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Thromboembolism after ovarian stimulation: successful management of a woman with superior sagittal sinus thrombosis after IVF and embryo transfer: Case report

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The current literature was reviewed in order to analyse the clinical manifestations, progression and management, and pregnancy outcome of thromboembolism in infertile patients undergoing ovarian stimulation. The first case of superior sagittal sinus thrombosis following IVF that was successfully managed with intracranial thrombectomy is also reported. This retrospective cohort study comprised 65 women who experienced thromboembolism after ovarian stimulation (64 from other published studies and the present case report). Thrombosis attack occurred at a mean (±SD) of 25.5 ± 20.1 days after oocyte retrieval. The onset timing in the intracranial thrombosis group (10.2 ± 4.6 days) was less ($P < 0.05$) than in those experiencing thromboembolism at other sites. Ovarian hyperstimulation syndrome (OHSS), haemoconcentration and high serum estradiol level were noted in 79, 62 and 54% of women respectively. Forty-eight of 55 patients (87%) who received anticoagulation recovered without sequelae. Among patients willing to continue pregnancy, 32% succeeded in term delivery with all healthy babies, and 23% were ongoing pregnancies. In conclusion, ovarian stimulation cycles accompanying high serum estradiol levels, haemoconcentration or OHSS are at potential risk of thromboembolism. Dose-adjusted heparinization is recommended as the first-line treatment of choice, while intravascular thrombolysis or operative thrombectomy is an aggressive but effective treatment. Continuation of pregnancy is considered safe, without any increased risk of fetal congenital anomalies.

Key words: intracranial thrombectomy/IVF/ovarian hyperstimulation syndrome/thromboembolism

Introduction

Ovarian hyperstimulation syndrome (OHSS) occurs in 1–10% of women undergoing ovarian hyperstimulation with exogenous gonadotrophin administration, and is a recognized and potentially life-threatening complication (Brinsden *et al*., 1995). It presents with a wide clinical spectrum ranging from mild abdominal discomfort to potentially lethal complications such as adult respiratory distress, renal failure and thromboembolism (Brinsden *et al*., 1995). Thromboembolic event is considered to be a dangerous and unpredictable manifestation of the syndrome, with an incidence of 0.04% (Arya *et al*., 2001). It is characterized by uncommon location, attack timing and unpredictable laboratory marker due to unclear pathogenesis. Thrombosis involving intracranial vessels is perhaps the most serious form. There may be a wide range of symptoms and signs at presentation, depending upon the extent of the thrombosis and the acuity of development.

Herein, the current literature was reviewed and a current case description included in order to describe the clinical presentations, management, outcomes and possible aetiology of thromboembolism after ovarian stimulation.

Literature search

A MEDLINE literature search was conducted using the following keywords: 'ovarian hyperstimulation', 'in-vitro fertilization (IVF)', 'ovulation induction' and 'thrombosis'. All pertinent peer-reviewed, English language articles were retrieved. A manual search of references was then conducted for additional articles. This included patients who underwent ovarian hyperstimulation following natural coitus, insemination or IVF, and one patient who had OHSS spontaneously without the use of an ovarian stimulating agent (Todros *et al*., 1999).

In order to assess the overall severity of OHSS, the syndrome was re-staged in each individual based on reports

of clinical signs and symptoms, ultrasonographic findings and laboratory data, according to a published classification system (Golan *et al*., 1989). The site of the thromboses, the timing of thromboses relative to oocyte retrieval, and possible predisposing factors as well as maternal and pregnancy outcomes following management was analysed.

Case report

A 29-year-old woman was admitted with suspected moderate OHSS, her chief complaints being progressive abdominal distension and shoulder pain while deep breathing 15 days after embryo transfer. Initially, the woman had presented with a 4-year history of secondary infertility due to a combination of ovulatory dysfunction and tubal damage. Laparoscopic electrothermal drilling for polycystic ovaries was performed at a community hospital 2 years previously, and 1 year later a right tubal pregnancy occurred that required a laparoscopic salpingectomy. Before visiting the present authors' infertility clinic, the woman had undergone eight cycles of intrauterine insemination all of which failed to conceive, and one cycle of IVF-embryo transfer that ended in abortion.

