CLINICAL RESEARCH

Case clustering in pityriasis rosea: support for role of an infective agent

A G MESSENGER, E G KNOX, ROY SUMMERLY, H L MUSTON, ELIZABETH ILDERTON

Abstract

One hundred and twenty-six cases of pityriasis rosea seen over two years in north Staffordshire were analysed for clustering in time and space. A statistically significant degree of clustering was found; this was evident among female patients considered separately but not among male patients. The incidence of the condition was higher in patients working in, or attending, educational establishments.

These findings support the hypothesis that pityriasis rosea is caused by an infective agent. A search for an infective organism and a transmission mechanism now seems justifiable.

Introduction

The cause of pityriasis rosea is not known, but the natural history and the rarity of second attacks have given rise to the belief that it is an infectious disease. Various micro-organisms, including fungi, spirochaetes, and streptococci, have been implicated without proof.[1] Apart from a single unconfirmed report of the isolation of a picornavirus-like agent from the scales of lesions in pityriasis rosea[2] virological investigations have been unproductive.[3 4] The epidemiological evidence for a possible infective aetiology consists of, firstly, seasonal variation in incidence[5]; secondly, an increased incidence among dermatologists[6]; and, thirdly, occasional reports of two or more cases occurring in the same family or intimate environment.[5]

Department of Dermatology, North Staffordshire Hospital Centre, Stoke-on-Trent, and Department of Postgraduate Medicine, University of Keele, Staffordshire

A G MESSENGER, MB, MRCP, registrar

ROY SUMMERLY, FRCP, FRCPED, consultant dermatologist and senior lecturer

H L MUSTON, MB, MRCP, senior registrar

ELIZABETH ILDERTON, research assistant

Department of Social Medicine and Health Services Research Centre, Medical School, University of Birmingham

E G KNOX, MD, FRCP, professor of social medicine

We examined the spatial and temporal distribution of the onset of pityriasis rosea for evidence of clustering by using two statistical methods, which detect low-order, space-time interaction and temporal clustering independent of geographical distribution.

Patients and methods

We undertook the study between September 1977 and August 1979. All general practitioners within the catchment area of the skin department, North Staffordshire Hospital Centre, were asked to refer by telephone call suspected cases of pityriasis rosea. Two further reminders were sent during the course of the study. Patients were seen within 24 hours of referral and the diagnosis established or rejected by clinical examination. Besides the usual patient-identifying data we recorded sex, age, and occupation, place of residence and place of occupation, and the date of onset of the rash. Geographical data were plotted on a street map (6·3 cm to the kilometre; four inches to the mile), and the national grid reference of the place of residence and place of occupation of each patient was recorded to the nearest 0·1 km. The data were transferred to a computer file for analysis.

STATISTICAL ANALYSES

First method—In a series of n cases there are $n(n-1)/2$ possible pairs. For every pair the time interval (t) and the distance interval (d) between them can be calculated. The question is then asked: Are short distances within pairs associated with short time intervals within pairs? In other words, are cases that occur immediately after an index case closer in distance than those arising much later? To detect an effect pairs are classified into those with distance apart less than or greater than d and with time intervals less than or greater than t. The number of pairs with a distance less than d and a time interval less than t is then compared with an expected number calculated in the usual way for 2×2 tables.[7 8] Significance is assessed with the χ^2 statistic or, when numbers are small, by calculation based on a Poisson distribution.

Second method—Temporal clusters considered independently of their geographical distribution may be detected sensitively by using a "moving window" test.[9] Given N cases distributed randomly over D days, what is the probability that n or more cases will be found in a restricted time-window of d days? Statistical calculation is laborious, but one of us (EGK) recently devised an approximation that gives results sufficiently close to the continuous scanning tabulations[9] and has been checked for accuracy by use of computer simulation methods. We examined our data using a "window" of 28 days.

Results

During the study 126 cases of pityriasis rosea were collected, 70 in the first year and 56 in the second. There were 45 male and 81 female patients (table I). The seasonal distribution (table II) showed an overall winter to summer ratio of 80:46 (1·74). A high incidence was found in patients working in, or attending, educational establishments, and the winter to summer ratio was 37:16 (2·06) compared with 43:40 (1·43) in other patients. The asymmetry was significant ($\chi^2 = 8{\cdot}32$, $p < 0{\cdot}01$) among the group at educational establishments but not among the remainder. The incidence was much higher in people at educational establishments than in pottery workers (table III), the difference being most noticeable between female schoolteachers (1·50) and female pottery workers (0·08).

