Acute Ulcerative Colitis Due to Klebsiella

Report of a Case Following Penicillin Therapy

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CONSIDERABLE INTEREST has recently been focused on the occurrence of acute enterocolitis following the use of antibiotics, particularly those of the broad spectrum group. No published reports, however, were found in which penicillin was the sole agent used before development of this syndrome.

The subject of this communication is a case in which penicillin therapy apparently led to acute ulcerative colitis and pure Klebsiella type 2 (B) grew on cultures of fecal matter.

CASE REPORT

A 47-year-old white man courthouse recorder was admitted to Peralta Hospital, Oakland, July 12, 1953, for a cerebral vascular accident. The past history included asymptomatic hypertension for ten years and excessive ingestion of alcohol.

Until the present hospitalization the patient had never received penicillin. There was no history of any gastrointestinal symptoms except for external hemorrhoids of about ten years' duration with occasional bleeding.

Examination revealed signs of typical left hemiplegia. The blood pressure was 180/110, the heart rate 112, the temperature 98° F., and respirations 24. The lungs contained occasional diffusely arising rhonchi in addition to numerous moist rales over the left lower lobe. Other positive physical findings included mild obesity, acne rosacea, reddening of the tongue, moderate emphysema, slight hepatomegaly and external hemorrhoids.

Results of laboratory studies, including blood cell count, urinalysis, Kahn test, cephalin flocculation, urea nitrogen content of the blood and spinal fluid examination, were within normal limits. Roentgenograms of the chest were normal except for tortuosity and elongation of the thoracic aorta. An electrocardiogram showed no abnormality other than occasional premature ventricular contractions. Intravenous pyelography showed a small parenchymal left renal calculus.

Treatment consisted basically of a 1,500 Calorie, low sodium diet with supplementary vitamins, and sedation with paraldehyde and phenobarbital. In addition, because of the physical signs of pneumonitis, 600,000 units of procaine penicillin daily was given intramuscularly for the first four hospital days. No other medications were employed.

The hospital course was smooth and the patient remained afebrile throughout his stay. The lungs became clear to physical examination in 24 hours, and there was gradual return of strength in the affected extremities. The blood pressure declined in several days to a normotensive level, and was never more than slightly elevated in subsequent determinations. At the time of discharge on July 18, 1953, the patient's only complaint was that of residual weakness of the extremities on the left side.

Second Admission: Directly after returning home from the hospital, three days after completion of penicillin therapy, the patient began to have persistent diarrhea. This gradually increased in severity until six or seven foul-smelling watery stools, containing blood at times in small amounts, were being passed daily. The patient also complained of moderate lower abdominal cramping, and noted some diminution of appetite. No fever or chills were observed.

Following an unsuccessful trial of symptomatic treatment with a bismuth and paregoric mixture, sigmoidoscopy was carried out August 6, 1953. The mucosa was severely inflamed and edematous throughout with numerous confluent shallow ulcers and oozing of blood from many of these sites. Microscopic inspection of aspirated material showed very numerous erythrocytes, moderate numbers of leukocytes and occasional epithelial cells. No amebae were found.

The patient was rehospitalized for further investigation and treatment. The temperature was 98.6° F., the blood pressure 120/82, the pulse rate 100 and respirations 20. The tongue appeared dry and slightly coated. The abdomen was soft and not distended. There was mild tenderness to palpation in the left lower quadrant. The liver edge was no longer palpable. Considerable improvement was observed in the acne rosacea previously noted. Upon neurological examination, residual effects of left hemiplegia were noted. Other physical findings were unchanged from the previous entry.

Results of examination of the blood and urinalysis were within normal limits and agglutination tests for typhoid and paratyphoid were negative. No amebae or other parasites were identified in examinations of sigmoidoscopic aspirates and fresh stools, utilizing techniques including concentrates and stained smears. Cultures of fecal material on blood agar and various inhibitory media done on August 6 and August 8 produced pure growth of a non-motile short plump Gram-negative rod which was at first tentatively classified as Aerobacter aerogenes. It was finally identified, however, as Klebsiella type 2 (B).*

A barium enema with double contrast technique showed many small shallow mucosal ulcers throughout the colon, most numerous in the rectum. The colon was normal in caliber and the wall appeared to be normally flexible throughout. A segment of the terminal ileum was filled and appeared normal.

