

# Postsplenectomy sepsis due to influenzal viremia and pneumococemia

G.T. ROBERTS, MB, BS, B SC; J.T. ROBERTS, FRCP[C]

**A 31-year-old man, who had undergone splenectomy 18 months previously because of hereditary spherocytosis, suddenly became ill, with fever, vomiting, epigastric pain and shock, and died 10 hours after the onset of his symptoms. Autopsy showed influenzal viremia, pneumococemia and bilateral adrenal hemorrhage. The rapid course of the patient's illness emphasizes the serious risk of sepsis for individuals who have had a splenectomy. Anti-influenza immunization in such patients should be considered.**

**Un homme de 31 ans, ayant subi 18 mois précédemment une splénectomie à cause d'une sphérocytose héréditaire, est tombé soudainement malade, avec présence de fièvre, de vomissements, de douleur épigastrique et d'un état de choc; il est décédé 10 heures après l'apparition des symptômes. L'autopsie a révélé une virémie grippale, une pneumococcémie et une hémorragie bilatérale des surrénales. L'évolution brutale de la maladie souligne le risque sérieux de septicémie chez les sujets qui ont subi une splénectomie. On devrait considérer chez ces patients la possibilité d'une vaccination contre l'influenza.**

The diminished ability of persons who have undergone splenectomy to combat infections successfully is now widely recognized. This complication of splenectomy has been most frequently observed in young children,<sup>1-3</sup> although older persons have been shown to be at some risk.<sup>4</sup> Bacterial infections have been responsible for most of the reported illness and death in these individuals,<sup>5</sup> but only rarely have viral infections been reported as a cause of postsplenectomy sepsis.<sup>6</sup>

In this paper we present a fatal case of postsplenectomy viremia complicated by pneumococcal sepsis.

## Case report

### Clinical history and findings

A 31-year-old man became ill Jan. 29, 1973 (during the 1972-73 influenza epidemic), 18 months after having had a splenectomy because of hereditary spherocytosis. He had been in good health until 10 hours before his death, when fever, chills, rigors, headache and low back pain began suddenly. Soon afterwards he had severe difficulty in breathing and epigastric pain radiating to the right shoulder, with nausea and vomiting. When he arrived at hospital 8 hours after the onset of symptoms he was in severe shock, with unrecordable blood pressure. He had striking cyanosis and conjunctival injection and was breathing in a gasping, grunting manner. There were no other physical abnormalities. Electrocardiogram revealed supraventricular tachycardia, at 150 beats/min.

Hematologic investigation was undertaken with the Coulter Counter, Model S (Coulter Electronics Inc., Hialeah, Florida) and by standard methods.<sup>7</sup> Hemoglobin value was 23 g/dl. Leukocyte count was  $36.0 \times 10^9/l$ , with the following differential: segmented neutrophils, 44%; bands, 33%; lymphocytes, 8%; monocytes, 8%; myelocytes, 6%; basophils, 1%; and nucleated erythrocytes, 2/100 leukocytes. A platelet count was not done and no comment was made on their relative numbers in the smear. Blood drawn into a clean tube, without anticoagulant, reportedly would not clot.

Large infusions of intravenous fluids, potassium supplements and furosemide were given. The patient's condition deteriorated suddenly 1 $\frac{3}{4}$  hours after admission and he died shortly thereafter in ventricular asystole.



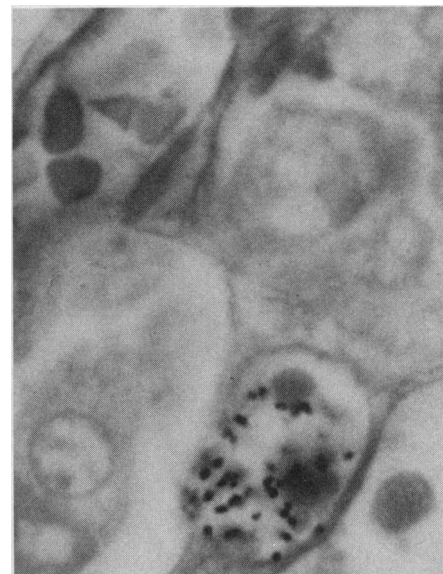
**FIG. 1—Above: hemorrhage in right adrenal. Below: normal adrenal from another subject.**

### Autopsy methods and findings

For histologic study, tissue specimens were fixed in buffered formalin, embedded in paraffin and stained with hematoxylin-eosin. Fibrin was identified in sections by the Martius scarlet blue technique. Bacteria were identified in paraffin-embedded sections after Gram-staining and counterstaining with neutral red.

