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Detection of subclinical abortion by assay of pregnancy specific β_1 glycoprotein

Detection of human chorionic gonadotrophin in blood or urine during the luteal phase led to the suggestion that many apparently infertile women may conceive but lose the pregnancy at the subsequent menstruation.[1] Schwangerschaftsprotein 1 is another placental product whose presence in the circulation is at least as reliable as that of human chorionic gonadotrophin in indicating pregnancy.[2] To see whether such occult pregnancy occurred we assayed Schwangerschaftsprotein 1 concentrations in one patient over seven successive menstrual cycles.

Case report

A 29 year old woman with nine years' unexplained infertility was treated with 100 mg clomiphene citrate for five days at the start of her menstrual cycle, followed by 5000 IU human chorionic gonadotrophin 10-12 days later. She was instructed to have intercourse after the injection of human chorionic gonadotrophin, and on two occasions her husband's semen was artificially inseminated. Her basal body temperature was recorded daily, and blood samples were taken four to six times during the luteal phase for measurement of serum concentrations of oestradiol, progesterone, β human chorionic gonadotrophin, and Schwangerschaftsprotein 1. During the fifth cycle a transient rise in concentration of Schwangerschaftsprotein 1 was noted just before menstruation, so in cycles 6 and 7 blood samples were taken daily from the time of injection of human chorionic gonadotrophin to menstruation. Concentrations of progesterone and oestradiol were measured by standard radioimmunoassay techniques using specific antisera. β Human chorionic gonadotrophin concentration was measured by radioimmunoassay using a commercial kit (Serono). All concentrations higher than 10 IU/l were taken as positive. Schwangerschaftsprotein 1 concentrations were measured by enzyme immunoassay using a kit (Behringwerke), the lower limit of sensitivity of which is 0·3 μg/l.

The first four cycles were normal ovulatory ones, in which progesterone concentrations found in conceptual cycles were reached,[3] but concentrations of β human chorionic gonadotrophin and Schwangerschaftsprotein 1 showed no evidence of conception. The table shows the results of assays in the last three cycles. Ovulation (day 0) was defined in terms of basal body temperature and change in steroid concentration. The rises in serum β human chorionic gonadotrophin concentrations immediately after ovulation in these three cycles were caused by the injections of the hormone and cannot be taken as evidence of pregnancy. On day 27 of the fifth cycle a transient rise in Schwangerschaftsprotein 1 concentration was recorded. On day 24 of the sixth cycle high concentrations of β human chorionic gonadotrophin and Schwangerschaftsprotein 1 were recorded, but Schwangerschaftsprotein 1 concentration was declining by day 27. Bleeding began on day 28, but a blood sample was not taken. In the seventh cycle concentrations indicating pregnancy were seen on day 27, coinciding with the premenstrual fall in progesterone concentration. They were still present on day 30, when a heavy period began. The high concentration of Schwangerschaftsprotein 1 persisted for the first two days of bleeding, but in view of the long half life of this protein[4] this does not necessarily indicate that trophoblastic tissue persisted for that time.

Concentrations of placental proteins and hormones during cycles 5 to 7 with presumed subclinical abortion (clomiphene citrate given at start of each cycle)

Days from menstruation	Days from ovulation (day 0)	Oestradiol (nmol/l)	Progesterone (nmol/l)	β Human chorionic gonadotrophin (IU/l)	Schwangerschafts-protein 1 (μg/l)
			Fifth cycle		
12*	− 1	2·46	1·95	3·4	<0·3
15	+ 2	0·50	28·95	40·8	<0·3
19	+ 6	1·16	>50·00	10·3	<0·3
20	+ 7	0·93	>50·00		<0·3
21	+ 8	1·04	>50·00	5·7	<0·3
22	+ 9	1·02	>50·00	4·9	<0·3
25	+12	0·94	30·75	5·7	<0·3
27	+14	0·36	4·70	3·8	0·64
			Sixth cycle		
13*	0	3·44	3·15	19·5	<0·3
14†	+ 1	2·93	12·65	97·1	<0·3
15	+ 2	0·86	11·95	57·0	<0·3
16	+ 3	0·55	42·10	42·7	<0·3
17	+ 4	1·22	48·80	32·5	<0·3
20	+ 7	2·18	>50·00	8·8	<0·3
21	+ 8	1·94	>50·00	9·3	<0·3
22	+ 9			4·0	<0·3
23	+10	2·03	>50·00	2·0	<0·3
24	+11	2·06	>50·00	116·0	1·28
27	+14	0·43	6·35	144·0	0·74
			Seventh cycle		
14*	− 1	3·96	2·90	2·5	<0·3
15	0	2·42	8·50	64·5	<0·3
16	+ 1	0·96	15·65	54·4	<0·3
17	+ 2	0·72	34·35	37·6	<0·3
18	+ 3	0·64	>50·00	25·9	<0·3
20	+ 5	1·26	>50·00	13·4	<0·3
21	+ 6	1·45	>50·00	9·1	<0·3
22	+ 7	1·76	>50·00	4·5	<0·3
23	+ 8	1·21	>50·00	3·8	<0·3
24	+ 9	1·39	>50·00	4·0	<0·3
25	+10	0·70	>50·00	3·6	<0·3
26	+11	0·56	>50·00	3·5	<0·3
27	+12	0·42	32·45	3·2	0·56
28	+13	0·68	22·25	2·6	0·60
29	+14	0·19	2·90	3·1	0·74
30‡	+15	0·20	1·60	2·7	0·82
31	+16	<0·13	2·10	3·3	0·60
32	+17	<0·13	<1·25	3·2	<0·3

*Human chorionic gonadotrophin 5000 IU given intramuscularly.
†Artificial insemination from husband.
‡Started to bleed heavily.
Conversion: SI to traditional units—Oestradiol: 1 nmol/l ≃ 272 pg/ml. Progesterone: 1 nmol/l ≈ 0·3 ng/ml.

Comment

We have no proof that fertilisation occurred, but the fact that two independent variables coincidentally indicated the possibility of conception, only after implantation could have occurred, makes fertilisation probable. The trend of Schwangerschaftsprotein 1 concentrations was quite different from that in our experience of normal pregnancy.[2] In this patient the concentration fell or stayed level, whereas in normal pregnancy it rises steeply.

A widely accepted estimate puts the incidence of subclinical abortion at not less than 40% of potentially fertile cycles.[5] Thus assay of Schwangerschaftsprotein 1 concentration may become a powerful tool in investigation of unexplained infertility.

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