp. 104.8°F). A haemogram at this stage revealed a leucocytic response with a total
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WBC count of $55.7 \times 10^3$/mm$^3$, a prominent neutrophilia (94%) and shift to left. The PCV was 23% and the BUN remained normal (11.8 mg%).

An ante-mortem blood culture at this time gave a pure culture of Serratia marcescens within 24 hr. The dog's condition deteriorated rapidly. Central nervous symptoms of dementia and paddling convulsions suggested a septicaemic meningitis. The animal died on 20 April 1971 despite therapy.

Case 4

On 25 April 1971 an 11-year-old female Wirehaired Terrier was presented in the postictal phase of a hypoglycaemic seizure characterized by generalized sporadic muscle twitching and flaccid weakness. The animal had suffered an epileptiform seizure 3 hr prior to presentation. The dog had a history of two seizure attacks within the last 4 years, each of which had followed excitation.

An initial blood examination suggested a hypoglycaemia associated with an insulinoma—PCV 57%, WBC $8.5 \times 10^3$/mm$^3$, blood glucose (BG) 35 mg%, BUN 11.0 mg%, serum glutamic pyruvic transaminase (SGPT) 54 RF units, TPP 7.6 g%, sodium 139 mEq/l, and potassium 3.1 mEq/l. A diagnosis of insulinoma was eventually confirmed by intravenous glucose tolerance test and blood insulin levels. During hospitalization the dog became febrile (temp. 103.2°F), and a blood culture was taken. Serratia marcescens was isolated, and a sensitivity test suggested the antibiotic of choice to be gentamicin. Treatment for the next 9 days was based on the monitoring of blood glucose, serum electrolytes, Na+, K+ and the haemogram, and included 50% dextrose saline, diazoxide, potassium therapy and intravenous gentamicin and chloramphenicol. Pyrexia persisted for the remaining 7-day course. The clinical condition showed very little improvement. Two days prior to death, a haemogram revealed a mild leucocytosis, WBC $18.7 \times 10^3$/mm$^3$, PCV 43%, BUN 9.1 mg%, and BG 80 mg%. The dog died 10 days after admission, with no obvious neurological signs except for somnolence and progressive weakness.

Case 5

On 28 July 1971 an 8-year-old female Schnauzer was operated on for a pyometra. Diagnosis had been based on clinical history, radiographic evidence of uterine enlargement, and haematological findings (WBC $23.2 \times 10^3$/mm$^3$ with a prominent regenerative shift to left). A jugular catheter was routinely inserted and the dog started on fluid therapy prior to surgery. Penicillin/streptomycin and dextrose saline were administered post-operatively for 2 days prior to discharge.

Seven days post-operatively the animal was re-presented in septicaemic crisis, prostrate and febrile (temp. 104.2°F), with pale mucous membranes and occasional petechiae on the gums and sclera, rapid heart rate, and weak pulse.

Clinical pathological findings again showed a leucocytosis (WBC $32.8 \times 10^3$/mm$^3$ with shift to left), mild responsive anaemia (PCV 28%, reticulocytes, 3.2%),
BUN 18.9 mg%, BG 95 mg%, TPP 7.2 g%, SGPT 164 RF units, and platelets 62,000/mm³. A blood culture collected at the time of presentation was positive for *Serratia marcescens* within 12 hr. The dog died before therapy was begun.

**Case 6**

Multiple myeloma was diagnosed in a 10-year-old male Airedale on 14 September 1971. Radiographs of the spine revealed extensive lytic lesions in the body and arch of the thoracic, and lumbar vertebrae. The serum protein was 12.5 g%; electrophoresis revealed a monoclonal spike in the beta and gamma fractions representing 78% of the serum protein. The spinal lesions were treated with 1,550 rads of cobalt radiation therapy from 13–22 October. Oral melphalan therapy was administered from 30 October to 4 November, and the animal was maintained on tetracycline (750 mg. daily) as prophylaxis to infection. The only side effects noted were gastrointestinal bleeding, progressive anaemia and leucopenia. On 5 November 1971 the animal was re-hospitalized because of a deteriorating clinical condition and marked anaemia (PCV 16%, WBC 8.3 x 10³/mm³). A blood transfusion was administered at this time. Other therapy included tetracycline, prednisolone, diphemanil methylsulfate and haematinics. Three days later the dog became febrile (temp. 104.5°F). Clinical pathological findings at this time were PCV 17%, WBC 13.2 x 10³/mm³, neutrophils 98%, band neutrophils 8%, metamyelocytes 2%, lymphocytes 2%, eight nucleated red cells/100 WBC's, platelet count 54,000/mm³, TP 8.1 g%, albumin 2.1 g%, globulin 6-0 g%, BUN 27 mg%, BG 75 mg% and SGPT 55 RF units. A blood culture was taken. The animal was discharged on high dose oral antibiotic therapy but failed to respond and died on 10 November 1971.

