

## HYPERSENSITIVITY REACTION AFTER GIVING THE CONTRAST MEDIA AT HYSTEROSALPINGOGRAPHY

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**H**ysterosalpingography is a radiologic procedure that uses contrast media to assess the morphology of the endometrium, uterus, and fallopian tube patency in infertile women and recurrent abortion. HSG procedure can detect abnormalities in the uterine cavity and fallopian tube, which has several advantages, such as safe, easy, useful, and affordable.

**Materials and methods.** A 32-year-old woman with 2 years of primary infertility, who underwent hysterosalpingography (HSG) to see abnormalities in the uterine cavity and fallopian tubes as one of the causes of her infertility. The subject tells no history of allergy, but she has a history of recurrent vaginal discharge (infection factor).

**Results.** Gynecological inspection of the external genitalia and in specular organs did not show any abnormalities, but somehow after giving the contrast media the subject feels swollen eyelids, facial edema, shortness of breath, and dryness in the throat and the eyes feel closed after 15 minutes to an hour. The subject gradually improved after 24 hours and 2 days of healing of the eyelids. Based on clinical symptoms, this case is an example of a moderate level of allergy. The subject occurred swelling of the palpebral (eyes area), a feeling of shortness of breath, and dry throat, all were the symptoms of hypersensitivity reaction. Furthermore, the subject's HSG features including type I (immediate) hypersensitivity reaction or anaphylactoid reaction.

Keywords: hypersensitivity, hysterosalpingography, antihistamine, clinical symptoms, corticosteroid.

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## РЕАКЦИЯ ГИПЕРЧУВСТВИТЕЛЬНОСТИ ПОСЛЕ ВВЕДЕНИЯ КОНТРАСТНОГО ПРЕПАРАТА ПРИ ГИСТЕРОСАЛЬПИНГОГРАФИИ

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**Г**истеросальпингография (ГСГ) – рентгенологическое исследование, при котором используется контрастное вещество для оценки эндометрия, полости матки и проходимости фаллопиевых труб у женщин с бесплодием и повторными абортами. Процедура ГСГ может выявить аномалии в полости матки и маточных трубах, а также имеет ряд таких

преимуществ, как безопасность, простота выполнения и доступность.

**Материалы и методы.** Для проведения гистеросальпингографии в клинику была направлена женщина 32 лет, с диагнозом «первичное бесплодие» в течение последних двух лет. ГСГ проводилась для выявления аномалий полости матки и маточных труб как одной из возможных причин бесплодия. Пациентка отмечала периодические выделения из влагалища, связанные с инфекционными процессами. В анамнезе аллергических реакций не наблюдалось.

**Результаты.** При гинекологическом осмотре не выявлено каких-либо отклонений от нормы. Через 15 минут после введения контрастного препарата в течение часа пациентка ощущала одышку и сухость в горле, появилась отечность лица, припухлость век и ощущение закрытых глаз. В течение следующих 24 часов пациентке постепенно становилось лучше, и через два дня отек век не наблюдался. Учитывая клиническую картину, данный случай является примером аллергической реакции средней степени тяжести. Все симптомы у пациентки были проявлениями реакции гиперчувствительности. Кроме того, реакция на контрастирование при гистеросальпингографии включает гиперчувствительность I типа (немедленную) или анафилактическую реакцию.

Ключевые слова: гиперчувствительность, гистеросальпингография, антигистаминный препарат, клиническая симптоматика, кортикостероиды.

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## Patient presentation

The subject of the study was a 32-year-old woman (without food and drug allergy) who had undergone HSG using ionic contrast Urographine 76% of 10 ccs, through the cervical canal of the uterine (nonvascular) for 2 years to treat clinical primary infertility. Additionally, there had been no prior examinations or injections with iodine contrast material. The HSG examination uses a cannula (HSG set) inserted into the cervical canal by opening the vaginal opening using a Graves speculum.

### Management and outcome.

Shortly after the HSG examination was complete, the subject experienced swollen eyelids (fig. 1).

Fifteen minutes later, the subject felt his eyes swell with a dry feeling in the throat and a little shortness of breath. About 2-4% oxygen was given to the subject through the nasal pass and then it showed a vital sign. Vital signs of the subject were: blood pressure 110/80 mmHg, pulse 90x/minute, temperature 36° C, respiratory rate 24x/minute.

Thirty minutes later, the subject felt the eye become more swollen and almost closed.

Subjects were observed and found that vital signs were still stable and were given 20-40% oxygen through the nasal cannula, antihistamines (Chlorpheniramine 4 mg), and Corticosteroids (Prednisone 10 mg), orally. After the subject felt more comfortable, she was sent home to rest and was prescribed an oral antihistamine and corticosteroid drugs 3x1 tablets per day.