She began a long stimulation protocol as described (Kung *et al*., 2003), consisting of GnRH agonist (Lupron; Abbott, North Chicago, IL, USA) for pituitary suppression, followed by three ampoules of recombinant FSH (Gonal-F, 75 IU/ampoule; Serono, Aubonne, Switzerland) for 11 days of stimulation. HCG (Pregnyl; Organon, Oss, Holland) was administered when there were six dominant follicles $\geqslant$17 mm in association with a serum estradiol level of 3707 pg/ml. Eight oocytes were recovered, and all were normally fertilized. Fluid accumulation with an echolucent space measuring 2 mm in the uterine cavity was found during oocyte retrieval. Transfer was postponed with extended embryo culture until the fluid accumulation had disappeared. Luteal support with oral micronized progesterone (Utrogestan; Piette International Laboratories, Belgium) together with vaginal suppository (total dose 800 mg per day) was used. Three blastocysts were transferred on day 5 without complication. At examination on day 9 after embryo transfer, the woman had symptoms of abdominal fullness, occasional shortness of breath, and a positive urinary pregnancy test.

On admission, ultrasonography revealed bilateral enlarged ovaries with a moderate amount of ascitic fluid. Laboratory findings were: haematocrit 33.9%; haemoglobin 12.1 g/dl; white blood cell count 12×10^3/μl; platelet count 235 000/μl; and both prothrombin time and electrolyte levels within normal limits. At 6 h after admission, the patient experienced a sudden-onset generalized seizure. Post-ictal confusion was noted about 20 min later, in addition to left-sided hemiplegia. The electroencephalogram showed diffuse slowing of cortical activity, while magnetic resonance imaging (MRI) showed multiple ill-defined subcortical white matter lesions with low signal intensity on T1-weighted image, and high signal intensity on T2/diffusion-weighted image over the right frontal and left frontal-parietal areas. Magnetic resonance venography showed non-visualized or occluded anterior superior sagittal sinus. A second grand mal seizure with projectile vomiting occurred. Digital subtraction angiography of the brain vessels showed thrombosis of the anterior superior sagittal sinus. Due to the patient's deteriorating neurological state, emergency intravascular treatment with medical thrombolysis and operative thrombectomy was performed. Initially, the occluded superior sagittal sinus was catheterized, after which urokinase (480 000 IU) was injected locally, and the blood clots macerated using a microballoon. Difficulty was encountered in complete canalization of the occluded sinus with residual blood clots. Right internal carotid artery angiography showed no significant opacification of the sinus that was suspected to have a cortical vein thrombosis. Anticoagulant treatment with intravenous heparin was then initiated and maintained to avoid any re-attack of thrombosis. The patient was placed on a rehabilitation programme during a 14-day hospitalization period after the event. At 55 days after embryo transfer, transvaginal ultrasonography demonstrated triplet gestation with three separate gestational sacs in the uterine cavity.

Neither family history nor coagulation deficiency was noted. Antithrombin III, protein C and antiphospholipid antibody levels were within the normal range. The free protein S level was 68% at the time of thrombosis attack and returned to within normal range 6 weeks later. The patient showed a gradual improvement in both thrombotic event symptoms and OHSS. At 33 days after admission, she was discharged with a sequela of mild weakness in her left upper extremity, and a surviving singleton with two vanishing fetuses. Full anticoagulation with subcutaneous low molecular-weight heparin twice daily was maintained throughout the pregnancy. The sequela of weakness in her extremities gradually decreased. Two episodes of seizure were noted, despite daily administration of phenytoin combined with folic acid. A healthy neonate weighing 2640 g was safely delivered by Caesarean section at 39 weeks gestation.

