Sextuplet Gestation

A CASE REPORT

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SUMMARY

Multiple gestations after human menopausal gonadotrophin (HGM) stimulation are not uncommon. Such pregnancies are at great risk from abortion, premature labour, placental insufficiency and intra-uterine death with maceration.

The present case report concerns a successful sextuplet gestation. Since recent advances in management were utilised and may have contributed to the successful outcome, the case was deemed to be worth reporting.

S. Afr. Med. J., **48**, 1449 (1974).

CASE REPORT

The patient, a 26-year-old White female, had had 2 earlier pregnancies, 7 and 5 years previously. These had resulted in the spontaneous delivery of a female and male infant weighing 4,0 kg and 3,6 kg respectively. No postpartum haemorrhage had occurred. After one year of taking an oral contraceptive (during which she became amenorrhoeic) no further spontaneous menstruation ensued.

She consulted her gynaecologist because of secondary amenorrhoea and infertility. History, examination and special investigations were non-contributory, apart from low gonadotrophin and oestrogen excretion. After the failure of three courses of clomiphene to induce ovulation, human menopausal gonadotrophin (HMG) was administered. Two of three courses resulted in apparent ovulation, but conception did not occur. The fourth course of HMG resulted in the sextuplet gestation. HMG 150 IU was administered daily for 5 days. Since no response was detectable in the cervical mucus, the dose was increased to 225 IU daily. On the second day at this dosage a cervical mucus response was detected, and a grade V^{15} response was attained within 3 days. Total urinary oestrogens assayed on the third and fourth days of 225 IU therapy were 43 and 162 µg per 24 hours respectively. HMG was withheld and the following day the excretion was 148 µg. Overstimulation was discussed with the patient, and it was decided to wait a further 24 hours before triggering ovulation. Human chorionic gonadotrophin (HCG) 4 500 IU was then administered on 14 and 15 May 1973, followed by HCG 3 000 IU twice weekly for 3 weeks.

On 7 June 1973 the patient complained of hyperemesis and was admitted to hospital for 5 days. Intravenous fluids and sedation were administered. On 13 June 1973 ultrasonography revealed large bilateral ovarian cysts, massive trophoblastic overgrowth, and at least 2 fetuses.

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Date received: 14 March 1974.

Course of Pregnancy

The course of pregnancy was complicated by anaemia (haemoglobin 10,0 g/100 ml on 29 September 1973). Total-dose Imferon was administered and the haemoglobin level responded well to this. Patient discomfort was excessive, necessitating almost total bedrest from 27 November 1973.

Ultrasonic examination was undertaken serially. The examination was made more difficult by supine hypotension, which caused one examination to be abandoned entirely. The means of at least 3 biparietal diameters are listed below. It is difficult to be certain exactly how many fetal heads were present at a single examination.

TABLE I. SERIAL BIPARIETAL DIAMETERS

6. 8.73	28 mm	
16. 8.73	30,5 mm	
12. 9.73	46,5 mm	
9.10.73	55 mm	
7.11.73	83 mm.	The small fetus was not identified
8.11.73	70 mm	
4.12.73	81 mm	

An identical reading was obtained for 3 fetuses, while the 4th reading was 74 mm. On 18 December 1973 the examination was abandoned.

The other striking feature of the pregnancy was excessive uterine activity. At 23 weeks' gestation, fenoterol 2,5 mg every 8 hours was started. The cervix was uneffaced. On three separate occasions (27 November 1973, 11 and 23 December 1973) uterine activity became painful and, in addition to the dose of fenoterol being doubled, diazepam 10 mg intramuscularly and an isoprenaline aerosol were utilised, which controlled the uterine activity satisfactorily. Later in pregnancy, aerosols of fenoterol or salbutamol were utilised as a routine. Cortisol (100 mg

every 6 hours for 48 hours) was administered weekly for 3 weeks, starting on 18 December 1973.

Despite this management, the cervix was noted to be effacing on 21 December 1973, and on 10 January 1974 it was noted to be 80% effaced and 2,5 cm dilated. At this time, the maternal weight had been static for 5 days and the urinary oestriol excretion was static (21,7 mg/24 hours on 2 January 1974 and 17,9 mg/24 hours on 5 January 1974).

It was therefore thought that the growth support margin of the uterus had been reached and that a Caesarean section should be performed in view of the risk of malpresentations, cord prolapse, abruptio placentae and asphyxia for the last fetuses during the birth process.

Delivery

A routine Caesarean section was performed on 11 January 1974 without complications. Points of note were:

(a) Pre-oxygenation in lateral position was followed by induction of anaesthesia with nitrous oxide and minimal halothane. Intubation was accomplished with succinylcholine in the lateral position. Maintenance anaesthesia followed, with nitrous oxide, oxygen and alloferin, until delivery was completed. No hypotension was noted at any stage. Two units of blood were infused. All babies cried immediately on delivery, although resuscitation was required later.

