CASE REPORT

Elevated liver function tests in a case of moderate ovarian hyperstimulation syndrome

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Ovarian hyperstimulation syndrome is a recognized complication of ovulation induction. Abnormalities in liver function have been considered to be a rare manifestation of the severe form of ovarian hyperstimulation syndrome (OHSS). A 28 year old woman with primary infertility underwent ovulation induction and intrauterine insemination. She was diagnosed with moderate OHSS and was followed as an outpatient. Early in her course of treatment she complained of upper right quadrant pain. Her work-up included an upper right quadrant ultrasound which showed only moderate ascites. Liver function tests at that time were elevated in a hepatocellular damage pattern. Liver function test elevations, as well as the ovarian hyperstimulation, resolved spontaneously in 10 days. Transient abnormalities in liver function do not appear to be limited to the most severe forms of OHSS.

Key words: ascites/hepatotoxicity/hyperstimulation/infertility

Introduction

While the mild form of ovarian hyperstimulation syndrome (OHSS) is common, the severe form occurs in <1% of cases and can be life threatening. The occurrence of abnormalities of liver function has been documented in six reports in the recent literature, all in association with the severe forms of OHSS. We present a case of a woman with moderate OHSS, treated as an outpatient, who developed ascites and abnormal liver function tests (LFT).

Case report

The patient is a 28 year old white female, gravida 0, para 0, with a 2.5 year history of infertility. Following an extensive work-up and an ovulation induction trial with clomiphene citrate, the patient underwent ovulation induction with 150 IU human menopausal gonadotrophin (HMG; Perganol; Serono Laboratories, Randolph, MA, USA) twice daily for 5 days. On day 6, her serum oestradiol concentration was 1674 pg/ml and an ultrasound examination showed a total of 17 follicles (three at 16 mm, five at 14 mm and nine at ≤12 mm). She was counselled about the risk of hyperstimulation but chose to proceed with the cycle. She was given 10000 IU human chorionic gonadotrophin on that day and an intrauterine insemination (IUI) was performed on the following 2 days.

The patient was monitored as an outpatient for moderate OHSS. Her weight was stable throughout her course of treatment. Her fluid output averaged 1000 ml/day. A pelvic ultrasound examination showed the largest ovarian size to be 10 cm in diameter. She had normal serum electrolytes, blood urea nitrogen (BUN) and creatinine, but she did develop a 26% rise in haematocrit, to 46%.

On post-IUI day 20, liver function studies were performed following complaints of upper right quadrant pain. Normal results were obtained for prothrombin time/partial thromboplastin time (PT/PTT), alkaline phosphatase, total bilirubin and hepatitis A and B, while AST, ALT, lactic dehydrogenase (LDH) and GGTP concentrations were elevated. Peak elevations occurred 2 days later, with an AST concentration of 182 IU/l (normal range 16-40), an ALT concentration of 183 IU/l (normal range 8-54), an LDH concentration of 307 IU/l (normal range 60-220) and a GGTP concentration of 50 IU/l (normal range 8-35). Other LFT remained in the normal range. An upper right quadrant ultrasound examination showed a normal liver and gall bladder. By day 26 post-IUI the patient reported the resolution of her symptoms, but normalization of the LFT did not occur until day 30. On day 36 post-IUI she was found to have a twin gestation. She is currently in her third trimester without further complications.

Discussion

Our case shows that liver dysfunction is not unique to severe OHSS but can also be present in moderate cases. Schenker and Weinstein (1978) defined the grades of severity of OHSS. According to their classification, moderate OHSS includes pronounced abdominal discomfort, nausea, vomiting and diarrhoea. In addition there is weight gain and an ovarian size <12×12 cm. Severe OHSS includes ascites, pleural effusion, an electrolyte imbalance, hypovolaemia and oliguria, as well as ovaries >12×12 cm in size. Our patient fits Schenker and Weinstein’s (1978) moderate picture, except for the presence of ascites.

Another classification system has been proposed by Navot et al. (1992). By their system, severe hyperstimulation is defined by variably enlarged ovaries, massive ascites with or without hydrothorax, haematocrit >45% or an increment of
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30% over baseline values, a white blood corpuscle number >15,000, oliguria, elevated creatinine concentrations, liver dysfunction and anasarca. According to this classification, our patient was moderate except for elevated LFT.

A review of the literature (Sueldo et al., 1988; Younis et al., 1988; Balasch et al., 1990; Ryley et al., 1990; Marsepoil et al., 1992) of reported cases of abnormal LFT associated with OHSS showed no correlation between increased LFT and the maximum oestradiol concentration (ranging from 1170 to 5600 pg/ml), or the amount of medication required for ovulation induction (from 18 to 30 ampoules). All but one patient became pregnant, and in those reports which listed the number of follicles, all had ≥17 follicles, with the number seeming to correlate directly with the severity of OHSS. Ascites was a common factor among patients. All patients, except for our case, were hospitalized, some with prolonged hospital stays requiring multiple paracenteses and thoracenteses. The duration of the elevated LFT ranged from 10 to 64 days.

The cause of elevated LFT in OHSS remains unclear. Hepatocellular damage from increased serum oestrogen concentrations has been proposed as a cause. Liver biopsies performed by Ryley et al. (1990) and Sueldo et al. (1988) showed ultrastructural changes consistent with an increased hepatic enzyme activity. These same changes have been seen in oral contraceptive users, both with and without LFT abnormalities. The clinical significance of the electron microscopic changes is unknown, because these changes are non-specific and can be found in a wide variety of conditions.

The maximum oestradiol concentrations in the series reviewed had a wide range, from 1170 to 5600 pg/ml. The maximum oestradiol concentration had no correlation with the severity of elevated LFT. There were three patients with maximum oestradiol concentrations <1800 pg/ml, a value which is common in ovulation induction (Forman et al., 1990). If these concentrations of oestradiol were enough to cause liver dysfunction, it should be seen as a common complication of ovulation induction. Another aetiology may explain why the elevated LFT are seen less often in ovulation induction with HMG.

A documented increase in the renin–angiotensin–aldosterone system in patients with severe OHSS (Navot et al., 1987) leads to increased vascular permeability. In the ovarian vasculature, increased vascular permeability accounts for the abdominal ascites, while in the hepatic vasculature, increased permeability has been hypothesized to cause hepatic oedema and hepatic damage. Ascites is the only common factor in all reported cases of elevated LFT in OHSS, including our own. This supports the role of increased vascular permeability in liver dysfunction.

Further study is necessary to understand the aetiology and significance of elevated LFT in OHSS. Our case of moderate OHSS with elevated LFT demonstrates the importance of the evaluation of LFT in even mild and moderate cases of OHSS. Our case also suggests that the incidence of hepatic dysfunction may be more common than reflected in the literature.

References

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