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discrepancy between our study and the previous reports remain unclear. Use of different antibodies might account for the different results. Larger prospective study of biopsied skin samples from ALS patients and from controls is necessary.

We thank David L McIlwain, Department of Physiology, University of North Carolina at Chapel Hill, for comments and encouragement.


Evidence of disturbed meiosis in a man referred for intracytoplasmic sperm injection

M H E C Pieters, R M Speed, P de Boer, J T M Vreeburg, G Dohle, P A In’t Veld

Intracytoplasmic sperm injection (ICSI) has become the treatment of choice in male infertility due to extreme oligozoospermia. Initially, the technique was limited to the selection and injection of motile spermatozoa with normal morphology; although it has now been shown that spermatozoa with abnormal morphology can also be used successfully.1 We describe a patient referred for ICSI who presented with phenotypically abnormal sperm and we show that in this patient the disturbed spermatogenesis was associated with chromosome abnormalities and abnormal meiosis.

A couple of south Mediterranean descent was referred to the in-vitro fertilisation clinic in Rotterdam for ICSI because of oligoasthenoterato-zoospermia in the 35-year-old man. His semen analyses showed a mean volume of 4.8 mL, mean sperm count of 7×10^6/mL, and a mean progressive motility of 6%. By WHO criteria, only 1% of the spermatozoa were of normal morphology. Most spermatozoa were malformed with a mean number of 3-3 abnormalities per sperm. The most frequent head abnormalities were absence of the acrosome in 65% of the spermatozoa, large and amorphous shape of the head in 32%, and of two to four tails in 61%.

Light microscopy showed normal seminiferous tubules and no evidence of inflammation or germ-cell neoplasia. The Johnson scores of right and left testes were five and six respectively. Microscopy of biopsy samples showed few spermatozoa and spermatids were found next to large spermatozoa with abnormal morphology. Most spermatozoa were malformed with a mean number of 3-3 abnormalities per sperm. The most frequent head abnormalities were absence of the acrosome in 65% of the spermatozoa, large and amorphous shape of the head in 32%, and of two to four tails in 61%.

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Fertility drugs and malignant germ-cell tumour of ovary in pregnancy

Krishnansu Tewari, G Scott Rose, Keith D Balderston, Manuel Porto, Matthew F Kohler

A 37-year-old white woman with a history of secondary infertility underwent attempted ovulation induction with clomiphene citrate, follicle-stimulating hormone, and gonadotropin-releasing hormone from September, 1996 to January, 1997. Ovulation induction was discontinued in February, 1997, when an 8×8 cm complex right ovarian mass was noted ultrasonographically and attributed to ovarian hyperstimulation. Prior ultrasound had demonstrated normal pelvic anatomy. In March, 1997, she conceived spontaneously. At 19 weeks’ gestation, a screening maternal serum alpha fetoprotein (AFP) was increased to greater than nine multiples of the median and she was referred to the University of California, Irvine. At 21 weeks’ gestation, a targeted ultrasound revealed no fetal abnormalities, and an amniotic fluid AFP was within normal limits. A 30 cm diameter complex adnexal mass was present with a cystic fluid content. The mass was adherent to the cervix and right adnexa and contained multiple areas of haemorrhage and necrosis. The patient was referred to the Department of Gynaecology for consideration of intervention.

In the absence of any evidence of malignancy, clinical examination was performed and an ultrasound of the abdomen and pelvis was obtained. The mass was found to be a complex cystic mass with solid components and multiple areas of haemorrhage and necrosis. The mass was adherent to the cervix and right adnexa and contained multiple areas of haemorrhage and necrosis. The patient was referred to the Department of Gynaecology for consideration of intervention.

The patient was referred to the Department of Obstetrics and Gynaecology for further evaluation. A biopsy of the mass was performed and histological examination revealed a malignant germ-cell tumour of the ovary. The patient was referred to the Department of Gynaecology for further evaluation.

