PITUITARY TUMOURS DURING PREGNANCY IN MOTHERS TREATED WITH BROMOCRIPTINE

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- 1 Out of 805 previously infertile women in whom pregnancy was achieved on bromocriptine treatment, 137 were diagnosed as having pituitary tumours.
- 2 In nine of these, tumour-related complications occurred during pregnancy, chiefly visual field impairment. Surgical intervention was considered necessary in two patients. In a third patient reinstitution of bromocriptine produced remission of symptoms.
- 3 Although the frequency of serious complications was low, the present state of knowledge indicates that surgery or irradiation of pituitary tumours should be preferred, at least as the first line of treatment, for patients contemplating pregnancy.

Introduction

It has long been known that the normal pituitary gland enlarges in pregnancy, with fairly rapid regression after delivery (Erdheim & Stumme, 1909). It is also generally accepted that pituitary tumours of the chromophobe type will increase in size during pregnancy, possibly causing complications (Child, Gordon, Mashiter & Joplin, 1975). The need for regular assessment of visual fields, leading to radiological evaluation of sella size and, if necessary, surgical intervention, has been repeatedly expressed (Rjosk, Fahlbusch, Huber & von Werder, 1978). Bromocriptine has been introduced for the treatment of infertility associated with hyperprolactinaemia, and a number of such patients may in fact have undetected pituitary adenomas. It is obviously important to know if bromocriptine treatment, which has a direct action on prolactin-secreting pituitary cells (Mashiter, Adams, Bread & Holley, 1977), can affect the expected change in pituitary size during pregnancy. One report exists of a patient in whom tumour enlargement occurred during a pregnancy which had been achieved with the help of bromocriptine; reinstitution of the drug was accompanied by improvement in visual field impairment and the pregnancy went to term (Bergh, Nillius & Wide, 1978). In our attempt to gather information on the infants born to mothers given bromocriptine in the early weeks of pregnancy, we have acquired some data on the health of the mothers (Griffith, Turkalj & Braun, 1978). The purpose of this paper is to provide some idea of the frequency of possible pituitary complications which may occur in bromocriptine-assisted pregnancies.

Methods

During the last 4 years over 800 pregnancies in bromocriptine-treated mothers have been reported to the medical research departments of Sandoz affiliated companies in different countries. We have obtained information on the course of pregnancy—abortion, multiple births, malformations—in a total of 805 completed pregnancies, using a simple questionnaire method (Griffith *et al.*, 1978). These cases were analysed for information on pituitary tumours in the mother—the questionnaire contained a passage concerning ‘course of pregnancy’ in which the doctor was able to comment on maternal health and events.

Results

Pituitary tumour was given as the diagnosis (definitive or tentative) in a total of 137 patients (Table 1). Twenty-five of these patients had received previous treatment (surgery or irradiation, or both). Although most tumours were obvious prolactinomas, acromegaly was diagnosed in four patients. Pregnancy ended in abortion in 21 patients, in seven of these abortion was induced for various reasons.

Of the 116 completed pregnancies, nine tumour-related complications were reported (Table 2). In eight of these, disturbances of vision were diagnostic features, and in the ninth severe headache was described. Craniotomy was done in two cases, bromocriptine was reinstituted in one, and caesarean sections were done in three cases. No intervention was deemed necessary in the remaining three patients.

Some of these cases have been published (see final column in Table 2).

Other findings reported during pregnancy in the 137 patients with pituitary tumours included hypertension and/or pre-eclamptic toxæmia in six patients, a pathological glucose tolerance test in one and cholestasis (not drug-related) in another. Delivery was spontaneous in 100 patients, induced in four and forceps-assisted in one. Caesarean sections were done in 11 patients. Data on the frequencies of spontaneous abortions, multiple pregnancies and malformations, as well as the average dose and duration of bromocriptine therapy show no relevant differences to those for the total collective (i.e. 805 patients).

