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CASE STUDY

Pleural effusion as a presenting symptom of ovarian hyperstimulation syndrome

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Pleural effusion as a presenting symptom of ovarian hyperstrimulation syndrome. A. Man, Y. Schwarz, J. Greif. ©ERS Journals Ltd 1997.

ABSTRACT: Pharmacological ovarian stimulation is an accepted technique for amplifying the normal process of follicular development and maturation. It has been in use for the past decade, especially in cases of infertility. Pleural effusion associated with ovarian hyperstimulation syndrome (OHSS), a complication of this therapy, may be more prevalent than is commonly accepted.

Four young women presented to our department with dyspnoea caused by pleural effusion as a result of ovarian hyperstimulation syndrome (OHSS).

The diagnosis of OHSS was based on a history of pharmacoligcal ovarian stimulation, clinical and laboratory evidence of ovarian enlargement and exclusion of other potential causes of pleural effusion in young women, such as infections, malignancy, pulmonary embolism and collagen vascular diseases. The fluid characteristics in all cases were exudative, with low to normal LDH. All of these patients required fluid evacuation for symptomatic relief. Resolution was achieved with supportive measures and rest.

Ovarian hyperstimulation syndrome may be common enough to warrant routine consideration in the differential diagnosis of pleural effusion in young women. *Eur Respir J 1997; 10: 2425–2426.*

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Pharmacological ovarian stimulation, a well-established therapeutic procedure in the field of infertility, has been widely used in the last decade [1]. This treatment modality has become the gold standard since the introduction of *in vitro* fertilisation (IVF). One of the more common complications of this treatment is the development of ovarian hyperstimulation syndrome (OHSS) which presents clinically in a mild form associated with ovarian enlargement, abdominal distention (grade 1), and with nausea or vomiting or both (grade 2). The moderate form includes ultrasonic evidence of ascites (grade 3), in addition to the other previously mentioned symptoms. A more severe form is associated with clinically apparent ascites with or without pleural effusion and dyspnoea (grade 4) and sometimes presents as a life-threatening situation (grade 5) characterized by additional changes in blood volume, haemoconcentration, coagulation abnormalities and reduced renal perfusion and function [2]. Here, we report the cases of four young women with a clinical presentation of OHSS that consisted of dyspnea and pleural effusion. The pathogenesis and clinical aspects of these cases are discussed.

Case Reports

Four women aged 24–29 yrs (mean 27 yrs) with a history of intensive hormonal treatment including human menopausal gonadotrophin (Pergonal®; Teva Pharmaceuticals Int., Herzylia, Israel) and human chronic gonadotropin (Chorigon®; Teva Pharmaceuticals Int.) for ovulation induction presented to our department with dyspnoea and cough due to pleural effusion. Their relevant characteristics are listed in table 1. All four patients had enlarged ovaries with a minimal amount of fluid in the Douglas sac; none had ascites. After evacuation of fluid, up to 7 days of rest and, in patients 3 and 4, cessation of the hormonal treatment, all the patients recovered fully. No evidence of pleural effusion was recorded in follow-up visits.

Discussion

We present four women with a mean age of 27 yrs who developed pleural effusion after hormonal treatment: one was being prepared for intrauterine insemination with concentrated sperm, one was suffering from infertility due to polycystic ovaries and two underwent treatment in association with IVF. In three of the four cases the fluid was located in the right side, it was exudative in all cases, the mean total protein was 47 $g \cdot L^{-1}$, none had leukocytosis and all had normal lactate dehydrogenase (LDH) levels.

The differential diagnosis of exudation pleural effusion in young women includes a wide spectrum of diseases, mainly pleuropneumonia, collagen vascular disease (systemic lupus erythematosus, rheumatoid arthritis), pulmonary embolism, malignancy and tuberculosis. Together these diseases account for over 80% of all exudates while other unusual causes account for the rest [3]. OHSS is a complication of pharmacological treatment for ovulation in cases of primary and secondary infertility. It usually includes a combination of human menopausal gonadotrophin (Pergonal®) with human chronic

Table 1. – Patient characteristics

	Patient 1	Patient 2	Patient 3	Patient 4
Medical history	Infertility due to polycystic ovaries	Infertility Intrauterine insemination	Pregnancy 4 weeks after IVF	Nine days after IVF
Hormonal therapy	Pergonal and Chorigon (4 weeks, last treatment 1 week prior to admission)	Pergonal and Chorigon (6 weeks, last treatment 10 days prior to admission)	Pergonal and Chorigon (12 weeks) Treatment with Chorigon continued up to admission	Pergonal and Chorigon (6 weeks) Treatment with Chorigon continued up to admission
Pleural effusion	Right side, moderate	Left side, extensive	Right side, moderate	Right side, moderate
Colour	Straw	Yellow	Yellow	Straw
Culture	Negative	Negative	Negative	Negative
WBC count cells·mL^{-1}	300	1100	300	400
Glucose mg·%$^{-1}$	87	84	86	82
LDH IU·L^{-1}	128	75	90	70
Total protein g·L^{-1}	48	50	45	45
Amount of fluid evacuated mL	2000	2000	1500	1200

IVF: *in vitro* fertilization; WBC: white blood cell; LDH: lactate dehydrogenase.

gonadotrophin (Chorigon®) [4]. The incidence of OHSS is rising, and this increase is associated with the treatment of women with polycystic ovaries or with the induction of pregnancy.

The syndrome has a clinical spectrum ranging from a mild form, which accounts for most cases, to moderate and severe forms that occur rarely, but deserve special attention since they are life threatening. Pleural effusion accompanies the severe forms (grades 4 and 5).

The pathogenesis of fluid exudation in OHSS is still obscure. The coincidence with high plasma oestrogen levels is well established, but the cause-and-effect relationships have not been proved and are controversial [5]. A predominant role of increased vascular permeability and sequestration of fluid into a third space due to vasoactive substances has been suggested. High levels of prorenin and angiotensin II were found locally in follicular fluid, while high plasma renin levels were found in patients with OHSS [6, 7]. The roles of prostaglandins [8], vascular endothelial growth factor [9] and interleukin (IL)-6 have been investigated as well. The origin of pleural effusion is believed to be secondary to fluid shift from abdominal ascites. Another explanation which has been suggested is capillary leak into the pleural space itself. The presentation of dyspnea due to pleural effusion without abdominal symptoms and ascites such as in the four cases described here is unusual. These findings, together with fluid characteristics of a serous exudate with high protein level, normal LDH and normal white blood cell (WBC) count support the presence of capillary leak and exudation appearing locally in the pleural space as the main pathogenetic mechanism of fluid formation in our cases.

We attribute the preferential right side location of the effusion to decreased lymphatic drainage as compared to the left side, as has been seen in congestive heart failure.

Ovarian hyperstimulation syndrome as a complication of hormonal treatment is usually mild in degree. The treatment is mainly supportive (bed rest and avoidance of further hormonal treatment), and the symptoms usually resolve spontaneously. We speculate that the presence of pleural effusion associated with ovarian hyperstimulation is more common than reported in the literature, since the effusion usually resolves spontaneously and chest radiographs are not done in most cases. Ultrasound and endocrine monitoring make prevention measures possible. This presentation aims to focus attention on the increasing prevalence of ovarian hyperstimulation syndrome which needs to be considered in the differential diagnosis of pleural effusion in young reproductive women.

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