For virus isolation, tissue was inoculated into the amniotic cavity of a 9- to 12-day-old chick embryo. The amniotic fluid was harvested after 72 hours and tested for the presence of virus by hemagglutination of guinea pig erythrocytes. The virus was identified by the hemagglutination-inhibition technique.<sup>8</sup> Titres of antibody to influenza viruses were determined by the hemagglutination-inhibition technique, using reference virus antigens.<sup>8</sup>

Petechial hemorrhages were widespread on the trunk, limbs and conjunctiva. Bilateral adrenal hemorrhage and virtual destruction of the adrenal cortical parenchyma were noted (Fig. 1). The lungs were congested but showed no evidence of active pneumonia. Multiple fibrin thrombi were present in the submucosa of the bronchi. No splenic tissue was noted. *Pneumococcus* type 12 was cultured from the lungs, blood, cerebrospinal fluid, adrenals and meninges. Gram-positive diplococci were demonstrated in histologic sections of the adrenals (Fig. 2). Post-mortem serum immunoglobulin values, determined with a nephelometer (Technicon Instruments Corp., Tarrytown, New York), were as follows: IgA, 406 mg/dl (normal, 90 to 400 mg/dl); IgG, 920 mg/dl



**FIG. 2—Gram-positive diplococci in adrenal cortical parenchyma (Gram's and neutral red stains; x100).**

From the departments of laboratory medicine, Henderson General Hospital and McMaster University medical school, Hamilton

Reprint requests to: Dr. J.T. Roberts, Department of laboratory medicine, Henderson General Hospital, 711 Concession St., Hamilton, ON L8V 1C3

Whenever  
the skin  
is infected or  
inflamed...

## LOCACORTEN® VIOFORM®

- anti-inflammatory
- antipruritic
- antifungal
- antibacterial

### INDICATIONS

The treatment of skin disorders complicated by bacterial and/or fungal infections with concomitant adequate systemic antibiotic cover if necessary. Recommended for preventing secondary infections, especially those associated with occlusive dressing therapy. It is indicated in: dermatomycosis, folliculitis, impetigo, pyoderma and infectious dermatitis. Locacorten-Vioform is also indicated in atopic dermatitis, seborrheic dermatitis, neurodermatitis, eczematoid dermatitis, psoriasis, anogenital pruritus, lichen simplex, lichen planus, chronic neurodermatitis, contact dermatitis (dermatitis venenata), nummular dermatitis, stasis dermatitis, acne, intertrigo, and many similar conditions. The cream has a slightly drying effect, primarily useful for moist, weeping lesions and in intertriginous areas. The ointment is especially indicated for dry lesions accompanied by thickening and scaling of the skin.

### APPLICATION AND DOSAGE

Locacorten-Vioform should be applied to the affected areas in a thin film three or four times daily. The site may, if necessary, be covered by a protective dressing. Treatment should be continued for at least a few days after clearing of the lesions.

### SIDE EFFECTS

Rarely, mild irritation. With occlusive dressings, a few cases of striae of the skin have been reported. Although rare, a sensitivity to Vioform may develop. If an exacerbation or allergic type reaction occurs, treatment with Locacorten-Vioform should be discontinued.

### PRECAUTIONS

Vioform, as well as other iodine-containing compounds, interferes with some thyroid function tests (such as PBI, radioactive iodine uptake and butanol-extractable iodine), which should therefore not be performed within a period shorter than three months following the use of Locacorten-Vioform. Other thyroid function tests, such as the T<sub>3</sub> resin sponge test, or the T<sub>4</sub> determination, are unaffected by Vioform. In prolonged occlusive therapy, the possibility of metabolic systemic effects should be kept in mind.

Locacorten-Vioform may cause staining of the skin, nails, hair, or fabrics.

### CONTRAINDICATIONS

Tuberculosis of the skin, chicken-pox, pregnancy, skin eruptions following vaccination, or in viral diseases of the skin in general. Locacorten-Vioform should not be employed to treat eye disorders, or syphilitic affections of the skin.

### SUPPLIED

*Cream*, containing 3% Vioform® (iodochlorhydroxyquin) and 0.02% Locacorten® (flumethasone pivalate) in a water-washable base; tubes of 15 and 50 Gm.

*Ointment*, containing 3% Vioform® and 0.02% Locacorten® in a petrolatum base; tubes of 15 and 50 Gm.

*Eardrops*, in controlled-drop plastic dispensers of 10 ml, containing Locacorten 0.02% and Vioform 1% in solution.

(normal, 500 to 1800 mg/dl); IgM, 68 mg/dl (normal, 60 to 250 mg/dl).

Influenza virus A<sub>2</sub>/England 42/72 was cultured from the lungs, adrenals and meninges. Postmortem serum samples showed a 1:40 titre of antibody to influenza virus A<sub>2</sub>/England 42/72 and a 1:80 titre of antibody to influenza virus A<sub>2</sub>/Hong Kong/72.

### Discussion

Several reports have emphasized the increased susceptibility to bacterial sepsis of persons who have undergone splenectomy, but viral infection as a cause of sepsis in these people has rarely been reported. Diamond, Allen and Magill,<sup>6</sup> reviewing their experience with children who had undergone splenectomy because of congenital hypoplastic anemia, found one fatal case of varicella. To our knowledge our case is the first to be reported of postsplenectomy sepsis in which both a viral and a bacterial pathogen were isolated.

