ABSTRACT OF ORIGINAL ARTICLE. This fundamental paper by a surgeon, Dr Gross, and a radiologist and radiotherapist, Dr Neuhauser, cleared up the existing information and conflicting results of therapy for Wilms’ tumor through 1947. There is a careful review of literature, comments about existing suggestions of preoperative radiation versus postoperative radiation versus radiation only and versus surgery without radiation. The authors then carefully analyze the experience at Boston Children’s Hospital over the period from 1914 to 1947. This material is carefully broken down into three periods, 1914 to 1930, 1931 to 1939, and 1940 to 1947. During period I, 1914 to 1930, 27 cases of Wilms’ tumor were seen and four cures were obtained for a survival rate of 14.9%. Beginning in 1931, under the able leadership of Dr William E. Ladd, a vigorous approach to the surgery for children with Wilms’ tumor was undertaken. The program consisted of a wide transabdominal incision rather than the more classic approach to kidney surgery by a flank incision. This surgical exposure allowed prompt identification and control of the renal vessels and removal, in most cases, of the entire tumor and kidney mass without rupture of the encapsulated tumor. Additionally, Dr. Ladd insisted on careful fluid and blood replacement before and during surgery and a meticulous approach to the anesthetic management of the child undergoing surgery. In previous experience at Boston Children’s and other reported centers, there had been a large number of intraoperative deaths. After 1932, there were no deaths from the surgery at Children’s Hospital in Boston. In the 1931 to 1939 experience, 31 patients were operated on and ten cures were achieved for a survival rate of 32.2%.

Beginning in 1940, Dr Gross and Dr Neuhauser instituted a program of immediate surgery and postoperative radiation to the bed of the tumor. Thirty-eight children were so treated with a survival rate of 47.3%. This group of patients was subsequently followed for 2 1/2 years so that cures, recurrences, and deaths could be accurately reported. This patient material also emphasized that babies in the first 12 months of life had a far better outlook than did older subjects. The authors also emphasized that if recurrences were to occur, they were usually evident within 9 months after operative removal and radiation therapy. Postoperative radiation therapy was given in daily doses of 200r alternately using three portals, anteriorly, laterally, and posteriorly over the tumor bed reaching a total of 4000 to 5000r using a 200KV machine.

COMMENTARY

This paper is fundamental in the evolution of therapy for Wilms’ tumor in childhood. A concise appraisal of surgical therapy is given based on the carefully worked out principles outlined by Dr Ladd. Although the authors admit that the tumor can be shrunk by preoperative radiation facilitating the operative exercise, they firmly state that there is no therapeutic benefit of preoperative radiation, because the surgery can be successfully carried out irrespective of the size of the tumor. They then make the point that the bed of the tumor can be fully irradiated and any residual tumor can be successfully treated by an operation. This clinical paper advertised and described for all pediatricians those clinical findings that would allow earlier diagnosis. A very interesting mention of chemotherapeutic agents is to be found in this paper: “...of chemotherapeutic agents nothing will be mentioned here since little value can be offered at this time; however, the rapid strides that are being made in this field for the treatment of other neoplasms rais[e] the hope that chemical agents will be found to control Wilms’ tumors that have already metastasized to other parts of the body.” Dr Sidney Farber, who analyzed the pathology in all the patient material in the present paper, was already hard at work in the laboratory to show that folic acid derivatives might be useful in the therapy of certain leukemias. It is certain he influenced the discussion of therapy for these tumors in this paper, published 1950. It would be only 6 years until Dr Farber began to show extraordinary success in the chemotherapy of Wilms’ tumor by actinomycin D!

In short, this seminal paper emphasized principles of diagnosis in the management of Wilms’ tumor, offered testimony to the fact that all Wilms’ tumors could be
successfully excised regardless of their size without the preoperative irradiation and further showed that postoperative radiation to the bed of the tumor increased survival. The study further suggested that preventive radiation to the lung fields might be helpful in certain circumstances but there were no data to support this. This study lined up all the surgical and radiotherapeutic principles on which successful chemotherapy in the form of actinomycin D was to be overlaid. It is worthy of note that Dr Gross and Dr Neuhauser, who represented the fields of surgery and radiation therapy, were subsequently joined by Dr Farber and the use of chemotherapy to lay down therapeutic principles for Wilms’ tumor. The three coworkers received the Lasker award for this work, which heavily influenced all subsequent therapeutic regimens, as well as the processing of therapeutic trials by the National Wilms’ Tumor Studies over the past 30 years.