TABLE I—*Distribution of patients by age and sex*

Age (years):	0–≤5	–≤10	–≤15	–≤20	–≤25	–≤30	–≤35	–≤40	–≤45	–≤50	>50
Males	1	3	7	11	4	3	8	2	3		2
Females		6	14	17	18	6	10	3	7	1	
Total	1	9	21	28	22	9	18	5	10	1	2

TABLE II—*Seasonal distribution of pityriasis rosea*

	Month												Total
	J	F	M	A	M	J	J	A	S	O	N	D	
Occupation in education	5	6	6	1	3	5	2	4	1	7	6	7	53
Others	8	4	3	2	8	1	9	3	7	6	15	7	73
Total	13	10	9	3	11	6	11	7	8	13	21	14	126

TABLE III—*Incidence of attacks of pityriasis rosea in subgroups of patients working in or attending educational establishments and pottery workers*

Occupation	Sex	No of patients	Approximate population	Incidence (cases/1000 population/year)
Schoolchildren	M	15	45 000*	0·17
	F	24	45 000*	0·27
Schoolteachers	F	8	2 640*	1·50
Pottery workers	M	6		
	F	6	40 000†	0·08

Data supplied by *local education authority and †personnel departments of local potteries.

TABLE IV—*Space-time interaction of cases of pityriasis rosea: analysis of all possible pairs (126 cases)*

Time interval	Distance apart		Total
	≤0·25 km	>0·25 km	
≤14 days	10	338	348
>14 days	69	7458	7527
Total	79	7796	7875

Expected number for time interval ≤14 days *and* distance apart ≤0·25 km = 3·49 ($p < 0{\cdot}005$).

An overall analysis of all possible pairs (table IV) produced 10 pairs exhibiting both short time (≤14 days) and short distance (≤0·25 km) intervals. The "expected" value would be 3·5, and the excess was significant ($p < 0{\cdot}005$). When analysed according to sex (table V) there were six female-female pairs exhibiting both short time and short distance intervals compared with an expected 1·4 ($p < 0{\cdot}005$). By contrast, there were no such male-male pairs and only four male-female pairs compared with an expected 1·7 ($p = 0{\cdot}05$).

These analyses were based on place of residence. Similar studies based on place of work produced no indication of space-time interactions. Among the 53 patients connected with educational establishments we found three pairs separated by less than seven days and less than one kilometre compared with an expected 0·77 ($p = 0{\cdot}04$ using Poisson distribution).

"Moving window" analysis showed a striking temporal cluster of 16 cases between 6 November and 3 December 1977 ($p < 0{\cdot}005$). There was also a strong suggestion that this was a double cluster, with five cases in the three days 14-16 November and six cases in the five days 28 November to 2 December. Twelve of the patients were female.

TABLE V—*Space-time interaction of cases of pityriasis rosea: analysis of different pair types*

Time interval	Distance apart		Total
	≤0·25 km	>0·25 km	
	Female-female pairs		
≤14 days	6*	139	145
>14 days	26	3069	3095
Total	32	3208	3240
	Male-male pairs		
≤14 days	0†	37	37
>14 days	10	943	953
Total	10	980	990
	Male-female pairs		
≤14 days	4‡	162	166
>14 days	33	3446	3479
Total	37	3608	3645

Expected numbers for time interval ≤14 days and distance apart ≤0·25 km: *female-female pairs 1·43 ($p < 0{\cdot}005$); †male-male pairs 0·37; ‡male-female pairs 1·69 ($p = 0{\cdot}05$).

Discussion

The pairs analysis provides statistical evidence in support of pityriasis rosea having an infective aetiology. If this is so then the need to use such sensitive techniques to show it suggests either that the infectivity is low or, more probably, that the infection is manifest clinically in only a small proportion of those infected, or possibly that transmission is effected through an alternative host. Burch and Rowell[10] proposed that pityriasis rosea might be an auto-aggressive disease affecting a small, genetically susceptible subset of the population and perhaps triggered by an infective agent. Such a mechanism would be compatible with our findings.

The validity of the space-time method is reasonably well established,[11-13] and results compare well with those obtained by computer simulation methods. The validity is unaffected by geographical heterogeneities of population density, provided that substantial geographical redistributions do not occur during the period of the study. Errors of diagnosis, and of attributing times and geographical locations to the events, reduce the chances of detecting clustering but do not increase the probability of spurious clusters. One source of spurious clusters arises when the diagnosis of one case increases a practitioner's awareness and raises the possibility that during a limited ensuing period he will more readily diagnose and refer cases that he would otherwise have missed. It is difficult to exclude this possibility entirely.