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administration and the development of an ovarian temporal relation (2 months) between fertility drug remains controversial. We report the first case of a germ-cell RESEARCH LETTERS to any possible carcinogenic influence of fertility drugs. Our mass adherent to the anterior abdominal wall and pelvic theatre and found to have a 40 cm diameter right ovarian for preterm labour prophylaxis. Final pathology revealed a increasing in size and the patient reported increasing abdominal pain, pressure, and dyspnoea. She was taken to seen (top figure). At 22 weeks' gestation the mass was notably appearing normal. Indomethacin had been successfully used for preterm labour prophylaxis. Final pathology revealed a grade 2 immature teratoma. Primitive cartilage, respiratory epithelium, sebaceous glands, and an early tooth were identified. Primitive neuroepithelial was thought to have been the source of the raised AFP (bottom figure).

Ovarian cancer may derive from coelomic epithelium, stromal (eg, granulosa) cells, and germ cells, the latter almost always arising in children and young adults during the first two decades of life. A positive association between prior treatment with fertility drugs and a risk for epithelial ovarian cancer and stromal tumours has been suggested14 but remains controversial. We report the first case of a germ-cell ovarian cancer arising in the setting of fertility-drug therapy. Since fertility drugs recruit follicles containing oocytes derived from germ cells, the germ cell may also be susceptible to any possible carcinogenic influence of fertility drugs. Our patient's normal antecedent pelvic ultrasound exam, the close temporal relation (2 months) between fertility drug administration and the development of an ovarian malignancy, and the diagnosis of a malignant ovarian cell tumour at the relatively late age of 37 years (perhaps suggesting an exogenous influence), all make a causal link between fertility-drug therapy and the development of a germ-cell tumour in our patient plausible. Because these tumours may grow rapidly, any adnexal mass associated with fertility drug use in pregnancy warrants close ultrasonographic surveillance and possible surgical intervention as clinically indicated.


Ultrasonography showing 30 cm complex adnexal mass at 21 weeks' gestation (top) and histological section of Immature teratoma (bottom)

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**Lamotrigine and topiramate may be a useful combination**

**Linda J Stephen, Graeme J Sills, Martin J Brodie**

Doctors who treat patients with epilepsy are able to choose from a range of antiepileptic drugs (AEDs).1 Nevertheless, around 30% of patients need to take two or more and many of them are still not free from seizures.2 Attempts are being made to identify synergism between newer AEDs.3 We report favourable outcomes in two patients treated with topiramate and lamotrigine. The validity of this observation is supported by their effectiveness together, but not individually, in abolishing pentylenetetrazol-induced generalised seizures in mice.

A 37-year-old woman with poorly controlled idiopathic generalised epilepsy was referred to our Epilepsy Unit in April, 1995, with frequent myoclonic jerks, absences, and tonic-clonic seizures despite treatment with sodium valproate to the limit of tolerability. Lamotrigine was substituted, leading to some reduction in seizures. As she was unable to tolerate a higher dose of lamotrigine, topiramate was added in June, 1996. The patient has remained seizure-free since August, 1996, on lamotrigine 175 mg in the morning, 200 mg at night (plasma concentration 27 µmol/L) and topiramate 50 mg twice daily (9 µmol/L).

An 18-year-old man with learning disabilities had fortnightly clusters of partial and generalised tonic-clonic seizures, despite a left temporal lobectomy and treatment with several AEDs. He was referred to the Epilepsy Unit in 1992 taking phenytoin. Vigabatrin did not improve his control. The addition of lamotrigine produced a small reduction in seizures. The patient's family then moved from the area. When he was re-referred in November, 1996, his AED consisted of phenytoin 300 mg and lamotrigine 500 mg daily. Seizure frequency and behaviour had worsened. Phenytoin was withdrawn and the lamotrigine dose increased to 400 mg twice daily without major benefit. The addition of low-dose topiramate led to marked improvement in control, alertness, and behaviour. He has remained seizure-free since April, 1997, on lamotrigine 400 mg twice daily (plasma concentrations 66 µmol/L) and topiramate 25 mg mane, 50 mg nocte (6.0 µmol/L).

Adult male ICR mice (25–30 g) were given lamotrigine (5