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Thomas L. Connolly

John R. Fischer

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Thomas L. Connolly, MD and John R. Fischer, MD*

A 35-year-old woman developed Serratia marcescens septicemia and purpura fulminans with evidence of disseminated intravascular coagulation. She was successfully treated with heparin sodium and antibiotics.

SERRATIA MARCESCENS, a gram negative bacillus, and member of the family Enterobacteriaceae, within the tribe Klebsiellae,[1] was previously considered to be non-pathogenic for man.[2] In recent years, however, this organism has been reported to cause various infections, including bacteremia,[3-6] endocarditis,[7,8] pneumonia,[9] empyema,[10] urinary tract infection,[11,12] osteomyelitis,[13] peritonitis,[14] wound infection,[15] meningitis,[16] and burn infection.[17]

Recent publications have stressed the importance of this organism as a cause of bacteremia in hospitalized patients. These reports do not mention the occurrence of cutaneous lesions associated with *Serratia marcescens* bacteremia. The following report describes a patient with *Serratia marcescens* bacteremia and purpura fulminans.

Case Report

A 35-year-old woman, in the 39th week of her pregnancy, was admitted to the hospital on February 28, 1973, with uterine contractions. Twenty-four hours of labor were ineffectual, due to cephalopelvic disproportion. A Caesarian section was performed, after a Foley catheter was inserted in the bladder. At the time of operation, the amniotic fluid was meconium stained, and the infant appeared severely ill, with respiratory distress.

The following day, the patient had a temperature of 38.4 C, and therapy with tetracycline, 500 mg intravenously, over each six-hour period, was initiated. The dosage was changed to 500 mg of tetracycline, orally, every six hours, on the second postoperative

*From the Division of Infectious Diseases of the Department of Medicine and the Department of Obstetrics and Gynecology, The Creighton University School of Medicine, Omaha, Nebraska

Dr. Connolly was a resident physician at Henry Ford Hospital from 1964-67. Address reprints to the authors at 527 Medical Arts Building, Omaha, NE 68102.

day. She became afebrile, and the tetracycline was discontinued on the third postoperative day. On the fifth postoperative day, she again had a temperature of 38.4 C, and she was given doxycycline, 100 mg orally, every 12 hours, and kanamycin, 500 mg intramuscularly, every eight hours. Both drugs were discontinued on the sixth postoperative day. Earlier, on the second postoperative day, she had complained of chest pain, and because of the possibility of her having had a pulmonary embolism, she was given heparin and coumadin. These drugs were given for three days, the last dose of each drug being given on the fourth postoperative day. Her chest pain abated after two hours, and serial enzyme determinations were normal, as were serial chest x ray films.

On the morning of the sixth postoperative day, she had shaking chills, a temperature of 39.5 C; and an area of erythema on the dorsal surface of the right foot. During the following 10 hours, the area of erythema became more intense and larger. The center of the involved area progressively became dusky, then dark blue to purple, and finally black. Bullae then developed in the center of the necrotic area. Similar lesions occurred on the lateral right hip and thigh, and right and left medial thighs. These areas evolved similarily to the foot lesion, over an 8-to-12-hour period. Not all areas progressed to the same extent. The patient's past history included an urticarial reaction to penicillin.

In consultation on the evening of the sixth postoperative day, examination revealed an acutely ill woman who was complaining of severe pain, involving the right foot and right hip. Inspection of the skin revealed lesions, as depicted in figures 1 and 2. Her mouth and throat appeared dry. Heart sounds were normal, except for sinus tachycardia. Lungs were clear to auscultation. The abdomen was mildly distended; moderate tenderness to deep palpation was noted across the lower abdomen; bowel sounds were decreased. Pelvic examination revealed moderate tenderness of the uterus and a slight amount of purulent drainage from the cervical os. Peripheral pulses, including pulses in the feet, were normal. The temperature was 40.5 C, the pulse 110, and respirations 24.

