

# 自然妊娠合并自发性卵巢过度刺激综合征1例 并文献复习

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## 摘要

目的: 探讨自发性卵巢过度刺激综合征(sOHSS)的病因、临床表现及诊治要点。方法: 对1例自然妊娠合并sOHSS患者的临床资料进行回顾分析并文献复习。结果: 患者为26岁妊娠期妇女, 停经12周, 腹胀加重1月, 查体右下腹扪及大小约14 cm囊性包块, 左下腹扪及大小约10 cm囊性包块, 活动欠佳, 无压痛。B超示宫腔内见胎儿回声, 心管搏动规律, 右侧卵巢大小141 × 100 mm, 左侧卵巢104 × 64 mm, 内均见多个液性暗区。胸部彩超提示右侧胸腔积液。血清甲胎蛋白(AFP)与糖类抗原125 (CA125)升高。临床诊断: 自发性卵巢过度刺激综合征。行腹腔镜下双侧卵巢打孔术 + 双侧卵巢楔形切除术, 术后感腹胀等症状较前减轻, 常规产检复查B超双侧卵巢体积较前减小, 并成功足月顺娩1健康女婴。结论: sOHSS发病率较低, 早期诊断和治疗可以有效避免严重的母胎并发症。

## 关键词

自发性卵巢过度刺激综合征, 自然妊娠, 诊断, 治疗

# A Case of Natural Pregnancy with Spontaneous Ovarian Hyperstimulation Syndrome and Literature Review

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## Abstract

**Objective:** To discuss the etiology, clinical manifestations, diagnosis and treatment of spontaneous ovarian hyperstimulation syndrome (sOHSS). **Methods:** The clinical data of a patient with natural pregnancy complicated with sOHSS were retrospectively analyzed and reviewed. **Results:** The patient was a 26-year-old pregnant woman with menopause for 12 weeks, and abdominal distension for 1 month. Her right lower abdominal palpation and a cystic mass of about 14 cm in size, and left lower abdominal palpation and a cystic mass of about 10 cm in size were examined. She had poor activity and no tenderness. Ultrasound showed that the fetal echo was seen in the uterine cavity, the heart tube beat regularly, the size of the right ovary was 141 \* 100 mm, the left ovary was 104 \* 64 mm, and multiple dark liquid areas were seen inside. Color Doppler ultrasound on the chest indicates a pleural effusion on the right side. Serum alpha-fetoprotein (AFP) and carbohydrate antigen 125 (CA125) are elevated. **Clinical Diagnosis:** Spontaneous ovarian hyperstimulation syndrome. Laparoscopic bilateral ovarian perforation + bilateral wedge resection of the ovary were performed, the postoperative symptoms of abdominal distension and other symptoms were alleviated compared with before, and the volume of bilateral ovaries on the routine obstetric review was reduced compared with that before. She gave birth to 1 healthy baby girl smoothly at full term. **Conclusion:** The incidence of sOHSS is low, and early diagnosis and treatment can effectively avoid serious maternal-fetal complications.

## Keywords

Spontaneous Ovarian Hyperstimulation Syndrome, Natural Pregnancy, Diagnosis, Treatment

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## 1. 引言

卵巢过度刺激综合征(ovarian hyperstimulation syndrome, OHSS)是辅助生殖技术中常见的一种严重并发症,多与医源性促排卵有关。过度刺激的卵巢释放的血管活性物质引起毛细血管通透性增加,导致血管液体渗漏和第三间隙液体积聚,从而出现胸腹腔积液、低蛋白血症、少尿和电解质失衡等临床表现[1]。而缺乏外源性促性腺激素刺激发生的OHSS,即自发过度卵巢刺激综合征(spontaneous ovarian hyperstimulation syndrome, sOHSS)发病率较低,约为0.2%~1.2% [2],文献报道多发生于妊娠8~14周[3]。2019年5月27日我院收治1例自然妊娠合并sOHSS患者,本文通过分析该病人的诊治经过(已获得病人的知情同意),复习国内外最新相关文献,归纳其发病机制与临床特点、诊断和治疗,为自然妊娠合并sOHSS的相关临床诊疗提供参考。

## 2. 病例资料

病人为26岁妊娠期妇女,身高154 cm,体重55 kg,首次妊娠,平素月经规律,因“停经12周,腹胀加重1月”于2019-05-27收住我院。近1周偶感下腹部疼痛及呼吸困难。既往“乙肝病史”10余年,查体右下腹扪及一大小约14 cm囊性包块,左下腹扪及大小约10 cm囊性包块,边缘清晰,活动欠佳,无压痛,妇科内诊未查。实验室检查AFP 13.8 ng/ml (正常 < 8.1 ng/ml), CA125: 393.2 U/ml (正常 < 30.2