Our chosen time interval of 14 days may be justified through general reference to a wide range of infectious processes, many of which have incubation intervals within this time. Sequential pairs and, more importantly, the varying incubation periods for many diseases should, therefore, be accommodated; thus pairs infected from a common source should be encompassed. The choice of a limiting distance of 0·25 km is less easily justified and the choice of the two values together is based as much on inspection of the data as on prior considerations. The significance values cannot therefore be considered in any precise quantitative sense, but the very small p values invite a qualitative assessment that such results are unlikely to have occurred simply through the operation of sampling processes.

Twenty-nine of our 126 cases occurred within 0·25 km and 28 days of another case. In one pair of sisters the onset was simultaneous and at the same address. The high incidence among schoolchildren, young adults, and female schoolteachers suggests environmental associations with educational establishments and seasons of the year. Although numbers are small, they also suggest transmission between female subjects and from female to male subjects or vice versa, but not, as a rule, between male subjects.

Temporal clustering observed early in the course of the study might have been due to initial enthusiasm of the referring practitioners, but examination of their referral patterns suggested that this was not the case. A determined search for an infective organism and a transmission mechanism now seems justifiable.

Requests for reprints should be addressed to Dr R Summerly, Department of Dermatology, Central Out-Patients' Department, North Staffordshire Hospital Centre, Stoke-on-Trent, Staffordshire ST4 7PA.

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Ultrasound-guided fetal intravenous transfusion for severe rhesus haemolytic disease

JENS BANG, JOHANNES E BOCK, DYRE TROLLE

Abstract

Intrauterine, intraperitoneal transfusion is associated with a poor survival rate in fetuses with hydrops and low gestational age. A method of direct fetal intravenous transfusion was used in two fetuses. One fetus with severe rhesus haemolytic disease was given transfusions in the 29th and 30th weeks of gestation, using an ultrasound-guided needle through the hepatic part of the umbilical vein without fetoscopy. In another fetus, an experimental cannulation of the umbilical vein succeeded in the 23rd week of gestation.

Ultrasound-guided fetal intravenous transfusion avoids the use of fetoscopy, which has limitations, and may improve the prognosis for rhesus-sensitised fetuses.

Introduction

Intraperitoneal transfusion of unborn infants with severe rhesus haemolytic disease gives poor results when the fetus has hydrops and a low gestational age.[1] Probably the fetal ascites prevents adequate resorption of erythrocytes, so that in many cases early delivery remains the treatment of choice.[2]

Rodeck *et al*[3] introduced a method of direct intravascular transfusion of fetuses under fetoscopic control at 23 to 26 weeks of gestation. Beyond that age, however, the method could not be used because of problems with the fetoscopic technique. We have therefore tried direct intravenous transfusion of fetuses through the hepatic part of the umbilical vein using a thin needle guided by ultrasound. The procedures conformed with the Declaration of Helsinki 1975.

Rigshospitalet, 2100 Copenhagen, Denmark

JENS BANG, MD, chief physician, university department of diagnostic ultrasound

JOHANNES E BOCK, MD, chief physician, university department of obstetrics and gynaecology

DYRE TROLLE, MD, professor of obstetrics and gynaecology

Materials and methods

Ultrasound scanning was performed with linear real-time equipment (Aloka). Gestational age was assessed from biparietal diameter and the fetus checked for hydrops and ascites. The intrauterine, intravenous transfusions were carried out under local anaesthesia.

A guide needle (1·2 × 150 mm) was introduced into the fetal abdomen 3-4 mm from the hepatic part of the umbilical vein, and through this a fine needle (0·6 × 180 mm) was inserted into the lumen of the umbilical vein. The procedure was visualised by ultrasound, the needle being passed through a special puncture transducer mounted on the scanner. The puncture transducer has a slit in the centre for introducing the needle, which may be fastened or released from the transducer with a wheel at the top. Also the puncture transducer was fitted with a movable scale calibrated in centimetres, by which the route of the needle could be monitored on the oscilloscope. When we scanned with the puncture transducer the scale was pointed directly at the umbilical vein and the tips of the guide needle and fine needle were visualised on the oscilloscope (figure).

Infusing blood into the umbilical vein produced some echoes, and the dispersal of the blood in the fetal vessels was seen on the oscilloscope. The fetal heart rate was measured before and after the transfusion.

Results

CASE 1

A 33-year-old woman, blood group O, rhesus-negative, was in her fifth pregnancy. The first had ended in spontaneous abortion, but the