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Luteal function in patients seeking AID

Artificial insemination from a donor (AID) is increasingly acceptable and demand for it is rising rapidly. Successful AID requires not only accurate timing of insemination but also suitable hormonal support for egg transport and implantation. Of all patients attending our NHS infertility clinic for donor insemination, however, 84% required clomiphene to improve luteal function; we decided to study this more fully.

Patients, methods, and results

All patients seeking AID between March 1976 and December 1978 were included. Out of 149 patients, 100 (67%) were found to have suboptimal serum progesterone concentrations (<30 nmol/l; <94·4 ng/ml) in the midluteal phase. Of 109 women attending the clinic who did not have oligomenorrhoea and whose husbands were normospermic, only 46 (42%) had suboptimal serum progesterone concentrations. This difference was significant ($P<0·001$). Furthermore, out of 16 patients whose midluteal progesterone concentrations were measured before their husbands were found to be infertile, only 6 (37·5%) had suboptimal values ($P<0·02$).

We also studied the temperature charts of our patients where these included accurate records of temperature during stages in treatment. The duration of basal temperature "hiphase" (number of days the temperature remained 0·1°C or more above the maximum temperature recorded in the week before the rise) was measured in each case. We studied the effects of the following stages: (1) from applying for AID to being put on the waiting list; (2) from the AID waiting list to starting treatment in patients not taking clomiphene; (3) from the AID waiting list to starting treatment in patients taking clomiphene; and (4) starting to take clomiphene in patients receiving AID. The table gives the results.

Duration of hiphase related to change in management

Management phase	Duration of hiphase in days (mean ± SD)	No of patients	Significance
Preclinic attendance	13·8 ± 1·1	10	P<0·001
Waiting list for AID	11·2 ± 1·7		
Waiting list, no clomiphene	12·3 ± 1·9	15	NS
AID started	12·6 ± 2·5		
Waiting list, taking clomiphene	14·4 ± 1·4	13	NS
AID started	13·9 ± 1·4		
AID without clomiphene	11·9 ± 1·6	17	P<0·001
AID with clomiphene	14·1 ± 1·4		

NS = Not significant.

Comment

We might expect that most women with infertile husbands would have normal fertility. We found, however, that 67% of patients receiving AID in our clinic had suboptimal midluteal progesterone concentrations. This prevalence was significantly higher than in infertile women with fertile husbands. A further 17% of patients required clomiphene because of irregular menstrual cycles or poor hiphase. Peyser *et al*[1] showed that psychological factors can affect the hypothalamic-pituitary-ovarian axis, which governs the hormonal basis of the menstrual cycle. We find that women presenting for AID undergo a change in duration of the hiphase and hence a change in their luteal function.

AID has, until recently, been subject to medical and lay disapproval, and is something that most couples find difficult to discuss with friends and relatives. It probably threatens the relationship between husband and wife, and causes more emotional stress than infertility alone. Preparating for and starting a course of AID is a major step for infertile couples, and pre-AID assessment is essential to increase the chances of success. AID counsellors, particularly those in clinics where treatment is undertaken, should adopt a relaxed approach with the couple seeking help. AID is best performed in centres where full hormonal evaluation and treatment can be undertaken.

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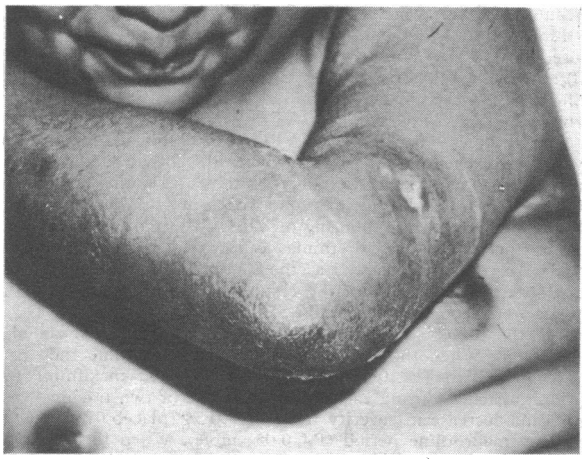
Successful treatment of systemic cryptococcosis with miconazole

Cryptococcosis associated with immunological deficiencies has a poor prognosis.[1 2] We report on a patient with dermatomyositis who developed systemic cryptococcosis and was successfully treated with miconazole; this is the first such case reported in the UK.

Case report

A 15-year-old girl presented in January 1973 with pain and swelling in her left calf. She developed a fever, and pain in her deltoid muscle and chest. Erythrocyte sedimentation rate was 100 mm in the first hour; serum immunoglobulin M, α^1- and α^2-globulins, lactate dehydrogenase, and creatine phosphokinase concentrations were all raised; and she was anaemic. Tests for antinuclear factor and LE cells were negative. A muscle biopsy showed polymyositis without vasculitis. She improved on oral prednisolone until September 1974, when she developed generalised muscle pains and weakness accompanied by dermatomyositic skin changes on her face and extremities. LE cell and antinuclear factor tests became positive. The prednisolone dosage was adjusted to between 10 and 20 mg daily. She developed many urinary and upper respiratory tract infections, but her chest *x*-ray films remained clear until August 1976, when an opacity was seen in the upper right lung. Tubercle bacilli were not found. That winter she had recurrent febrile attacks, associated with exacerbations of muscle or skin changes. These symptoms were controlled by increasing the dose of prednisolone. Early in 1977 her fever returned, and painful swellings appeared on her buttocks, elbow, and forearm. She was given ampicillin, but the next week some of the swellings ulcerated (fig). No organisms were seen in Gram films, but *Cryptococcus neoformans* was isolated in pure culture from an aspirated swelling and three times subsequently from ulcers, but not from blood. The culture grew on blood agar at 37°C with added CO_2, but its "germination time" varied from two to eight days, after which profuse growth suddenly appeared on plates previously blank. The organism was sensitive to 5-fluorocytosine (5-fc) amphotericin, and miconazole. Cryptococci were seen in biopsy specimens from the lesions and a in a blood film. Neither cryptococci not tubercle bacilli were found in her sputum, and her cerebrospinal fluid was normal.