Literature review

A review of 52 articles yielded 64 patients who had experienced a thromboembolic event. Among 65 cases (including the present patient) there were 10 with lower-extremity thrombosis (Crooke *et al*., 1964; Mozes *et al*., 1965; Nwosu *et al*., 1974; Dalrymple *et al*., 1982; Kaaja *et al*., 1989; Benshushan *et al*., 1995; Choktanasiri and Rojanasakul, 1995; Kligman *et al*., 1995; Ludwig *et al*., 2000; Sobande *et al*., 2000), 10 with upper-extremity thrombosis (Mills *et al*., 1992; Hollemaert *et al*., 1996; Stewart *et al*., 1997b; Loret de Mola *et al*., 2000; Heinig *et al*., 2001; Mancini *et al*., 2001), 19 with neck thrombosis (Rajah *et al*., 1991; Fournet *et al*., 1991; Ong *et al*., 1991; Ayhan *et al*., 1993; Hignett *et al*., 1995; Hulinsky and Smith, 1995; Horstkamp *et al*., 1996; Moutos *et al*., 1997; Ellis *et al*., 1998; Todros *et al*., 1999; Lamon *et al*., 2000; Schanzer *et al*., 2000; Arya *et al*., 2001; Belaen *et al*., 2001; Tavmergen *et al*., 2001), 18 with intracranial thrombosis (Table II), and eight with thrombosis at other sites (Aurousseau *et al*., 1995; Huong *et al*., 1996; Germond *et al*., 1996; Ludwig *et al*., 1999; Turkistani *et al*., 2001; Akdemir *et al*., 2002; Andrejevic *et al*., 2002).

The onset of disease, degree of OHSS, peak serum estradiol level, predisposing factors and outcome of pregnancy in 65

Table I. Characteristics of thromboembolism in 65 patients undergoing ovulation stimulation

Characteristic	Site of thrombosis					
	Lower extremity	Upper extremity	Neck	Intracranial	Others[a]	Total
No. of patients	10	11	19	18	7	65
Onset (day)[b]						
Mean ± SD	24.8 ± 25.4	30.2 ± 17.0	39.8 ± 19.2	10.2 ± 4.6	15.0 ± 12.2	25.5 ± 20.1
Range	5–84[c]	6–49	11–105	3–21	2–35	2–105
Classification of OHSS						
Severe (*n*)	2	5	11	11	1	30 (49.2)
Moderate (*n*)	2	2	5	4	0	13 (21.3)
Mild (*n*)	1	1	1	1	1	5 (8.2)
None (*n*)	4	3	2	2	2	13 (21.3)
Haematocrit >42% per total cases	2/6[d]	4/9[d]	13/16[d]	12/18[d]	2/4[d]	33/53[d] (62)
Peak serum E_2 level >3000 pg/ml per total cases	2/4[d]	4/8[d]	6/11[d]	5/9[d]	2/3[d]	19/35[d] (54)
Predisposing factor[e]	4	2	5	2	3	16/43[d] (37)
Inherited thrombophilia per total cases	2/4[d]	1/7[d]	5/14[d]	1/12[d]	1/6[d]	10/43[d] (23)
Pregnancy outcome						
Term delivery	2	3	9	3	1	18 (31.6)
Ongoing pregnancy[f]	2	4	7	0	0	13 (22.8)
Miscarriage	1	1	1	1	1	5 (8.8)
Elective termination	1	0	0	5	0	6 (10.5)
Failure to achieve pregnancy	2	2	1	7	3	15 (26.3)
Maternal outcome						
Recovery	9	10	17	8	5	49 (79)
Neurological sequela	1	1	1	7	1	11 (18)
Death	0	0	0	2	0	2 (3)

Values in parentheses are percentages.
[a]Includes two patients with myocardial infarction, one retinal arterial infarction, one renal vein thrombosis, one intracardiac thrombosis, and one pulmonary embolism.
[b]Onset indicated days after oocyte retrieval.
[c]One case developed a deep calf vein thrombosis before administration of hCG was excluded.
[d]The denominator was the number of total cases with data available.
[e]Predisposing factors included inherited thrombophilia, infection, personal or family history, and vessel anomaly.
[f]Includes two patients with twins but one died, one patient with twins but one vanished, and one patient with triplets but two vanished.

