A Paraplegic Fathering a Child after an Intrathecal Injection of Neostigmine: Case Report

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Summary

This paper reports a 33-year-old male paraplegic (T6) who fathered a child by artificial insemination following an intrathecal injection of neostigmine. His wife was healthy and pregnancy was achieved after the 10th insemination. She delivered a mature female child weighing 3,100 g in August 1984. To our knowledge this is only the fourth successful case in the world following neostigmine injection.

Key words: Paraplegic; Ejaculation; Intrathecal neostigmine injection; Artificial insemination; Pregnancy and delivery.

Introduction

Ejaculation induction for paraplegics, using an intrathecal injection of neostigmine (Guttmann, 1949), has been tried by several clinicians with variable results (Spira, 1956; Piera, 1973; Chapelle *et al.*, 1974; Iwatsubo *et al.*, 1984; Ishido *et al.*, 1985). Since 1981, we have attempted artificial insemination with husband's semen (AIH) obtained by this method for those paraplegics who hoped to father a child. A successful case is reported.

Case report

A 33-year-old male sustained a compression fracture of T6 following a 3-metre-high fall in November 1980, resulting in complete paralysis below the T9 segment. In December 1980, spinal fusion was performed and in March 1981, transurethral lithotripsy of a bladder stone was necessary. He voided urine freely by the Credé and Valsalva maneuver and a cystometrogram showed a low compliance bladder, with a capacity of 350 ml, without autonomic hyperreflexia.

Sexual life

In March 1980, 7 months before his injury, he was married, and then had a normal sex life with his wife. In June 1980, his wife conceived but aborted.

After the injury he had weak erections which persisted only briefly without ejaculations and had no opportunity for coitus with his wife. His wife was aged 25 years and was healthy. Her menstrual cycle was 30 days.

Course of AIH

In March 1983, the first intrathecal injection of neostigmine (Vagostigmine 0.75 mg, Shionogi) was tried and 1 ml of semen (sperm count of $3 \times 10^6/\text{ml}$, motility of 0%) was collected 4 hours later. It was inseminated by a gynecologist, but his wife did not conceive. AIH was repeated on 8 occasions 30 days apart at the time when it was believed the patient's wife was most likely to be ovulating, but all failed despite remarkable improvement in the spermatogram during this period (Fig. 1). On December 9, 1983, the 10th AIH was done with 2 ml of semen induced by 1.0 mg neostigmine (sperm count of $90 \times 10^6/\text{ml}$, motility of 70%). Following this AIH the wife became pregnant and she delivered a healthy female child weighing 3100 g on August 24, 1984.

Figure 1. Number of sperm and percentage of motility induced by neostigmine injection. These parameters improved gradually up to the 10th trial except the 7th and 8th ejaculates.

Discussion

There are numerous reports on the sexual function of male paraplegics, and we reviewed the 13 major series comprising 2461 patients shown in Table 1 (Munro *et al.*, 1948; Horne *et al.*, 1948; Kuhn, 1950; Talbot, 1955; Zeitlin *et al.*, 1957; Bors and Comarr, 1960; Tsuji *et al.*, 1960; Comarr, 1970; Miyazaki, 1970; Kimura, 1970; Hayashi *et al.*, 1973; Fitzpatrick, 1974; Miyazaki, 1982). While 1548 patients (63%) had erections after the injury, only 355 patients (14%) experienced ejaculations; erections were preserved about four times as often as ejaculations. Furthermore only 44 paraplegics (1.8%) were successful in causing their partners to conceive. The belief that paraplegics cannot have sexual intercourse is no longer true, since various penile prostheses are now

Table 1 Sexual function of male paraplegics

Reporter	No. of patients	Erection	Ejaculation	Coitus	Progeny
Munro <i>et al.</i>	84	62	8	—	2
Kuhn	25	25	2	—	0
Talbot	408	270	92	94	20
Zeitlin <i>et al.</i>	100	86	3	26	1
Comarr	150	123	19	57	1
Bors & Comarr	529	321	80	262	18
Horne <i>et al.</i>	18	11	3	5	2
Tsuji <i>et al.</i>	638	341	60	32	—
Miyazaki	324	180	50	60	—
Hayashi <i>et al.</i>	52	48	19	11	—
Miyazaki	62	35	7	—	—
Fitzpatrick	14	12	6	3	0
Kimura	57	34	6	3	—
Total	2461	1548 (63%)	355 (14%)	553 (22%)	44 (2%)