In experimental studies investigating the mechanisms of failure of immune protection in mammals who have had a splenectomy, bacteria have almost invariably been used; as a result, the available knowledge is limited to the interactions between bacteria and these mammals.

Little is known about the pathogenetic mechanisms leading to an increased susceptibility to bacterial sepsis in humans who have had a splenectomy. Whitaker<sup>9</sup> has provided evidence that the filtering function of the spleen may be important in the early clearance of a potentially lethal load of blood-borne bacteria. It appears also that the spleen is involved in the production of antibody, especially IgM, the immunoglobulin class that is associated with the early humoral response to antigenic stimulus. However, no consistent correlation has been found between serum antibody concentrations after splenectomy and susceptibility to infection. Serum opsonin activity seems to be diminished after splenectomy, and Constantopoulos and colleagues<sup>10</sup> have presented evidence indicating that an opsonic factor is deficient in the serum of individuals who have had a splenectomy. Confirmation of their findings is required.

Our case showed the classic features of overwhelming postsplenectomy sepsis: fulminant pneumococemia, with indirect laboratory evidence of disseminated intravascular coagulation, terminating in the Waterhouse-Friderichsen syndrome and death. The unusual feature was that a viral pathogen, influenza virus A<sub>2</sub>/England 42/72, seems to have contributed to this patient's death. The virus was isolated from lungs, adrenals and meninges, which indicates that viremia must have

been present. The pneumococcus was also isolated from these sites and it would therefore appear that the action of the two infective agents was related. The association between influenza pneumonia and subsequent bacterial pneumonitis and subsequent bacterial pneumonia is well known. An association between meningococemia and infection of the upper respiratory tract with echovirus was noted by Levitt and colleagues.<sup>11</sup> Young and associates<sup>12</sup> observed a highly significant association between the acquisition of group B meningococci and serologic evidence of acute influenza. They hypothesized that influenza may directly affect the host in a way that enhances the likelihood of acquisition of meningococci on exposure to them.

Thus, we consider that our patient's terminal illness almost certainly started as an influenza infection, which is in keeping with the clinical features of the early phase of the illness. The subsequent acquisition of pneumococcal infection, which rapidly became overwhelming, resulted in the patient's death.

Immunization against the various types of pneumococcus has been advocated for individuals who have had a splenectomy, but the value of this procedure has not been tested. However, we believe that anti-influenza immunization for these individuals should be considered. It would be relatively easy to administer the appropriate vaccine during or at the onset of an epidemic.

Permission to publish this case was granted by Dr. Thomas Ryan, who, with Dr. R. Bloch, cared for the patient.

### References

1. KING H, SCHUMACKER HB JR: Splenic studies I. Susceptibility to infection after splenectomy performed in infancy. *Ann Surg* 136: 239, 1952
2. FINLAND M: Serious infections in splenectomized children. *Pediatrics* 27: 689, 1961
3. HORAN M, COLEBATCH JH: Relation between splenectomy and subsequent infection. A clinical study. *Arch Dis Child* 37: 398, 1962
4. BISNO AL: Hyposplenism and overwhelming pneumococcal infection: a reappraisal. *Am J Med Sci* 262: 101, 1971
5. SINGER DB: Post-splenectomy sepsis, in *Perspectives in Pediatric Pathology I*, ROSENBERG HS, BOLANDE RP (eds), Chicago, Year Book Med, 1973, p 285
6. DIAMOND LK, ALLEN DM, MAGILL FB: Congenital (erythroid) hypoplastic anemia: a 25-year study. *Am J Dis Child* 102: 403, 1961
7. DACIE JV, LEWIS SM: *Practical Hematology*, 4th ed, London, J & A Churchill, 1968
8. ROBINSON RQ, DOWDLE WR: Chap 11 of *Diagnostic Procedures for Viral and Rickettsial Infections*, 4th ed, LENNETTE EH, SCHMIDT NJ (eds), New York, Am Public Health Assoc, 1969, p 423
9. WHITAKER AN: The effect of previous splenectomy on the course of pneumococcal bacteraemia in mice. *J Pathol Bacteriol* 95: 357, 1968
10. CONSTANTOPOULOS A, NAJJAR VA, WISH JB, et al: Defective phagocytosis due to tuftsin deficiency in splenectomized subjects. *Am J Dis Child* 125: 663, 1973
11. LEVITT LP, BOND JO, HALL IE, et al: Meningococcal and ECHO-9 meningitis. Report of an outbreak. *Neurology (Minneapolis)* 20: 45, 1970
12. YOUNG LS, LAFORCE FM, HEAD JJ, et al: A simultaneous outbreak of meningococcal and influenza infections. *N Engl J Med* 287: 5, 1972