(b) No lateral tilt was necessary, since the weight of the uterus held it at an angle of at least 15°.

(c) No postpartum haemorrhage occurred and uterine retraction was excellent.

Postpartum, the mother remained in excellent condition, apart from an episode of peripheral cyanosis and tachypnoea. This was thought to be due to peripheral sludging as a result of polycythaemia (packed cell volume 53%) and it responded to fluid administration. A diagnosis of benign amniotic fluid embolism was considered. Mild intravascular coagulation was detected 11 hours postpartum but settled spontaneously.

Paediatric Care

The paediatric care of a sextuplet pregnancy involved certain preparations before anticipated delivery of the infants by Caesarean section. At birth each baby was to be attended by a paediatrician and a paediatric nursing sister. (An intensive care room was equipped to accommodate 6 additional infants who might be immature and suffering from respiratory distress.)

The multiple pregnancy was terminated by elective Caesarean section at approximately 36 weeks of gestation. All 6 babies were delivered and transferred to their allotted resuscitation table within 2 minutes. Five infants failed to establish spontaneous breathing and had Apgar scores under 3/10 at 1 minute of age (Table II). They were intubated and their lungs were inflated with oxygen. The sixth infant maintained normal breathing from the time of birth (Apgar 6/10) and required additional oxygen for a further 2 minutes. All babies breathed normally at 3 minutes of age and were transferred in warmed incubators to the intensive care unit.

TABLE II. BIRTH ORDER, SEX AND MEASUREMENTS OF SEXTUPLETS

Birth order	Sex	Weight (g)	Head circumference (cm)	Apgar score (1 min)	Bilirubin highest level (mg/100 ml)
1	Male	2 020	34,5	2	7,5
2	Female	1 260	29,0	6	9,5
3	Male	2 080	32,0	1	9,0
4	Female	1 820	31,0	2	9,0
5	Male	1 880	34,0	1	9,5
6	Female	1 980	33,0	2	9,0

The placental tissue weighed 2 700 g and consisted of six separate organs which were joined to each other. The placenta which had supported the growth of the smallest infant was centrally situated and decidedly smaller than the other organs.

Each infant showed some physical evidence of retarded intra-uterine growth. The gestational ages scored at 24 hours[1] gave readings of 36 weeks in all cases. The weights of 5 babies ranged from 2 080 g to 1 820 g, and fell just above or below the 3rd percentile on an intra-uterine growth chart,[2] while the weight (1 260 g) of the remaining infant fell well below this level. No congenital abnormalities could be detected, nor was there evidence of respiratory distress caused by hyaline membrane disease.

The babies received 10% invert sugar solutions through a scalp vein in volumes of 60 ml/kg/day. Blood sugar checks were performed every 3 hours in order to maintain a level above 45 mg/100 ml. At 24 hours of age additional calories were provided by a one-third strength evaporated milk in quantities of 30 ml/kg/day. The milk was administered continuously through a nasogastric tube by means of an infusion pump. Intravenous fluid was discontinued after 72 hours and the volume of milk feeds was increased to 100 ml/kg/day.

Serum bilirubin levels were checked every 6 hours and five infants received phototherapy at 72 hours of age as their total bilirubin levels were in the region of 10 mg/100 ml (Table II). All signs of jaundice disappeared within 72 hours and phototherapy was discontinued.

The 5 larger infants were placed in cots at 7 days of age and were offered bottle feeds. These were increased in volume over 4 weeks to 200 ml/kg/day. The smallest infant was weaned from her incubator at 3 weeks of age and within the next 10 days was taking bottle feeds of 200 ml/kg/day every 3 hours.

All received additional vitamins, folic acid and iron.

DISCUSSION

The incidence of multiple gestations following gonadotrophin administration is 30 - 50%.[3,4] The incidence of

more than twins is 20%. The reason for this is that several follicles are always stimulated to the stage of readiness for ovum release rather than the single large follicle of normal ovulation.[5] A fine balance is therefore drawn between multiple gestations and no pregnancy. A fourfold variation in response, by the same patient to the same dose, is often found in successive treatment cycles.

Urinary oestrogen estimations are the routine way of monitoring for overstimulation, but even these may be misleading. It is apparent from this case and those of Liggins and Ibbertson[6] and Juwelewicz *et al.*[7] that the most sensitive index of overstimulation is the rate of rise of oestrogens rather than the absolute levels achieved. Further evidence may be evinced from the studies of Edwards.[13] Biological monitoring is satisfactory for assessing adequacy of response, although no guide to overstimulation, as the case of Campbell and Dewhurst's quintuplets illustrates.[8]

With multiple gestations the major risks are abortion, premature delivery, placental insufficiency and intra-uterine death. A difficult clinical decision must be made between premature delivery with neonatal death from the sequelae of being born too soon and intra-uterine death from an inadequate growth support margin and resultant placental insufficiency. This appeared to be achieved in this case by a combination of clinical skills and special investigations.