U/ml), D-二聚体 4.50 mg/l (正常 < 0.55 mg/l), 人绒毛膜促性腺激素(human chorionic gonadotropin, hCG) 173,384 mIU/ml, 红细胞压积 32.1% (正常 > 36%)。癌胚抗原(CEA)与附睾蛋白 4 (HE4)水平正常。血肌酐、尿素氮、电解质、雌二醇、卵泡刺激素(FSH)及甲状腺功能测试均正常。B 超示宫腔内见胎儿回声, 心管搏动规律, 大小符合孕周。右侧卵巢大小 141 × 100 mm (如图 1(a)所示), 左侧卵巢大小 104 × 64 mm (如图 1(b)所示), 内均见多个液性暗区, 较大者大小约 60 × 32 mm, 内透声好。胸部 B 超示右侧胸腔探及片状无回声, 透声可, 最大深度约 2.6 cm。提示右侧胸腔积水。患者入院后腹胀、呼吸困难等压迫症状加重, 遂行腹腔镜下双侧卵巢打孔术 + 双侧卵巢楔形切除术, 术中见子宫增大如孕 3 月余, 双侧卵巢均增大, 左卵巢直径约 12 cm, 右卵巢直径约 14 cm, 均呈多囊样改变, 囊肿直径 1~6 cm 不等, 部分囊内含黄体组织。将双侧卵巢囊肿穿刺放液, 囊内液清亮, 缩小卵巢体积, 减少压迫症状, 组织剪楔形切除少许卵巢组织送活检, 排除卵巢恶性肿瘤。经放液缩小体积后, 双侧卵巢直径约 8 cm。术中快速冰冻病理提示(双侧卵巢)黄体囊肿, 术后诊断: 重度自发性卵巢过度刺激综合征。术后予监测生命体征、体重、腹围、液体出入量和肝肾功等。术后 5 天复查腹部 B 超示: 宫腔内见胎儿回声, 心管搏动规律。右侧卵巢大小 105 × 94 mm, 左侧卵巢大小 73 × 48 mm, 内均见多个液性暗区, 较大者大小约 47 × 34 mm, 内透声好。患者腹胀、呼吸困难等症状较前减轻并顺利出院。常规产检, 复查 B 超双侧卵巢体积较前减小。并于孕 38 周成功足月顺娩 1 健康女婴, 重 3100 g。产后 6 周超声检查示双侧卵巢恢复正常, 胸水也完全消失。



Figure 1. (a) Right ovary 14 × 10 cm; (b) Left ovary 10 × 6 cm  
图 1. (a) 右侧卵巢 14 × 10 cm; (b) 左侧卵巢 10 × 6 cm

### 3. 讨论

#### 3.1. sOHSS 病因及发病机制

sOHSS 的病因及发病机制尚不完全清楚, 主要有两种理论解释, 即糖蛋白激素过度分泌(通常并发多胎妊娠[4]、妊娠滋养细胞肿瘤[5]、垂体腺瘤[6]、甲状腺功能减退和分泌 hCG 的肿瘤)和/或卵泡刺激素受体(FSHR)突变[7] [8]。此外, 有报道称绒毛膜羊膜炎的存在也可能会增 hCG 水平[9]。Arora 等人报告了一例在葡萄胎妊娠清除术后 3 天出现了严重的 sOHSS [10]。Davoudian 首次报道了一名患有胎盘肿大的 sOHSS 孕妇, 发现与之相关的胎盘间质发育不良(PMD)衍生的血管内皮生长因子刺激卵巢[11]。肿瘤坏死因子  $\alpha$  和内皮素-1 的产生增加也被认为是增加血管通透性导致液体在第三间隙积聚的关键因素[12]。Carlo 等人发现 sOHSS 存在遗传易感性[13]。Burgos 报道了一例胸腔神经内分泌肿瘤异位分泌 FSH 引起的 sOHSS [14], 在另一项关于 FSHR 突变的研究发现, Ser680Asn 基因位点突变的存在可以预测 sOHSS