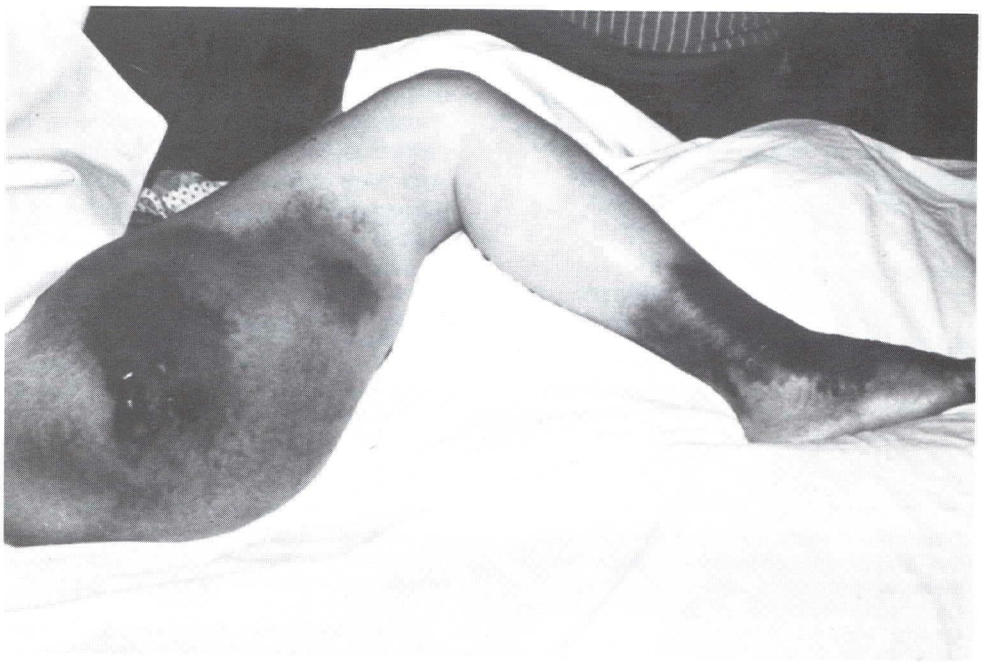

Figure 1
Purpura fulminans secondary to *Serratia marcescens* **septicemia.**

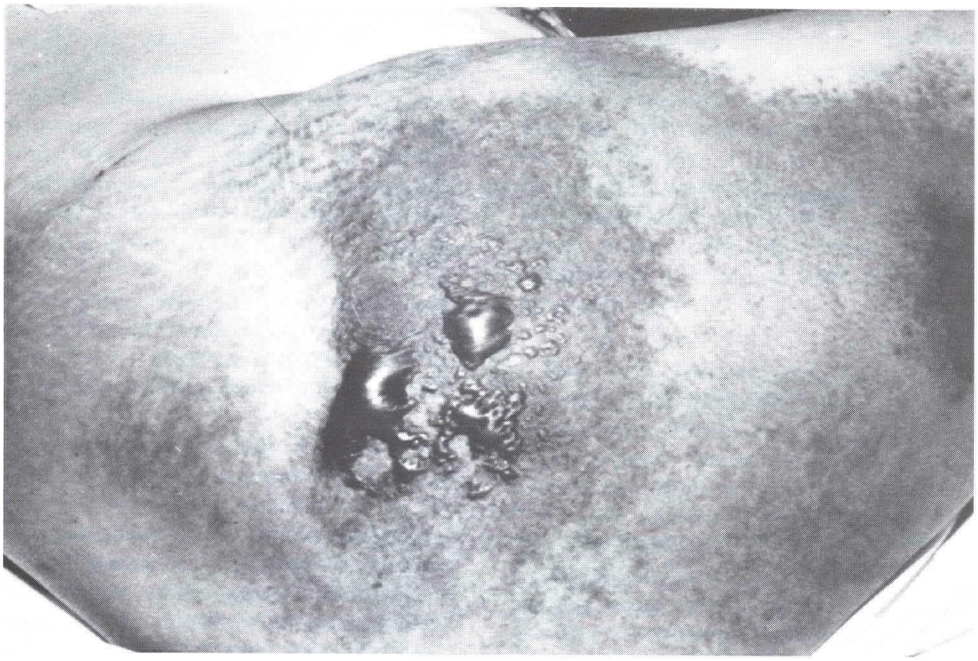

Figure 2
Purpura fulminans secondary to *Serratia marcescens* **septicemia, closer view.**