McKeown and Record[14] calculated that spontaneous multiple gestations resulted in retardation of fetal growth when the total fetal mass exceeded 3 kg. This occurs at 30 weeks in twins and at 26 weeks in quadruplets. Their results are shown in Table III.

TABLE III. MEAN GESTATIONAL AGE IN MULTIPLE PREGNANCIES

	No. of deliveries	Mean birthweight (kg)	Mean gestational age (days)
Singletons	**22 454**	**3,4**	**280,5**
Twins	**325**	**2,4**	**261,6**
Triplets	**249**	**1,8**	**246,8**
Quadruplets	**27**	**1,4**	**236,8**

It can be seen from Table III that the mean gestational age decreases for increasing fetal numbers, but that the total fetal weight does not increase proportionately. Berbos *et al.*[9] report a quintuplet gestation which delivered at 218 days with a total fetal weight of 6,4 kg.

Pregnancies resulting from induced ovulation are known to have a much greater incidence of 'placental insufficiency' than spontaneous pregnancies. Of the reported gonadotrophin-induced multiple gestations, the total fetal weights and gestational ages were as shown in Table II. It can be seen that the quality of survival of the present series is in excess of previously reported multiple gestations with regard to gestational age, total fetal mass, average fetal weight, placental mass and number of survivors.

There are several possible reasons for this favourable outcome. It might be merely fortuitous in view of our patient's previous large infants. Liggins and Ibbertson's case,[6] with the next largest fetal weight, had had a previous neonate weighing 4,24 kg which was larger than both of the present subject's previous infants.

The second possible reason is the advanced gestation of the present infants. While it cannot absolutely be ascribed to the systematic and intensive use of the second generation β adrenergics, three clear episodes of painful uterine contractions were averted by intensification of the regimen. Only isoxuprine and alcohol appear to have been used previously, and then only sporadically.

These findings do not explain the other facet of the case, viz. that the total fetal mass, the placental weight and the fetoplacental weight ratio were far in excess of other reported cases (Table IV). It is possible that placentation was improved by the administration of HCG, which is undoubtedly placentotrophic,[10] administration resulting in placental growth.[11] The growth support margin may therefore have been increased, although the neonates were small for dates by singleton standards. In both reports of the 2 next-largest total fetal weights,[6,7] HCG or luteinising hormone had been given to the mothers.

The infants were born in optimal physical health. Their lungs were normal at birth despite the shortened period of gestation. It is difficult to attribute this early maturation of lungs to the antenatal use of cortisone, since all infants showed evidence of growth retardation. This fact in itself can be associated with an acceleration of lung maturation, irrespective of the gestation of an infant.[12]

Other facets of the case bear mentioning. Post-partum tachypnoea and cyanosis were reported by Aiken,[16]

TABLE IV. COMPARISON WITH OTHER REPORTED CASES

Author	No. of fetuses	Survivals	Gestation at delivery (+14 days)	Total fetal weight (kg)	Mean fetal weight (kg)	Range	Placental weight (kg)
Aiken[16]	**7**	**3**	**±210**	**7,3**	**1,04**	**—**	**2,04**
Juwelewicz *et al.*[7]	**5**	**NS***	**239**	**8,6**	**1,7**	**—**	**NS**
Campbell and Dewhurst[8]	**5**	**NS**	**212**	**NS**	**NS**	**1,10-1,56**	**NS**
Lachelin *et al.*[3]	**7**	**6**	**224**	**NS**	**NS**	**0,74-1,22**	**NS**
Liggins and Ibbertson[6]	**5**	**5**	**238**	**8,8**	**1,76**	**—**	**1,13**
Present report	**6**	**6**	**253**	**11,0**	**1,83**	**—**	**2,7**

* NS = not stated.

who found a central venous pressure of 11 cm. In our case the central venous pressure was low (possibly engendered by diuretics), and was thought to be due to peripheral sludging in association with a packed cell volume of 53%. Another possible explanation was a non-particulate amniotic fluid embolus, in view of the benign course and evidence of intravascular coagulation. The latter could, however, possibly be accounted for by the large placental site.

The final point of note was that multiple skills, ranging from private practitioner to haematology department, were necessary to ensure the favourable outcome. This illustrates that a successful outcome can be anticipated where such patients have access to the multiple skills available at a teaching hospital.

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