Treatment was initiated on August 6, 1953, with sulfadiazine, which was discontinued three days later

*Confirmation of the organism as Klebsiella (Aerobacter) was made by the Bacteriology Laboratory of the California State Department of Health. Dr. P. R. Edwards of the Communicable Disease Center, U.S.P.G.S., performed the serological identification. Information forwarded with the report[1] stressed the biological similarity and close serological relationship of the Klebsiella and Aerobacter groups. It was pointed out that until recent years the placement of an organism in either of these groups depended largely on the source of the original culture.

because of microscopic hematuria and crystalluria. Aureomycin was then given for the next five days, pending reports of sensitivity determinations. During these first eight days of therapy the patient continued to pass five or six watery stools daily. There was some symptomatic improvement, however, with subsidence of abdominal cramps and diminution of bowel urgency. The temperature remained normal except for slight elevations on two occasions.

When sensitivity studies were completed on the Klebsiella which was isolated, it was found that this organism was highly sensitive to terramycin, moderately sensitive to streptomycin and chloramphenicol, and resistant to penicillin, aureomycin and erythromycin.

The antibiotic therapy was accordingly changed to terramycin on August 14, 1953. During the next 72 hours the stools became partially formed and diminished in number to three daily. The patient then improved progressively to complete recovery.

Upon sigmoidoscopic examination on August 18, no ulcers were visible and the mucosa appeared normal except for slight granularity.

Additional stool cultures after treatment was begun produced a mixed flora with diminishing numbers of Klebsiella. A culture on August 10 showed a predominant growth of Klebsiella, moderate numbers of diphtheroids and a few colonies of beta-hemolytic Staphylococcus albus. A culture on August 17, after terramycin therapy, showed moderate growth of Staphylococcus albus with only a few colonies of Klebsiella.

All medications were stopped when the patient was discharged from the hospital on August 19, 1953. During the next four days the stools became fully formed and declined in number to one normal stool daily. No symptoms recurred during a follow-up observation period of six months.

DISCUSSION

Analysis of this case points strongly toward penicillin as the cause of the ulcerative colitis. This conclusion is favored by the absence of any previous intestinal disorder, by the onset of symptoms after penicillin therapy, by the pure cultures of a penicillin-resistant Gram-negative organism in the stools, and by the therapeutic response to an agent effective against this organism *in vitro*.

It has been well established that acute enterocolitis may result from the administration of other antibiotics,[2, 3, 4, 6, 7] notably aureomycin and terramycin, as well as chloramphenicol or a combination of penicillin and streptomycin. Bacteriologic studies of the stools in these cases have shown the frequent exclusive or predominant growth of resistant staphylococci. Pseudomonas and proteus[4] have also been found in similar circumstances, but Klebsiella has not been previously inculpated in this manner.

The fundamental pathogenetic factor in enterocolitis of this type is generally acknowledged to be an alteration of the normal bowel flora. Sensitive bacteria are suppressed or eliminated, and rapid multiplication of certain resistant organisms takes place. Although these organisms are ordinarily innocuous within the intestinal tract in smaller numbers, under these conditions their prolific growth is at times associated with an inflammatory reaction in the wall of the bowel. This may be manifested by simple erythema and edema of the mucosa, but ulcerative lesions and pseudomembraneous colitis have also been observed.

Diarrhea is the most common symptom of this disorder, although it does not invariably occur. Nausea, vomiting and anorexia are other complaints that may be encountered. Systemic symptoms are in some instances entirely absent or there may be various degrees of fever, toxemia, azotemia and circulatory collapse, leading at times to death.

Treatment of this condition is based upon the use of supportive therapy and appropriate antibacterial agents. Emphasis upon the frequent etiological role of staphylococci has led to therapeutic trials of erythromycin with favorable results.[2, 5] The case reported here, however, indicates the need to guide therapy by accurate identification of the offending organism and appraisal of its sensitivity.

SUMMARY

A case of acute ulcerative colitis secondary to penicillin therapy is presented. The causative organism appeared to be Klebsiella type 2 (B), which was present in pure growth on cultures of stools.

Cure followed the administration of terramycin, which was the most effective agent *in vitro*.

The subject of enterocolitis due to antibiotics is briefly discussed.

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