**Bacteriology**

Ante-mortem blood cultures were collected using aseptic techniques following close shaving and double sterilization with 70% alcohol and povidone-iodine of the site over the cephalic vein.

Approximately 8–10 cc of blood was collected by venepuncture and transferred to 50 cc of Trypticase Soy Broth—Baltimore Biological Laboratories, Cockeysville, Md. 21030 U.S.A.—in two cases on thioglycollate media containing 1% sodium polyanethol sulfate (Von Haebler & Miles, 1938) in four cases. Following 12–24 hr incubation at 37°C, when growth had appeared in the media, as evidenced by turbidity of the broth, a subculture to a 5% sheep blood agar plate and Levine eosin methylene blue (EMB) media was made.

At necrospy of the heart, blood was routinely cultured. Thioglycollate broth was used as the basic isolation media, incubated 12 hr at 37°C before subculturing on to blood and EMB agar plates. Cultures from obvious lesions, such as valvular heart lesions, the kidney and, in two cases, swabs from the bone marrow, were inoculated directly onto blood agar and EMB plates. The organism grew readily
on blood agar producing medium-sized (2–3 mm in diameter) entire glistening opaque greyish-yellow non-haemolytic colonies at 24 hr. Levine EMB media also revealed medium-sized dull purplish-black colonies. Stained films revealed uniform gram-negative bacilli averaging 0.5–1.0 μ in length. The organisms were motile, and subsequent biochemical studies (summarized in Table 1) identified them as Serratia spp. (Edward & Ewing, 1972; Oberhofer & Hajkowski, 1970). Confirmatory classification of all isolates was made by the Communicable Disease Center, Atlanta, Georgia, where the organisms were typed as Serratia marcescens, slightly related to O14:H12.

**Table 1. Biochemical and biophysical characteristics of Serratia marcescens isolated from six dogs with septicaemia.**

<table>
<thead>
<tr>
<th>Test</th>
<th>Reaction</th>
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<tbody>
<tr>
<td>Urea</td>
<td>—</td>
</tr>
<tr>
<td>Hydrogen sulphide</td>
<td>—</td>
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<tr>
<td>Citrate</td>
<td>+</td>
</tr>
<tr>
<td>Oxidase</td>
<td>—</td>
</tr>
<tr>
<td>Indole</td>
<td>—</td>
</tr>
<tr>
<td>Lysine decarboxylase</td>
<td>+</td>
</tr>
<tr>
<td>Ornithine decarboxylase</td>
<td>+</td>
</tr>
<tr>
<td>Desoxyribonuclease activity</td>
<td>+</td>
</tr>
<tr>
<td>Motility</td>
<td>+</td>
</tr>
<tr>
<td>Sugars</td>
<td>—</td>
</tr>
<tr>
<td>Lactose</td>
<td>Acid</td>
</tr>
<tr>
<td>Dextrose</td>
<td>Acid</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Acid</td>
</tr>
<tr>
<td>Maltose</td>
<td>Acid</td>
</tr>
<tr>
<td>Mannitol</td>
<td>Acid</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>Acid</td>
</tr>
<tr>
<td>Ducitol</td>
<td>—</td>
</tr>
<tr>
<td>Inulin</td>
<td>—</td>
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<tr>
<td>Raffinose</td>
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</tbody>
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Routine antibiotic sensitivity testing was carried out on each ante-mortem isolate using 5% Mueller Hinton sheep blood agar plates and antibiotic impregnated sensitivity discs (Table 2).