COMMENTARY

Pseudomonas aeruginosa Infection as a Complication of Therapy in Pancreatic Fibrosis (Mucoviscidosis), by Sterling D. Garrard, et al, Pediatrics, 1951;8:482

Comments by Bonnie W. Ramsey, MD

ABSTRACT OF ORIGINAL ARTICLE. This landmark article represents the first report of Pseudomonas aeruginosa as a significant clinical pathogen in patients with cystic fibrosis (CF). The authors summarize the case histories of four consecutive patients with CF admitted to a Chicago pediatric teaching hospital. In all four, P. aeruginosa was the predominant organism cultured from tracheobronchial secretions. The histories were remarkably similar. The patients (two male, two female) were very young, ranging from 14 months to 5 years of age, and had previously been diagnosed with “pancreatic fibrosis” based on the absence of pancreatic digestive enzymes. The four patients had received pancreatic enzyme replacement (pancreatin) and prolonged antibiotics prophylaxis. The antibiotic regimens consisted of a variety of oral antibiotics, including sulfonamides, penicillin, aureomycin, and zephiran, as well as aerosol polymyxin, prescribed as treatments for Staphylococcus aureus tracheobronchial infections.1,2

The patients presented with acute respiratory distress and were diagnosed as having diffuse bronchopneumonia based on physical examination and chest radiography. Treatment consisted of intramuscular streptomycin (or terramycin) and penicillin. Repeated bronchial lavage was attempted to clear airway secretions. The two female patients did not respond to therapy and died within hours. The two males responded briefly, but subsequently died at 8 weeks and 1 year after initial culture of P. aeruginosa. Similar postmortem findings in all patients included pancreatic fibrosis, suppurative bronchiitis, multiple pulmonary abscesses, and bronchiectasis.

In their discussion, the authors emphasize several salient features of CF pulmonary disease. First, they raise the potential role of prolonged antimicrobial therapy in altering tracheobronchial flora. S. aureus, the predominant pathogen in all initial descriptions of the illness,3,4 was being eliminated by antistaphylococcal antibiotic therapy. In its place, was emerging P. aeruginosa. This phenomenon of shifting bacterial flora had been reported recently in other illnesses,5,6 but not in CF. Second, the authors address the importance of P. aeruginosa as an emerging opportunistic infection in the tracheobronchial tree, noting rapid development of antibiotic resistance attributable to its ability to “develop genetic mutations” and alter its “morphologic appearance”.7,8 Third and most important, the authors challenge the pediatric community to “critically examine” the clinical recommendation1,2,9 for prolonged antibiotic prophylaxis. Realizing the effectiveness of this regimen against S. aureus, they suggested that physicians also weigh the risk of emergence of resistant strains of P. aeruginosa. They recommended, “Effective antibiotics should be employed judiciously and changed when specifically indicated based upon cultures of tracheobronchial secretions. To minimize the appearance of resistant strains, combinations of two antibiotics having different mechanisms of action are desirable.”

COMMENTARY

When the authors reported their four case reports of Pseudomonas aeruginosa in 1951, did they understand the impact that this pathogen would have on patients with cystic fibrosis (CF)? At that time, CF had only been described as a clinical disease of the pancreas and lung for 13 years,3 and its genetic inheritance only understood at a rudimentary level. The median life span was ~5 years. Pancreatic enzyme replacement and antibiotic therapy were only palliative. Staphylococcus aureus, the major pathogen colonizing patients’ airways, led to overwhelming pneumonia and death in infancy.1,4,5 Thus, early CF clinicians1 advocated liberal use of antistaphylococcal antibiotics in a desperate attempt to control the rapidly progressive bronchopulmonary disease. In this landmark article, Garrard et al, raise concern that prolonged antibiotic usage may be “altering the flora of the tracheobronchial tree”. They note that P. aeruginosa, previously regarded as a “relatively harmless contaminant,” had become an in-
Treatment of Mixed Tumors of the Kidney in Childhood, by Robert E. Gross, MD, and Edward B. D. Neuhauser, MD, Pediatrics, 1950;6:843-852
Judson Randolph
Pediatrics 1998;102:209

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