Cryptococcal swellings and ulcer on arm.

The girl became critically ill, and her high-swinging fever continued. Systemic cryptococcosis was diagnosed and treatment started with 5-fc, 2·5 mg six hourly by mouth. She did not improve, and so two weeks later intravenous amphotericin was added, 0·25 mg/kg body weight daily, and the dose doubled after the first week. After 16 days of combined treatment her leucocyte count fell below 1×10^9/l (1000/mm^3), with under 30% granulocytes. Both drugs were discontinued and six units of blood (two fresh) transfused. Her white cell count rose steadily to normal, but her fever and abscesses persisted. Nine days later miconazole was given, 600 mg eight hourly by intravenous drip for four weeks and then 750 mg thrice daily by mouth for 13 months. She tolerated miconazole well, and gradually became afebrile; her abscesses healed. Intravenous hydrocortisone, given during the acute illness, was replaced by oral prednisolone at a maintenance dose of 12·5 mg daily. Despite a raised erythrocyte sedimentation rate and minor intercurrent infections, she was well two years after the diagnosis.

Comment

The cryptococcosis probably disseminated in 1976 when a pulmonary shadow appeared, and subsequent fevers arose from cryptococcosis rather than dermatomyositis. The cryptococcus was sensitive to serum concentrations obtained with each drug, but 5-fc was ineffective and amphotericin toxic. Miconazole was given for 14 months. Her serum appeared milky during intravenous treatment and her lipid patterns were abnormal; these effects have been observed before.[3 4] Cryptococcal antigen and antibody were never detectable in her serum and are not invariably found in cryptococcosis. Records at the Mycological Reference Laboratory show that latex agglutination tests for antigen are positive in 96% of patients in whom the central nervous system is affected but negative in 50% of those with cutaneous manifestations.[5]

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Doppler ultrasound and subjective assessment of fetal activity

Non-stress fetal heart rate (FHR) monitoring is an accepted method of assessing fetal wellbeing,[1] and subjective assessment of fetal activity by counting the number of fetal movements daily is reportedly a useful non-invasive test of placental function.[2] It has been suggested that Doppler ultrasound (US) increases fetal activity.[3] Because subjective assessment of fetal activity and ultrasonic monitoring of FHR are often combined, we decided to investigate the effect of US compared with phonocardiography (PHONO) on fetal activity.

Subjects, methods, and results

Twenty patients at 32-42 weeks of gestation were investigated by means of electronic FHR monitoring using PHONO and US with a Hewlett-Packard 8030A cardiotocograph. Patients taking sedatives or with ruptured membranes or polyhydraminos were excluded because of the possible effect of these factors on their ability to recognise fetal activity.[4] Each patient was monitored in bed semi-recumbent and tilted to right or left. The fetal heart was auscultated with a Pinnard stethoscope and the FHR transducer positioned over the point of loudest sound. Elasticated straps were placed around the abdomen to stabilise the FHR and tocodynamometer transducers.

Two examinations were performed on each patient on successive days. PHONO was used as a control, and the tests were conducted according to the following protocol. (1) The tocodynamometer transducer was positioned over the uterine fundus and the US (or PHONO) transducer over the fetal heart. (2) Ten minutes later the power was turned on and monitoring began. (3) FHR was recorded for 15 minutes, an event marker being used to indicate the moment the patient reported any fetal movements. Continuous movement for up to 30 seconds was counted as one movement and occurred in two examinations. (4) After 15 minutes the power was turned off and a PHONO (or US) transducer substituted. A further 10 minutes elapsed before beginning another 15 minutes of monitoring and recording movements as above. (5) On day 2 the PHONO and US sequence was reversed. Whether PHONO or US was used in the first 15 minutes of investigation on the first day was decided at random. In all cases a recording of the fetal heart was obtained. At no time during the investigation was the abdomen palpated or the transducer repositioned.

The table gives the results. Student's *t* test for paired samples failed to show any significant difference between the US and PHONO groups, either for the individual days or for the total number of movements overall.

Movements felt on days 1 and 2 of investigation

Case No	Day 1		Day 2		Total	
	US	PHONO	US	PHONO	US	PHONO
1	1	8	6	7	7	15
2	84	36	25	48	109	84
3	25	23	1	19	26	42
4	0	10	1	15	1	25
5	0	0	0	0	0	0
6	15	1	11	3	26	4
7	9	5	6	9	15	14
8	4	1	2	3	6	4
9	5	23	24	12	29	35
10	2	14	19	4	21	18
11	3	0	7	4	10	4
12	41	26	5	36	46	62
13	29	33	15	11	44	44
14	2	7	0	1	2	8
15	4	3	5	6	9	9
16	3	5	7	7	10	12
17	0	4	0	0	0	4
18	2	3	6	11	8	14
19	2	3	15	22	17	25
20	5	14	2	5	7	19
Mean SD	11·8 20·31	10·9 11·29	7·8 7·84	11·1 12·27	19·6 24·97	22·1 21·72
Student's *t* test for paired samples	P = 0·7		P = 0·2		P = 0·3	

Comment

David *et al*,[3] who studied 36 patients, reported an increase in fetal movements recorded subjectively in patients monitored with US. They did not mention whether continuous fetal movement was present during their studies or indeed how it would have been recorded in terms of number of movements. We encountered such a problem in two patients, and our method of reporting it is explained. Using PHONO as a control, we could not substantiate the findings of David