thromboembolic patients after controlled ovarian hyperstimulation are listed in Table I. The mean time of occurrence of the thrombotic event was 25.5 ± 20.1 days after oocyte retrieval. Thrombosis occurred before the day of hCG administration in only one case (Ludwig *et al*., 2000). Otherwise, one patient with antiphospholipid antibodies suffered from intracardiac thrombosis 5 years after four cycles of ovulation induction. Although it was possibly triggered by ovulation induction, this was not included in the timing statistic (Andrejevic *et al*., 2002). The time to attack was earlier in the group of intracranial location [mean 10.2 (range 3 to 21) days] than in the group of other locations (Tables I and II). Forty-eight of 61 cases (79%) had available information in the original reports for assessment of various degrees of OHSS. Among those with OHSS, the condition was severe in 49.2% of cases, moderate in 21.3% and mild in 8.2%. Haemoconcentration defined as a haematocrit ⩾42% was noted in 33 (62%) of 53 cases with available data. Peak serum estradiol levels >3000 pg/ml were noted in 19 (54%) of 35 cases with available data. There were 16 (37%) patients who were thought to have predisposing factors including inherited thrombophilia, personal or family history, infection and vessel anomaly.

Among 57 patients for whom information was available with regard to pregnancy outcome after ovarian hyperstimulation, 42 (74%) achieved pregnancy. Eighteen of these succeeded in term deliveries (including the present patient) (Crooke *et al*., 1964; Nwosu *et al*., 1974; Rizk *et al*., 1990; Fournet *et al*., 1991; Ong *et al*., 1991; Hulinsky and Smith, 1995; Horstkamp *et al*., 1996; Stewart *et al*., 1997b; Ellis *et al*., 1998; Todros *et al*., 1999; Lamon *et al*., 2000; Loret de Mola *et al*., 2000; Arya *et al*., 2001; Turkistani *et al*., 2001; Elford *et al*., 2002; the present case), 13 are ongoing pregnancies, five ended in miscarriage and six underwent elective termination. Of the 13 ongoing pregnancies, only two had a vanished fetus (Moutos *et al*., 1997; the present case).

With regard to the maternal outcome of 62 patients, 49 (79%) experienced complete recovery without sequelae, while the remaining 13 had sequelae which included two mortalities (Mozes *et al*., 1965; Cluroe and Synek, 1995), two had amputations (Mozes *et al*., 1965; Mancini *et al*., 2001), two had permanent hemiparesis, and seven had impairment of daily activity. The two patients who died both had intracranial thrombosis. Furthermore, the chance of complete neurological recovery after treatment of thromboembolic events was 47% (8/17 patients) in the intracranial group, this being less than the value of 91% (41/45 patients) in other groups.

Discussion

There is an increased risk of thromboembolic disease during pregnancy and the puerperium (Cunningham *et al*., 2001), the mechanism being thought due to a hypercoagulable state associated with haemostasis and thrombophilias.

Table II. Location, onset and OHSS classification following ovulation induction, and maternal and pregnancy outcomes: summary of 18 patients with intracranial arterial or venous thrombosis