The hemoglobin was 9.2 gm/100 ml; the hematocrit was 29%; the white blood cell count was 19,200, with 60% neutrophils, 30% band forms, 7% lymphocytes, and 3% monocytes. On peripheral blood smear, platelets appeared normal but helmet cells were observed. Marked toxic granulation of the neutrophils was noted. The urinary sediment contained 10 to 12 white blood cells per high power field. The blood urea nitrogen was 4 mg and the serum sugar 131 mg/100 ml. The serum sodium was 126, the serum potassium 4.5 and the serum bicarbonate 15 millequivalents per liter. Prothrombin time, two hours before the skin lesions first appeared, was 15.5 seconds, with a control of 12.3 seconds. Approximately eight hours later, before anticoagulation therapy, the prothrombin time was 27 seconds, with a control of 12.7 seconds.

The fibrinogen was 360 mg/100 ml and the platelet count was 384,000. The Lee-White clotting time was ten minutes. The chest roentgenogram revealed minimal atelectasis in the right lower lung field, but was otherwise not remarkable. The electrocardiogram recorded sinus tachycardia and minor nonspecific ST-T wave changes. Serum protein electrophoresis was normal, and serum immunoglobulin levels, obtained on the twelfth postoperative day, were IgA, 300 mg/100 ml (normal 165-410), mildly elevated IgG 2000 mg/100 ml (normal 600-1200), and mildly elevated IgM 250/100 ml (normal 50-110). One blood culture, obtained on March 5, five days after admission and two blood cultures, obtained two days after that, revealed *Serratia marcescens* that produced red pigment at room temperature. Cultures of urine and cervical drainage contained *Esherichia coli*. A culture taken from a skin lesion on the foot produced no bacterial growth. Antibiotic sensitivities of the cultures obtained are listed in Table I. Cultures of the infant's blood revealed *Escherichia coli*.

A skin biopsy was taken from the edge of the cutaneous lesion, but did not include the most involved necrotic area. The biopsy revealed subepidermal bullous formation. Bacteria were not seen in the biopsy specimen.

Table 1. Source and Sensitivities of Organisms Isolated.

Antibiotic	E. Coli (2 species) Cervix 1.	2.	E. Coli Urine	Serratia marcescens Blood	E. Coli (Infant's Blood)
Streptomycin	R*	S*	R	S	S
Tetracycline	R	S	R	R	S
Cephalothin	S	S	S	R	S
Chloramphenicol	R	S	S	S	S
Carbenicillin	R	S	R	S	S
Kanamycin	S	S	S	S	S
Ampicillin	R	S	R	S	S
Colistin	S	S	S	R	S
Polymixin	S	S	S	R	S
Gentamycin	S	S	S	S	S
Sulfa	R	S	R	S	S

R* Resistant
S* Sensitive

Heparin sodium was given initially 7500 units intravenously, and then 5000 units intravenously every four hours. Gentamycin, 100 mg intravenously, initially, and then 60 mg intravenously every six hours was administered along with cephalothin, two grams intravenously every three hours. The patient was also given a tranfusion of 1000 ml of whole blood. Her response to therapy was dramatic. The skin lesions, which had been visibly progressing by the minutes, abruptly became stationary and no new areas of the skin involvement developed. Within eight hours, the temperature had decreased to 38.1 C and it did not rise above 37.8 C after 36 hours of therapy. The dosage of antibiotics was reduced after 48 hours and heparin was discontinued after five days of therapy. The areas of skin involvement slowly improved, with areas of redness abating over the next week and the necrotic areas healing over the next four weeks. Skin grafting was not necessary.

Comment

Purpura fulminans is a serious complication of bacterial or viral infection. It has occurred secondary to infection with numerous organisms;[18,19] however, *Serratia marcescens* bacteremia has not been previously implicated as a cause of this disorder. Disseminated intravascular coagulation plays an important role in the pathogenesis of this entity.

