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Nosocomial Varicella

Part I: Outbreak in Oncology Patients at a Children's Hospital

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Twenty cases of varicella occurred in patients or siblings of patients in a 41-day period in a children's hospital. Most cases were among oncology patients, with transmission occurring in both the inpatient and outpatient areas. One patient died after visceral dissemination of varicella. Neither pooled immunoglobulin nor zoster immune plasma was effective in preventing clinical varicella, although zoster immune plasma appeared to ameliorate the illness. Recommended control measures included strict isolation or discharge of infected patients, and respiratory isolation or discharge of exposed susceptibles. Although apparently too late to be effective in this outbreak, similar measures are warranted should nosocomial outbreaks of varicella occur elsewhere.

WHILE VARICELLA is usually a benign disease of childhood, it can cause severe or fatal illness in patients with impaired immunity.[1-4] Nosocomial outbreaks of varicella-zoster illness have resulted in serious morbidity and mortality,[5-10] especially on oncology wards where numerous patients with impaired immunity may be exposed simultaneously.[11] In recent years many pediatric oncology units have combined outpatient, inpatient and intermediate care facilities into "therapeutic communities" to allow patients to enjoy a more normal life style while receiving necessary therapy. However, with the establishment of such therapeutic communities, potential mechanisms for the spread of nosocomial infection have become more complex and, accordingly, more difficult to control. This paper describes an outbreak of 20 cases of varicella in such a unit for pediatric oncology patients, and discusses the control measures that were used in an attempt to halt the spread of varicella.

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Part I of a two-part article. Part II: Suggested Guidelines for Management, will be published in a subsequent issue.

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Background

The Children's Hospital at Stanford University is a 60-bed hospital with four separate inpatient wards, outpatient facilities located within the hospital, and a physically separate but nearby intermediate care facility. Two wards and most beds in the intermediate care facility are used by the oncology service, which is organized as an open therapeutic community. Oncology patients have access to the inpatient units, the intermediate care

facility and the outpatient department unless precluded by medical considerations including infections; parents and other family members may "live in" on the hospital ward. In addition, nononcology patients share the outpatient, intermediate care and inpatient recreational facilities with the oncology patients, and are free to visit the oncology wards.

Methods

The period of varicella communicability in normal persons is variable, though in general communicability is considered to end when all lesions have crusted;[12] however, varicella may occasionally be communicable as early as four days before rash onset in normal children[5] and up to a week or more after rash onset in immunosuppressed patients. Because of these uncertainties regarding the period of communicability in individual patients, the inclusive period of varicella communicability for the purpose of this epidemiologic investigation only was arbitrarily defined as two days before rash onset to five days after rash onset. High risk of exposure to varicella was considered to exist on days when a patient within this communicable period was an inpatient (ward or intermediate care) or attended the outpatient clinic without being isolated. For patients in whom varicella subsequently developed, the likely time of exposure was considered to be between 10 and 21 days before rash onset (usual minimum and maximum incubation periods). Only the month of March was analyzed since isolation procedures were instituted in April. It was necessary to use varicella histories in the estimation of attack rates since preexposure serology findings were not available. The probable source of exposure as described in the text was derived from dates of inpatient admissions and outpatient visits as well as from available information about community exposures.

Results

The Outbreak

Between March 6 and April 20, a total of 20 cases of varicella occurred among patients and their siblings (See Figure 1). Fourteen cases were in oncology patients, four in their normal siblings and two in nononcology patients. In two oncology patients hemorrhagic varicella developed, and another died with visceral dissemination of varicella five days after onset.

The index case and the next three cases (one in a nononcology patient) occurred in children who had been exposed during the customary peak of varicella activity in the general community, though two of the latter cases may also have been exposed to the index patient on his day of admission. Of the 11 subsequent cases in oncology patients, ten occurred after nosocomial exposure. Only one of these ten patients had had any possible community exposure. In the 11th case, the patient had a known community exposure. Three of the four cases among siblings also occurred after hospital exposure; none had a known exposure in the community. Both nononcology patients had been inpatients during periods of potential risk but one had also been exposed in the community as noted above. In both, varicella developed after discharge, and no additional cases occurred in nononcology patients.

Forty-three oncology patients were exposed on at least one high-risk inhospital day. Eight cases of varicella developed among this group, for an overall attack rate of 19 percent. Of these 43 oncology patients, 21 were historically susceptible to varicella at the time of exposure, and all eight cases occurred in this group, for an attack rate of 38 percent. No cases appeared among the 22 oncology inpatients with a history of previous varicella.

A total of 104 oncology patients attended the

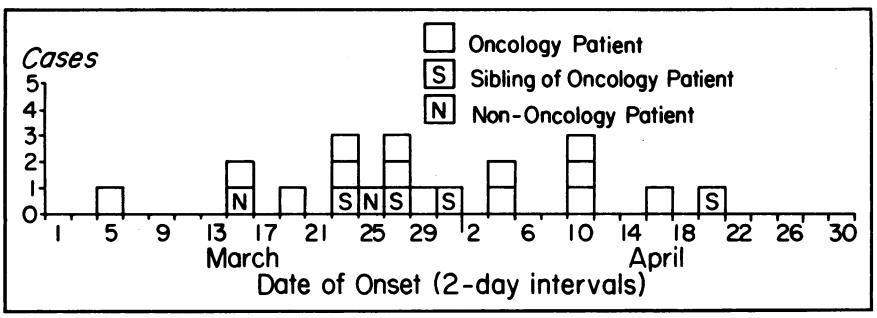

Figure 1.—Varicella among patients and family members, by date of onset, March-April 1974.