**PATHOLOGY**

The lesions found at necropsy were consistent with a fulminating septicaemia. Lesions were typically found in the heart, lungs, kidney, brain, liver and reticuloendothelial system. Cardiac lesions were the most conspicuous. Valvular
endocarditis was present in all cases. Acute haemorrhagic irregular vegetative lesions had involved the mitral valve cusps in six dogs (Fig. 1), the tricuspid valve in two dogs, and the aortic valve in one dog. Subendocardial ecchymoses and petechiation were also common findings. Histopathological examination revealed septic valvular endocarditis as well as extensive myocarditis and endocarditis in four dogs. Two dogs had small myocardial infarcts.

TABLE 2. Antibiotic sensitivities of six clinical isolates of *Serratia marcescens*.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Disc concentration (mcg)</th>
<th>Number of isolates sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Lincomycin</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>Neomycin</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Penicillin (units)</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Polymixin B (units)</td>
<td>300</td>
<td>0</td>
</tr>
<tr>
<td>Sulphadimethoxine</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>30</td>
<td>2</td>
</tr>
<tr>
<td>Triple Sulfa</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*Sensi Discs, Baltimore Biological Laboratories, Cockeysville, Maryland.*

Large aortic and venous thromboses were present in two cases. Multiple disseminated septic emboli and infarcts were present in all the major organs. The lungs and kidneys were consistently involved in all dogs. Grossly, the lungs revealed some degree of oedema and congestion. Multiple subpleural haemorrhages were found diffusely scattered over the surface of the lobes. Microscopically, the lungs showed disseminated foci of septic inflammation, microabscesses, haemorrhage and pneumonitis. Grossly, the kidneys of all dogs revealed bilateral multiple small (up to 5 mm in diameter) subcapsular haemorrhagic infarcts. In three dogs the area of infarction was more extensive. One dog showed gross evidence of bilateral pyelonephritis. Microscopically, lesions included disseminated microabscesses and areas of septic embolism with necrosis throughout the kidney.

The brains in five dogs had extensive subdural hyperaemia and haemorrhages over the surface of the cerebrum (Fig. 2) and cerebellum. Haemorrhagic menin-
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Gioencephalitis with cerebral infarcts was seen on microscopic examination (Fig. 3). A Gram stain revealed many Gram-negative bacillary elements present within the inflammatory exudate of the subarachnoid spaces (Fig. 4).

The spleen in two cases had been removed. Lesions in the spleen of the other four dogs at necropsy were multiple blackened nodules of hemorrhagic infarction. Microscopically, other areas showed diffuse splenitis characterized by lymphoid depletion, oedema and increased infiltration of neutrophils.

![Fig. 1. Heart, left atrium and mitral valve, dog 6. Acute vegetative endocarditis involving the valve cusps with subendocardial haemorrhage within the atrial wall.](image)

The liver was grossly involved in three dogs. Although normal in size, it was diffusely mottled and there was overall pale-reddish discoloration. The texture was friable. Microscopic findings were dilatation of the hepatic sinusoids with oedema and mild congestion and increased infiltration of polymorphonuclear leucocytes. Degenerative changes and necrosis, when present (two dogs), were centrilobular in distribution.

Other lesions varied with the initial disease for which the animal was presented. Haemorrhagic gastroenteritis with haemorrhagic, oedematous mesenteric lymph nodes was present in dog 2. Neoplastic lesions were present in three dogs and included such lesions as heart-base tumour (dog 4), gastric leiomyoma (dog 3), pancreatic islet cell carcinoma with multiple hepatic metastasis (dog 4), and
FIG. 2. Brain, dorsal view, dog 3. Extensive meningeal vascular hyperaemia with scattered areas of subarachnoid haemorrhage.