Table 2 Successful AIH using semen obtained by intrathecal injection of neostigmine

Reporter	Level of injury	Age	Period after injury	Wife	Number of AIH	Sperm count	Sperm motility
Spira (1956)	T6	31	6y	?	4	200 × 10 ⁶ /ml	50%
Chapelle <i>et al.</i> (1976)	T7	28	7y	?	1	40 × 10 ⁶ /ml	?
Miyazaki (1982)	C6	28	6y	28y paraplegia (L1)	2	245 × 10 ⁶ /ml	74%
Our case (1985)	T6	33	3y	25y normal	10	90 × 10 ⁶ /ml	70%

available. But fertility in these patients is still extremely low because of impaired spermatogenesis and inability to ejaculate.

There have been three methods to induce ejaculations artificially: transrectal electrostimulation (Thomas *et al.*, 1975; Francois *et al.*, 1978; Brindley, 1981), electro-vibration of the external genitalia (Francois *et al.*, 1980; Brindley, 1981), and the present method originally reported by Guttmann in 1949. The last technique has been applied for many patients but so far only three patients have succeeded in fathering their own children. To our knowledge our case is the 4th successful one in the world (Table 2).

The longer the period after the spinal injury, the poorer the spermatogenesis, which is true for all paraplegics. Miyazaki (1982) analyzed the semen of 11 patients obtained by neostigmine injection and found that the number of sperm averaged $19 \times 10^6/\text{ml}$ and the average motility was 34 per cent. In our patient the sperm count and the motility improved gradually as artificial ejaculation was repeated (Fig. 1), which confirmed the statement of Guttmann and Walsh (1971). Consequently we feel strongly that doctors should not desist from the neostigmine induction procedure even if the spermatogram is significantly impaired at the first or second trial.

The mechanism of ejaculation following intrathecal injection of neostigmine is unclear but a twofold action is suspected (Bors and Comarr, 1960). The first action is the direct stimulation of the spinal sexual centre by neostigmine. The spinal sexual centres are divided into two parts: that for seminal emission is

the sympathetic centre linked to the hypogastric nerves, extending from T11 to L2. The other for ejaculation proper is the somatic centre associated with the pudendal nerves, arising in cord segments S2, 3 and 4 (Tarabulcy, 1972). Since S2-4 is also a centre for erection, in most cases intrathecal injection of neostigmine also provokes erections (Guttmann and Walsh, 1971). The second action is the removal of skeletal muscle reflexes which may inhibit sexual function.

There is a practical problem in applying the intrathecal injection of neostigmine for AIH as autonomic hyperreflexia (Head and Riddoch, 1917) sometimes occurs. This dangerous phenomenon, which is provoked by the contraction of the seminal vesicles and bulbocavernous muscles during ejaculation, tends to occur in paraplegics with a lesion above T5 (Guttmann and Walsh, 1971). The signs and symptoms of autonomic hyperreflexia are headache, nausea, vomiting and hypertension. Guttmann and Walsh (1971) reported a case (complete C6-7 lesion) who died of cerebral haemorrhage after the injection of 0.3 mg neostigmine. Ushiyama *et al.* (1984) encountered a patient with C5 lesion in whom the removal of an intracranial haematoma was necessary for a right frontal lobe haemorrhage following the injection of 0.3 mg neostigmine. Autonomic hyperreflexia can be controlled by atropine or pentolinium intravenously (Guttmann and Walsh, 1971). The following precautions should be observed: 1) taking nothing by mouth for several hours before the neostigmine injection, 2) securing an intravenous line, 3) keeping atropine and a ganglionic blocking agent at hand, and 4) monitoring blood pressure and pulse rate for several hours after the injection. Recently Chapelle *et al.* (1983) reported the use of subcutaneous injections of physostigmine which can be injected at home by the patient himself. Since this modified technique seldom provokes autonomic hyperreflexia, it will be worth pursuing further.