Reference	Site of thrombosis	Onset (day)	OHSS	Maternal outcome	Pregnancy outcome
Arterial origin					
Mozes *et al*. (1965)	Left internal carotid artery extending intracranially	5 days post hCG	Severe	Death	Non-pregnant
Rizk *et al*. (1990)	Right middle cerebral artery	12[a]	Severe	Recovery	Term delivery
Kermode *et al*. (1993)	Left internal carotid artery, left frontal	8[a]	Severe	Ambulant with frame	N/A
Inbar *et al*. (1994)	Right middle cerebral artery	11[a]	None	Recovery	Non-pregnant
Aurousseau *et al*. (1995)	Cerebral ischaemia, right terminal internal carotid	14[a]	None	N/A	Termination
Cluroe *et al*. (1995)	Right middle cerebral artery	6 days post ET	Severe	Death	Non-pregnant
Hwang *et al*. (1998)	Right middle cerebral artery	11 days post ET	Severe	Neurological deficit	Termination
EL Sadek *et al*. (1998)	Left basal ganglia, corona and left choroidal artery	6[a]	Severe	Recovery	Non-pregnant
Yoshii *et al*. (1999)	Right internal carotid artery, multiple cerebral infarction	7[a]	Severe	Recovery	Termination
Davies and Patel (1999)	Right middle cerebral artery	N/A	Moderate	Permanent hemiparesis	N/A
Worrell *et al*. (2001)	Left distal internal carotid artery, left middle cerebral artery; intracardiac thrombus	9[a]	Severe	Residual hemiparesis	Chemical pregnancy
Koo *et al*. (2002)	Right middle cerebral artery	14 days post ET	Mild	Walk with device	Termination
Elford *et al*. (2002)	Right middle cerebral artery	7 days post ET	Severe	Mild left inferior quadrantanopia	Term delivery
Venous origin					
Waterstone *et al*. (1992)	Right transverse sinus	10[a]	Severe	Impaired in writing	Chemical pregnancy
Aboulghar *et al*. (1998)	Cortical area	11[a]	Moderate	Recovery	Non-pregnant
Aboulghar *et al*. (1998)	Left parieto-occipital area	9[a]	Moderate	Recovery	N/A
Tang *et al*. (2000)	Cortical vein; femoral vein extend to lower inferior vena cava	15[a]	Severe	Recovery	Termination
Ou *et al*. (2002, present case)	Superior sagittal sinus, right frontal, left frontoparietal area	20[a]	Moderate	Recovery	Ongoing

[a]Onset indicated days from oocyte retrieval.
ET = embryo transfer; N/A = data not available.

Thromboembolism with an incidence of 1 per 1000 pregnancies has continued to be a prominent cause of maternal deaths (Rochat *et al*., 1988). Intracranial thrombosis is the major type of ischaemic stroke during pregnancy or the puerperium (Cunningham *et al*., 2001), and may cause maternal death.

Patients undergoing ovarian stimulation with exogenous high-dose gonadotrophin administration for ovulation induction are at risk of thromboembolic disease (Kodaman *et al*., 1996). A hypercoagulable state with secondary supraphysiological hyperestrogenaemia and haemoconcentration after ovarian hyperstimulation have been proposed to induce attack of thromboembolism. In addition, some inherited deficiencies referred to as thrombophilias, such as antithrombin III, protein C and protein S deficiency, factor V Leiden mutation, and antiphospholipid antibody syndrome that can lead to hypercoagulability are thought to be predisposing factors. It has been reported (Kim *et al*., 1981) that hyperestrogenaemia might cause an increase in platelet count, fibrinogen and von Willebrand factor, and a decrease in antithrombin III level. A combination of iatrogenic hyperestrogenism and established pregnancy may have a synergistic effect on the risk of thromboembolism. In the present review, 54% of patients had a peak serum estradiol level >3000 pg/ml, and 74% achieved pregnancy after ovulation induction, which was similar (72%) to that reported elsewhere (Stewart *et al*., 1997a). At the present authors' institution, the average serum estradiol level on the day of hCG administration in patients undergoing IVF was 1384 ± 923 pg/ml, and 67% of patients had a level <2000 pg/ml (Lan *et al*., 2003). Hence, those patients with a peak serum estradiol level ⩾3000 pg/ml should be managed with care.