The generalized Shwartzman reaction has served as an important experimental model in illustrating many features of disseminated intravascular coagulation. Classically, this reaction has been produced in rabbits by the intravenous injection of two appropriately spaced doses of endotoxin. Pathologically, the hallmark of the generalized Shwartzman reaction is renal cortical necrosis, due to fibrin thrombi in glomerular vessels.[20] Thomas and Good demonstrated that *Serratia marcescens* possesses a potent endotoxin capable of producing the generalized Shwartzman reaction in rabbits.[21] Graber et al reported a generalized Shwartzman-like reaction in a man with *Serratia marcescens* septicemia, secondary to an infected burn. Intravenous injections of endotoxin, extracted from the organism, produced the renal lesions of the generalized Shwartzman reaction in rabbits.[17] At autopsy engorgement of the glomerular capillaries was found by eosinophilic staining material. This was probably due to fibrin. Skin lesions were not noted in their patient.

It is likely that our patient's skin lesions appeared as a result of dissemi-

nated intravascular coagulation secondary to the *Serratia marcescens* septicemia. Although the platelet count, 384,000 cu mm, and fibrinogen, 360 mg/100 ml were not reduced, the prothrombin time changed from 15.5 seconds, (control 12.3 seconds) to 27.0 seconds (control 12.5) in several hours, and helmet cells were observed on the peripheral smear.

The effect of heparin in abruptly halting the previous rapid progression of the skin lesions suggests that disseminated intravascular coagulation was occurring.

It has been shown that pregnant rabbits[22] and rabbits pre-treated with steroids are more susceptible to the development of the generalized Shwartzman reaction, following a single intravenous dose of endotoxin. It is theoretically possible that our patient's recent pregnancy could have made her more susceptible to the development of disseminated intravascular coagulation. She had not received steroids. It has also been reported that the generalized Shwartzman reaction can be precipitated by giving a single dose of *Serratia marcescens* endotoxin, followed by the injection of one of the synthetic heparin-like acidic polymers, such as dextran.[24] Our patient had not received dextran and the last dose of heparin had been 50 hours prior to the development of her skin lesions.

Necrosis of skin and subcutaneous tissue has been reported with the use of coumarin derivatives.[25] Over 90% of the patients have been women, and the lesions have appeared between the third and tenth day of therapy. Sodium warfarin only rarely has been reported to cause this entity. Coumarin derivatives, other than warfarin, are more commonly used in Europe, where this entity has been widely reported. A direct toxic effect of the coumarin compounds on the vessel walls has been cited as the possible mechanism involved.[26] It is unlikely that coumarin toxicity played a role in the genesis of our patient's skin lesions. She had not received coumadin for 50 hours, and the effect of the coumadin on the coagulation system, as measured by the prothrombin time of 15.5 seconds, had largely subsided. Further, the skin lesions occurred in a setting of profound septic illness with high fever, chills, leukocytosis with a left shift, and demonstrated bacteremia.

The skin lesions associated with Pseudomonas bacteremia have features in common with the lesions observed in our patient. These dermal lesions, known as echthyma gangrenosum in their fully developed form, usually also pass through these stages of edema, erythema, hemorrhagic bullae, and necrosis which were observed in our patient.[27] Pathological invasion of vein walls by bacteria is noted in skin lesions associated with *Pseudomonas* bacteremia. Bacteria were not demonstrated in the biopsy specimen from this patient and reports of patients dying of *Serratia marcescens* bacteremia have not mentioned invasion of blood vessels by bacteria.[3,6] It is unlikely that direct invasion of blood vessels by *Serratia marcescens* organisms occurred in this case.

Reports of bacteremia due to *Serratia marcescens* in hospitalized patients have increased in recent years. *Serratia marcescens* bacteremia has characteristically been observed in seriously ill or debilitated patients who have received prior antibiotic therapy, often with more than one drug.[3,6] This organism is often resistant to many antibiotics, but has universally been susceptible to gentamycin.[4,6,28,29] It appears that purpura fulminans, due to *Serratia marcescens* bacteremia, should be vigorously treated with both gentamycin and heparin.

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