Conclusion

Successful AIH using neostigmine injection in a 33-year-old male paraplegic is reported. This case is only the fourth one reported in the literature. The physician must prepare for potentially serious side effects, when this specific treatment modality is attempted.

Résumé

Un paraplégique complet qui a obtenu une enfant par sa propre insémination artificielle après une injection sous-archnoïdienne de vagostigmine est rapporté.

Notre patient est un homme âgé de 33 ans qui s'est fracturé par compression la vertèbre Th-6 après sa chute accidentale de 3 m il y a 3 ans (en novembre, 1980) et a présenté le syndrome spinal complet au dessous du segment Th-9. Après l'accident il est quelquefois entré en érection, mais il n'a fait aucune éjaculation, de sorte qu'il a visité notre clinique dans l'espoir de gagner un enfant. Au 4 mars, 1983, 0.75 mg de vagostigmine a été injecté dans l'espace sous-archnoïdien, et 4 heures après 1 ml de semence (nombre des spermatozoïdes: 3×10^6 /ml, motilité: 0%) a été collecté. La première insemination artificielle a été faite à l'aide de ce semence, mais sa femme n'est pas devenue prégnante. Quoique sans succès, l'IAM a été faite 8 fois à la même manière la première. Au 9 décembre, 1983, la dixième IAM a été faite à l'aide de 2 ml de semence (nombre des spermatozoïdes: 90×10^6 /ml, motilité: 70%) obtenu par l'injection sous-archnoïdienne de 1 mg de vagostigmine, ce qui a fait sa femme prégnante et ainsi normalement accoucher d'une bébé maturée pesée de 3100 g au 24 août, 1984.

Le présent cas personnel est le 4^{ème} dans le monde, qui concerne l'accouchement à term fait avec succès par l'insemination artificielle après l'injection sous-archnoïdienne de vagostigmine.

Zusammenfassung

Es wird über einen vollständig querschnittsgelähmten Mann berichtet, der durch künstliche Befruchtung nach intrasubarachnoidaler Einspritzung von Vagostigmin Vater eines Mädchens geworden ist.

Unser Patient ist ein 33 Jahre alter Mann, der vor 3 Jahren (Nov. 1980) nach einem Fall von 3 m einen Kompressionsbruch des Wirbelsäulenknochens Th6 erlitt, wodurch es zu einem vollständigen Wirbelsäulensyndrom unterhalb des Segments Th9 kam. Nach der Verletzung hatte er einige Erektionen, aber es kam zu keinen Ejakulationen, und er kam zu unserer klinik in der Hoffnung, der Vater eines Kindes zu werden.

Am 4. März 1983 wurden 0.75 mg Vagostigmin in den subarachnoidalen Raum eingespritzt und 1 ml Samen wurde gesammelt (Samenzählung: 3×10^6 /ml, Motilität: 0%). Mit diesem Samen wurde die erste künstliche Befruchtung versucht, aber die Frau wurde nicht schwanger. Nach der ersten künstlichen Befruchtung wurden 8 weitere Versuche nach der gleichen Methode durchgeführt, die jedoch nicht erfolgreich waren. Am 9. Dez. 1983 wurde die zehnte künstliche Befruchtung mit 2 ml Samen durchgeführt, die durch intrasubarachnoidale Einspritzung von 1 mg Vagostigmin erhalten worden waren (Samenzählung: 90×10^6 /ml, Motilität: 70%). Hiernach wurde die Frau schwanger und gebar am 24. August 1984 ein voll ausgetragenes weibliches Baby mit einem Gewicht von 3100 g durch normale Geburt. Unser Fall ist der vierte erfolgreiche Bericht der ganzen Welt in Bezug auf eine abgeschlossene Schwangerschaft durch künstliche Befruchtung nach intrasubarachnoidaler Einspritzung von Vagostigmin.

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