FIG. 3. Histopathological section of the cerebral meninges of dog 3 showing acute septic haemorrhagic meningitis with extensive oedema, red cell extravasation and leukocyte infiltration within the subarachnoid space. H & E, x70.
**DISCUSSION**

The history of *Serratia marcescens* has been well reviewed (Gaughran, 1969). Its importance as an emerging nosocomial pathogen has been emphasized in the human medical literature (Clayton & Von Graevenitz, 1966; Denney, Kaye & Hagstrom, 1967; Dodson, 1968; Duma, Warner & Dalton, 1971; Ewing, *et al.*, 1962; Fields *et al.*, 1967; Magnuson & Elston, 1966; Smith & Reynolds, 1970; Wilfert, *et al.*, 1968; Williams *et al.*, 1971). In small animal medicine it has not been accepted as a true pathogen (Bruner & Gillespie, 1966; Wilson & Miles, 1959); and in fact, is at times overlooked because of the morphological similarity of non-chromogenic strains to other coliform organisms such as *Escherichia coli*, *Enterobacter* spp., *Aeromonas* spp. and the Paracolon group (Bottone & Allerhand, 1970; Fields *et al.*, 1967). Infections in man due to this organism have been reported with increasing frequency and the pathogenicity of the organism has been described (Clayton & Von Graevenitz, 1966; Ewing *et al.*, 1962; Magnuson...
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& Elston, 1966; Williams et al., 1971). Most frequently encountered infections have included urinary tract disease, wound infections, otitis, sinusitis, pneumonia, septicaemia, bacterial endocarditis and meningitis.

Septicaemia due to this organism has been frequently encountered as a hospital acquired infection (Dodson, 1968; Magnuson & Elston, 1966; Wilfert et al., 1968; Williams et al., 1971). Predisposing factors associated with the establishment of infection have included previous antibiotic, corticosteroid or cytotoxic drug therapy, pre-existing infections, underlying chronic and debilitating diseases, immunological deficiencies, protracted intravenous fluid therapy and postsurgical complications.

Indwelling intravenous and intraperitoneal catheters, instrumentation of the urogenital or respiratory tract or surgical intervention have been the most frequent portals of entry (Duma et al., 1971; Smith & Reynolds, 1970). Of the six cases reported in this paper, all had been treated with fluid therapy via indwelling jugular catheter, and it is believed that this was the site of entry of the organisms. A positive culture of Serratia marcescens was obtained from the catheter tip in one dog. The organism was isolated from the urine of one dog. The necropsy findings confirmed pyelonephritis, but there was no evidence of cystitis to suggest an ascending infection.

The limited data on in vitro disc sensitivity testing of the strains isolated from the dogs revealed that, as with human strains, they are resistant to many commonly used antimicrobial agents (Clayton & Von Graevenitz, 1966; Dodson, 1968; Magnuson & Elston, 1966; Williams et al., 1971). Most frequently they are sensitive to gentamicin (Wilfert, Barrett & Kass, 1968; Williams et al., 1971), chloramphenicol, erythromycin and kanamycin. Gentamicin or a combination of chloramphenicol and kanamycin has been recommended as therapy for human bacteremia (Dodson, 1968; Wilfert et al., 1968; Williams et al., 1971). Despite the fact that five dogs were treated with the appropriate antibiotic therapy—gentamicin—none responded. Early therapy with high dose rates of antibiotics may in future prove more beneficial. In addition, the restoration of adequate blood perfusion of vital tissues by aggressive fluid therapy, as well as ensuring adequate pulmonary gas exchange and the cautious use of steroids and heparin, are standard therapeutic measures that must also be instituted in the management of Gram-negative septic shock.

ACKNOWLEDGEMENTS

The author thanks Dr George J. Hermann, assistant chief, Enterobacteriology Unit, National Communicable Disease Center, Atlanta, Georgia, for confirming and typing the isolants; Dr Arthur Hurvitz, head of pathology, The Animal Medical Center, for assistance with the pathology; and Mrs Nancy Sturge, editorial secretary, The Animal Medical Center, for assistance in preparation of the manuscript.
REFERENCES

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Résumé. On a isolé, avant la mort et à l'autopsie, une souche non-pigmentée de bactérie prodigieuse (Serratia marcescens) du sang de six chiens soumis à des soins vétérinaires intensifs. L'évidence clinique, bactériologique et pathologique a confirmé que la mort était associée à une septicémie de cet organisme gramnégatif.