TABLE 1.—*Varicella Attack Rate Among Historically Susceptible Oncology Outpatients by Number of High-Risk Exposure Days in Clinic*

No. High-Risk Days on Which Patient Made Clinic Visit	No. of Patients	No. Susceptible by History	Varicella Cases	Attack Rate Among Susceptible Patients* (Percent)
0	34	14	0	0
1	62	33	1	3
2	20	9	2	22
≥3	22	10	3	30
TOTAL	138	66	6	9

*Progression of attack rates significant $p < .02$, $X^2 = 10.3$, 3df.

outpatient clinic on at least one high-risk day. Six cases of varicella developed among this group for an overall attack rate of 6 percent. All six cases occurred among 52 patients (12 percent) who were historically susceptible to varicella. Within this historically susceptible group, attack rates increased with increasing numbers of clinic visits on high-risk days (Table 1). No cases were observed among the 52 oncology outpatients with a history of previous varicella, nor among any of the 34 patients who attended the clinic on no high-risk days. There was no apparent relationship between underlying illness and the likelihood of varicella developing in this group of patients.

Fifty nononcology inpatients and 221 nononcology outpatients were likewise exposed on at least one day with high risk of exposure. Two cases of varicella developed in the inpatient group for an overall attack rate of 4 percent; both cases occurred among a group of 13 patients who were historically susceptible (an attack rate among susceptible patients of 15 percent). Only one case developed in the outpatient group for an overall attack rate of 0.5 percent. This particular nononcology outpatient was also the brother of an oncology patient, and had "lived in" the intermediate care facility during a high-risk period.

Use of Passive Immunization

Most of the oncology patients were passively immunized in an attempt to prevent or modify illness. A total of 35 patients received commercial pooled immunoglobulin intramuscularly in a dose of 0.4 ml per kg of body weight, whereas 14 patients received zoster immune plasma (ZIP) in doses ranging from 1.5 to 10.2 ml per kg of body weight. Although in some instances the varicella-zoster titer of the ZIP was 1:32 by complement fixation,[13] in most cases the titer of the plasma was unknown; all plasma units were negative for hepatitis-B surface antigen. Some patients received both immunoglobulin and ZIP.

Neither pooled immunoglobulin nor ZIP in these doses appeared to prevent clinical varicella. However, all four patients who received ZIP 6 to 21 days before the onset of rash had illnesses judged "atypically mild" by the attending physicians. Conversely, nine of ten patients not receiving ZIP had clinical courses considered to be "usual," or had complications of varicella (prolonged lesions, hemorrhagic varicella and fatal visceral dissemination of varicella) ($p = 0.005$ by Fisher's exact test).

Control Measures

Rigid isolation measures were not instituted until the large cluster of cases appeared in late March. Inpatients with active varicella were placed in strict isolation (private room with use of gown, gloves and mask), while exposed inpatients who were historically susceptible were placed in respiratory isolation until discharge or until 21 days had elapsed since their last exposure (usual maximum incubation period). Patients for hospital admission were carefully screened for history of previous varicella and for recent exposure to varicella. Exposed susceptible patients were placed in respiratory isolation when admitted, and segregated from unexposed susceptible patients. Whenever possible, exposed and infected patients were discharged.

In the outpatient clinic, exposed susceptible patients and patients with active varicella were seen in separate rooms. Passage between areas was limited during the period of the epidemic. The census of the intermediate care facility was purposely decreased, with as many patients being cared for in their homes or other local hospitals as possible.

Discussion

This outbreak illustrates the potential severity of varicella among immunosuppressed patients in an open therapeutic community. All cases occurred in patients who were historically susceptible to varicella, and attack rates in the outpatient setting were related to crude frequency of exposure. Uncontrolled observations suggested that passive immunization with zoster immune plasma may have modified the severity of illness. Unfortunately, strict isolation procedures were not instituted until the scope of the outbreak became

apparent at the end of March. By that time 13 of the eventual total of 20 cases had already occurred. Indeed, the cessation of this outbreak was probably due to the exposure of most susceptible patients within two incubation periods. The isolation procedures may have helped reduce the number of tertiary cases, though most cases had almost certainly been exposed by the time the control measures were instituted.

The usual distinction between inpatient, outpatient and intermediate care areas is clouded in this type of open-hospital arrangement, and the opportunities for exposure were presumably greater than in the usual hospital situation. In addition, normal siblings were also involved in the outbreak. These factors undoubtedly contributed to the high attack rate among historically susceptible oncology patients, which was 38 percent during the month of March. Nononcology patients were minimally affected; one of the two nononcology inpatients with varicella had a known community exposure while the one nononcology outpatient with varicella was almost certainly exposed in the intermediate care facility.

The value of the isolation procedures recommended in this outbreak cannot be overemphasized, however. The use of strict isolation for varicella, which is spread by the respiratory route as well as direct contact,[14] should be a routine procedure. Respiratory isolation for exposed susceptibles is also recommended because varicella has been shown to be communicable up to four days before the onset of rash, presumably by the respiratory or airborne route.[5] The most important spread of varicella in hospitals may occur before the appearance of rash and, therefore, before the diagnosis becomes obvious. Infected and exposed patients should always be discharged from the hospital when possible.

The use of prophylactic agents may be ineffective in the control of epidemic varicella though obviously not in the attenuation of illness. Although zoster immune plasma and zoster immune globulin are apparently effective in modifying varicella,[15-19] the effects on viral excretion and the period of communicability are not known; varicella may be communicable even when attenuated. In this outbreak the modification of illness by zoster immune plasma hindered appropriate control measures in one patient because of increased difficulty in diagnosing clinical varicella.

The intent of this report is to emphasize the potential danger of nosocomial varicella, especially in such an open therapeutic community. The described control measures should be instituted immediately both to reduce the spread of infection and to prevent or modify the course of illness among susceptible patients with impaired immunity.

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