Haemoconcentration has been thought to be a contributing factor to thromboembolism in patients with OHSS. In the present review, 33 (62%) of 53 cases had haemoconcentration with a haematocrit >42%. Interestingly, this was more prevalent in the neck and intracranial thrombosis groups (81 and 67% respectively). In addition, 48 (79%) of 61 patients had OHSS, and in most of these cases the condition was either moderate or severe. Either haemoconcentration itself or in association with OHSS is able to increase both the viscosity of blood and the concentration of coagulation factors. It has been reported that ovarian stimulation in IVF is associated with an increase in both fibrinogen level and clot lysis time, as well as a decrease in antithrombin III level (Aune *et al*., 1991). Although others (Delvigne *et al*., 2002) reported no differences in coagulation test between OHSS and control groups, they investigated patients for only a short period of time after completion of IVF treatment rather than during an attack of OHSS. Another group (Kodaman *et al*., 1996) demonstrated significant differences in serum fibrinogen, thrombin–antithrombin III complex, plasmin-α2 antiplasmin complex, D-dimers and prekallikrein between the OHSS and control

groups. These authors also found that activation of the coagulation cascade system occurred within 2 days after hCG administration, while activation of the fibrinolytic system occurred a few days later in OHSS patients. Early activation of the fibrinolytic system may indicate the occurrence of subclinical thrombus formation. The onset was seen to be earlier in the intracranial group because the diameter of intracranial vessels is much smaller than that of other vessels in other groups. Furthermore, activation of these systems will continue for approximately 3 weeks after the onset of OHSS if pregnancy is established (Kodaman *et al*., 1996). Further investigations are needed to elucidate the different timing of thrombosis occurrence during pregnancy between patients who conceived naturally and those after controlled ovarian stimulation.

The prevention of OHSS is important for patients who are at risk of OHSS. When high estradiol levels (>3000 pg/ml) were noted before hCG administration, coasting—which involves withholding gonadotrophin and delaying hCG—might be beneficial in minimizing the risk of thromboembolism development. With regard to the high incidence (62%) of thrombotic events in patients with haemoconcentration, maintenance of adequate hydration to restore intravascular viscosity is mandatory, although it would lead to an increase of fluid accumulation in the third space, and intravenous fluid administration should be titrated downward as the haematocrit returns to normal.

Protein C, protein S and antithrombin III deficiencies, antiphospholipid antibody syndrome and factor V Leiden mutation have each been linked to this complication, and may result from activated protein C resistance. It is believed that factor V Leiden mutation occurs with a frequency of 2–4% in the general population, and of 40–60% among those with a personal or family history of thrombosis (Todros *et al*., 1999). Recently, it has been shown that mutations in the prothrombin gene and the factor V gene are associated with cerebral vein thrombosis (Martinelli *et al*., 1998). The simultaneous presence of the above-mentioned mutations and OHSS might enhance the risk of cerebrovascular thrombosis (Rad and Helmerhorst, 1999). In the present study, among 43 patients with available information, 10 (23%) were found to have inherited thrombophilia, including seven (17%) who showed an association with factor V Leiden mutation. Others (Delvigne *et al*., 2002) reported similar prevalence rates of thrombophilia in IVF patients who did or did not develop OHSS. Thus, further studies are required to determine whether all patients with OHSS should be screened for inherited thrombophilia.