Discussion

Our information, although perhaps sketchy, gives some indication of the likelihood with which pituitary-related complications can occur in bromocriptine-assisted pregnancies. The mean duration of infertility for the tumour patients was 6.7 years. Without bromocriptine, most of these patients would not have become pregnant; it is known that pregnancy is unusual in patients with radiologically evident pituitary tumours (Child *et al.*, 1975). Thus a comparison between the frequency of complications in bromocriptine-treated and non-treated patients is not possible. In the nine cases with tumour-related complications, surgical intervention was necessary in only two—a frequency of 1.4% in patients with tumours. Although caesarean sections were done in three of the other cases, the duration of pregnancy ranged between 36 and 42 weeks, so that it does not seem as if a relevant reduction in the duration of pregnancy is necessary in the majority of patients presenting with symptoms of tumour enlargement.

At this point it may be asked whether bromocriptine treatment in fact produces a shrinkage in tumour size, so that continued use throughout pregnancy would avoid just those complications which are feared. Animal studies have shown that ergot derivatives can hinder the growth of pituitary tumours (MacLeod & Lehmeyer, 1973). At least seven patients (some non-pregnant) have been reported where bromocriptine has reduced pituitary tumour size (Corenblum, Webster, Mortimer & Ezrin, 1975; Sobrinho, Nunes, Santos & Mauricio, 1978; Nillius, Bergh, Lundberg, Stahle & Wide, 1978; Huth & Tyson, 1977; Vaidya, Aloorkar & Sheth, 1977). Furthermore, symptomatology disappeared in our case 7 with the reinstitution of bromocriptine therapy at the 30th week of pregnancy.

At present, our knowledge is inadequate for us to recommend a change in policy regarding the treatment of pituitary tumours in relation to pregnancy. If a tumour has been diagnosed (or is even suspected) contraception should be practised. When pregnancy is desired, a tumour should be treated if necessary either by surgery or irradiation (Thorner, Besser, Jones, Dacie & Jones, 1975; Rubenstein, 1977). Visual fields should be evaluated carefully throughout pregnancy in any mother with a suspected pituitary tumour (especially in those with high serum prolactin levels), whether receiving bromocriptine or not. Until more is known about a possible protective action of bromocriptine, the drug should be discontinued as soon as pregnancy is diagnosed. Marked visual changes or indeed other evidence of rapid pituitary enlargement is an indication for surgical intervention. In our opinion, there is at present insufficient evidence to advocate that such patients should be treated with bromocriptine to reduce the size of the pituitary. However, it may be that future reports will change this viewpoint.

Table 1 Incidence of pituitary tumour and treatment in patients who had received bromocriptine

Indication	Number of pregnancies	Previous therapy					Abortions
		Surgery	Irradiation	Surgery and irradiation	Births (at term)		
Pituitary tumour	100	12	12	1	86		14
Agromegaly	4	0	0	0	3		1
Pathological sella	19	0	0	0	13		6
Suspicion of tumour	14	0	0	0	14		0
Total	137	12	12	1	116		21

Table 2 Tumour-related complications in nine of the 116 completed pregnancies

No.	Age (years)	Clinical diagnosis	Bromocriptine			Clinical symptoms	Measures	Duration of pregnancy (weeks)	References
			Dose (mg/day)	Duration total (months)	Duration of treatment in pregnancy (days)				
1	30	Pituitary microadenoma	5.0	6	19	Visual disturbances in 5th month, disappeared in 7th month	None	40	
2	20	Chromophobe adenoma	5.0	6	23	Bi-temporal hemianopsia	Craniotomy	42	
3	24	Chromophobe adenoma	5.0	5	42	Visual field defect	Craniotomy	41	Burry <i>et al.</i> (1978)
4	39	Pituitary tumour	7.5	4	51	Small field defect for red	None	38	Thorne <i>et al.</i> (1975)
5	32	Pituitary tumour	5.0	1	17	Visual field defect with bi-temporal hemianopsia	Caesarean section	38	Corbey <i>et al.</i> (1977)
6	25	Sella enlargement during pregnancy	5.0	1	21	Headaches	None	41	Bergh <i>et al.</i> (1978)
7	25	Pituitary tumour	15.0	4	41	Visual field defect at 30th week	15 mg bromocriptine daily led to normalization	39	Bergh <i>et al.</i> (1978)
8	28	Pituitary tumour	5.0	4.5	30	Visual field defect with bi-temporal hemianopsia	Caesarean section	38	Lamberts <i>et al.</i> (1977)
9	31	Pituitary tumour	3.75	2	—	Optic nerve compression	Caesarean section	36	—

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(Received November 28, 1978)