的临床严重程度[15]。

### 3.2. sOHSS 的临床表现及分型

sOHSS 既可以发生在孕期，也可以发生在非孕期。其危险因素包括年轻、低体重指数、多囊卵巢综合征病史、既往 OHSS 病史、高水平的抗 Muller 激素(AMH)和较高剂量的促性腺激素等。sOHSS 的临床表现包括卵巢肿大、腹水、少尿、腹痛及电解质失衡，少数患者会出现外阴水肿[16]。在严重情况下，血液浓缩和凝血功能紊乱可导致血栓栓塞、肝肾功能衰竭、急性呼吸窘迫，甚至死亡[4]。sOHSS 根据严重程度分为三类，轻度 sOHSS：双侧卵巢增大至 8 cm，伴有腹胀和轻微腹痛；中度 sOHSS：卵巢增大至 12 cm，伴胃肠道症状(恶心、呕吐、腹泻等)及腹水；严重 sOHSS：约占 2%，巨大卵巢囊肿，严重腹水，血钾  $> 5$  mmol/L，血钠  $< 135$  mmol/L，血清白蛋白(ALB)  $< 35$  g/L，少尿和低血容量性休克，肝功能障碍，极易发生动静脉血栓栓塞[17] [18]。根据临床表现和 FSH 受体突变情况，De Leener 将 sOHSS 综合征分为四种类型。I 型是指 hCG、促甲状腺激素(TSH)和 FSH 水平正常的 FSHR 突变病例。FSHR 基因突变不仅可以被促卵泡激素激活，还可以被具有相同  $\beta$  亚基的糖蛋白激素如促性腺激素、促黄体生成素和人绒毛膜促性腺激素激活，增加其对自然妊娠期间产生的促性腺激素释放激素的敏感性，从而导致自然妊娠期卵巢过度刺激综合征的发生。目前已鉴定出多种 FSHR 基因突变，如 Asp567Asn、Thr449Ala、Iso554Thr、Thr449Ile、Asp567Gly、Ser128Tyr、Ala307Thr、Arg634His 和 Thr449Asn 等。II 型最为常见，为高 hCG 水平的病例如葡萄胎和多胎妊娠等。III 型与高 TSH 水平的甲状腺功能减退有关。IV 型与分泌 FSH 或 LH (黄体生成素)的促性腺素腺瘤有关[19]。12%~20%的 sOHSS 患者中可出现卵巢扭转或囊肿出血等并发症[20]。因为 sOHSS 在产后也会发生，有胃肠道症状的产褥期妇女也应值得我们关注。

### 3.3. sOHSS 的诊断和处理

虽然 sOHSS 为自限性疾病，早期诊断和治疗也尤为重要，在诊断过程中，一线检查是盆腔超声检查，这是一种经济有效的非侵入性检查，可以反映胎儿、卵巢和腹水的状况。在全面认识 sOHSS 的基础上，还需注意与妊娠黄体瘤、复发性卵泡膜黄体囊肿、卵巢癌和黄体高反应性鉴别，避免误诊和漏诊。sOHSS 患者卵巢多为双侧多囊，囊壁较薄。相比之下，卵巢恶性肿瘤的特征是单侧实性囊性囊肿，囊壁较厚。由于 CA125 在妊娠早期升高，对妊娠期卵巢肿瘤的诊断不准确[21] [22]。sOHSS 的治疗取决于其严重程度。轻度患者，持续的心理支持和心理咨询在治疗中起着非常重要的作用[13]。严重的 sOHSS 需要入院并及时处理，静脉补液以补充丢失的血管内容量，防止潜在的致命并发症，特别是肾功能衰竭和血栓栓塞。利尿剂的使用通常只限于治疗肺水肿时，因其可提高血液浓度，增加静脉血栓形成的风险。静脉血栓形成是 sOHSS 最重要的威胁生命的并发症。大卵巢或腹水对盆腔血管的压力以及妊娠高雌激素水平引起的高凝状态是 sOHSS 血栓栓塞的危险因素，肝素是血栓预防的推荐药物[23]。对于有明显腹水的患者，穿刺术可能会有所帮助，可降低腹内压，改善肾血流，增加尿量。阴道后穹窿穿刺的好处是更容易接近和避免卵巢创伤。胸腔穿刺术可能是避免呼吸窘迫的必要手段。在 sOHSS 合并垂体促性腺激素腺瘤的病例中，切除垂体腺瘤可以使增大的多囊卵巢消退和恢复正常的月经周期，但易复发[24]，除了垂体切除等治疗方式外，生长抑素类似物奥曲肽也可以作为良好的选择[24]。患有 sOHSS 合并甲状腺功能减退的患者可以用左旋甲状腺素治疗[6]。卡麦角林多为巴胺激动剂，通过抑制血管内皮生长因子(VEGF)的产生抑制血管通透性，在预防 sOHSS 方面很有效，单独使用卡麦角林或与白蛋白联合使用，可降低中重度 sOHSS 的发病率，少数病例会出现胃肠道症状等副反应[25]。sOHSS 手术治疗增加了流产的风险，仅在卵泡破裂、出血或卵巢囊肿扭转的情况下实行[26]，当涉及母亲的生命危险时需终止妊娠。与伴有甲状腺功能减退的 sOHSS 相比，hCG 浓度升高引起的 sOHSS 预后不良的风险相对更大[25]。扭转病例中，右附件扭

转比左附件扭转更常见, 也有双侧附件扭转的报道[27]。

sOHSS 临床较为罕见, 其原因多种多样, 常与伴有腹胀、腹水和卵巢肿大的卵巢肿瘤相混淆。主要采取保守治疗。由于 sOHSS 不可预测, 对有高危因素的人群孕前要进行严密监测, 如多囊卵巢综合征、甲状腺功能减退、OHSS 病史等, 做到对 sOHSS 的早诊断和早治疗, 可改善患者预后, 影响妊娠结局。

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