Cerebral venous thrombosis has a mortality rate of between 5 and 30% (Benamer and Bone, 2000), and is more hazardous if thrombosis occurs in the cerebral sinus. The affected patient usually presents with sudden-onset headache, sometimes associated with pallioedema and vomiting, seizure and disorder of consciousness. Fortunately, the recent progression in radiological technologies such as cerebral angiography and MRI now permit a rapid and precise diagnosis, even for treatment. Furthermore, it has been reported that cerebral venous thrombosis related to pregnancy and the puerperium has a better outcome than those unrelated to pregnancy (Cantu' and Barinagarrementeria, 1993). In the present review, 47% of patients with intracranial thrombosis and 79% with thrombosis at any site after ovulation stimulation had complete recovery, without sequelae. It appears that patients with an intracranial thrombosis have a poorer prognosis than those with other thromboses. It has been speculated that cerebral infarction might be overlooked in patients who are asymptomatic or who show only mild neurological deficits (Yoshii *et al*., 1999). Others (Cluroe and Synek, 1995) reported an autopsy case of widespread multiple cerebral infarctions with marked congested vessels of varying size. These authors supposed that the mechanism was due to multiple areas of local thrombosis with haemoconcentration or thromboembolism. The present literature review also revealed that haemoconcentration was more likely to occur in both intracranial and neck thromboses; therefore, intracranial thrombosis after ovulation induction should be managed aggressively and may even require operative intervention. Supportive management with dose-adjusted heparin has been the first-line choice for cerebral venous thrombosis (Benamer and Bone, 2000). Interventional treatments including intravascular local thrombolysis and thrombectomy should be reserved for patients with extensive or clinically deteriorating neurological deficits during conservative management. Intravascular thrombectomy followed by the use of a thrombolytic agent has been recommended in the treatment of cerebral sinus thrombosis (Dowd *et al*., 1999; Chow *et al*., 2000). The bulk thromboses in the dural sinuses were large compared with those which occurred within the cerebral arteries, and would be eliminated with restoration of venous outflow more rapidly by this procedure. In the present patient, repeat attacks of generalized seizure and failure of effective lysis of the intracranial thrombotic clots by urokinase administration locally led to the performance of intravascular thrombectomy in order to re-canalize the occluded vessel and re-establish blood perfusion. The risk of any escape of macerated clots into the systemic circulation during thrombectomy is low because the amount of thrombus released during this procedure was quantitatively too small to induce symptomatic pulmonary embolism (Novak *et al*., 2000).

In the past, the use of heparin to treat cerebral venous thrombosis was thought to be safe, though controversy over the efficacy of this approach persists (Benamer and Bone, 2000). The common complication with heparinization is haemorrhage, and the long-term major complications are heparin-induced thrombopenia and osteoporosis. In the present review, 55 patients received anticoagulation therapy (mostly heparinization) for which the rate of recovery was 87%. Only one patient was found to have a haematoma near the gestational sac, and after reduction of the heparin dose the pregnancy was uneventful, with a healthy baby born in the 36th gestational week. In contrast, four cases were reported without heparinization or with early discontinuation of heparinization (Yoshii *et al*., 1999). Of these four patients, two had neurological sequelae (Hwang *et al*., 1998; Koo *et al*., 2002), and one patient had complications of pulmonary embolism (Nwosu *et al*., 1974). Hence, it is recommended that dose-adjusted heparinization be used as the first-line choice for this disease and maintained throughout pregnancy.

The study of pregnancy outcome after thromboembolism recognized as a complication of OHSS was limited. Of 42 patients with pregnancy, 18 succeeded in term delivery, 13 with ongoing pregnancy at the time of writing of the original reports, five ended in miscarriage, and six underwent elective termination. The miscarriage rate after management of thrombosis was 8.8%.

With regard to the obstetric prognosis, eight cases had one or more of the following complications: preterm labour, premature rupture of membrane, intrauterine growth restriction and fetal demise. With regard to the effect of radiation exposure on embryonic or fetal growth during surgical intervention, the radiation dose for computed tomography or angiography is much less than 5 rads, and this poses little or no risk to the fetus (Brent, 1999). The present review showed that among 27 newborn, none of the infants was found to have either congenital anomaly or neonatal morbidity and mortality.

In conclusion, the first case of superior sagittal sinus thrombosis following IVF-embryo transfer and subsequent pregnancy has been reported. This patient was successfully managed with intracranial thrombectomy following prophylactic heparinization. Care should be taken in patients with predisposing factors for a thromboembolic event. Prophylactic heparinization may be effective for these patients, especially for those with associated OHSS, but when thromboembolism is diagnosed supportive treatment with optimal-dose heparin or low molecular-weight heparin is recommended, and should be maintained throughout pregnancy. For thrombus in the intracranial vessels, aggressive use of intravascular thrombolysis or thrombectomy should be reserved as an effective remedy. The continuation of an established pregnancy is considered safe, without carrying the increasing risk of fetal congenital anomalies.

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