Subject was asked to immediately come to the Emergency Room if allergy symptoms come again. During 24 hours of observation, the subject did not feel any new allergic reactions, only swollen eyes and cannot be opened properly. The subject was still taking the prescribed medicine. The next day after 24 hours the complaints slowly reduced, and the swollen eyes disappeared completely after 2 days. Vital signs and examination of generalist status before action showed normal limits. Additional tests and HSG examination results showed a normal uterine cavity with slippery walls, no visible mass, or signs of chronic inflammation. Both patent tuba and contrast intravasation were seen in bilateral peritubular and around the uterine cavity (fig. 2).

### Discussion.



**Fig. 1 (Рис. 1)**

**Fig. 1. Photos.**

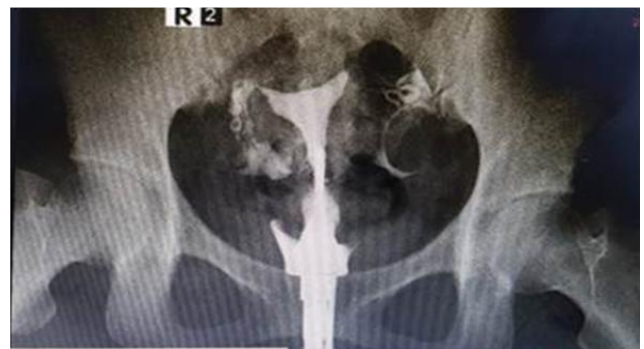
Stages of the physical process: the eyelids begin to swell after examination, followed by the eyes becoming increasingly closed and swelling in the face after 24 hours. Source: Author's photo document.

**Рис. 1. Фотографии.**

Стадии развития процесса: после исследования веки начали опухать, после чего глаза все больше закрывались, через 24 часа появились отеки на лице. Источник: собственность автора.



**Fig. 2 a (Рис. 2 а)**



**Fig. 2 b (Рис. 2 б)**

**Fig. 2. Hysterosalpingography examination.**

a – Normal uterine cavity, smooth wall, and both patent tubes. Intravasation of contrast in bilateral peritubal pars 1/3 proximal.

b – It shows a contrast agent at the perimetrium showing level 2 (medium). Source: Documentation from the Asri Medical Center Clinical Radiology Section.

**Рис. 2. Гистеросальпингография.**

а – визуализируется нормальная полость матки, стенки четкие, ровные, обе трубы проходимы. Определяется интравасация контраста в перитубарную область на 1/3 проксимальнее с двух сторон.

б – визуализируется контрастный препарат в области периметрия, соответствующий уровню 2 (средний). Источник: Documentation from the Asri Medical Center Clinical Radiology Section. .

Hysterosalpingography is a radiologic procedure that uses contrast media to assess the morphology of the endometrium, uterus, and fallopian tube patency in infertile women and recurrent abortion. HSG procedure can detect abnormalities in the uterine cavity and fallopian tube, which has several advantages, such as safe, easy, useful, and affordable [1, 2]. HSG quality is high compared to the gold standard and has a theoretic value [3-5]. HSG is also used as an initial or preliminary examination before other radiological examinations, such as hystero-graphic ultrasound, pelvic ultrasound or magnetic resonance imaging (MRI) [6, 7]. The sensitivity and specificity values of HSG are 90.91% and 77.78% , a few studies have also found these to be 85-100% [8].

Indications and contraindications of HSG are very important to record to identify the signs of inflammation in genitalia organs, such as inflammation in the vagina, portio, and cervix area. This condition happens because HSG can easily incorporate pathogenic microorganisms through contrast media and instruments used in the uterus and tubal cavum and peritoneal cavity, which can result in a greater spread of infection. Inflammation of the gynecologist organs is also at risk of disseminated intra-vacory incidence as well as systemic reactions that induce anaphylactoid reaction [9, 10]. Allergic reactions of contrast material in HSG procedure that occur in subjects are very rare considering the contrast administration through the cervical canal, nonvascular so that systemic reactions that cause hypersensitivity reactions are very rare [1, 2, 8].

It is important to provide lessons for us to examine subjects before HSG is performed, including anamnesis of hypersensitivity reactions to drugs, food, contrast material, history of genital infection, and vaginal discharge. Therefore, this study is to identify the level of allergic reactions that occur after hysterosalpingography procedure based on clinical symptoms and the level image of the contrast intravasation pattern. The results of this examination will help HSG operators in selecting a non-ionic low osmolar contrast material that is safer against hypersensitivity reactions [11, 12]. We can also see the results of the HSG in the subject if the radiograph shows the intravasation of the contrast material, and the level so that we are more careful to observe the possibility of anaphylactoid reaction in the subject [2].

The use of contrast material often conducted on radiological imaging include HSG, gastrointestinal imaging, cystography, and sialography [5, 9]. In this case, the subject undergoes HSG to treat clinical primary infertility.

The common complications of the HSG procedure include infections, vaginal bleeding, radiation exposure, vagal reactions, uterine trauma, and intravasation. However, it rarely causes an allergic reaction due to the use of contrast material.

Contrast material given to this subject is Urographine 76% as much as 10 ml which is inserted into the uterine cavity and fallopian tubes through the external uterine ostium using a cannula (nonvascular). Urographine contains a mixture of sodium amidotrizoate and meglumine amidotrizoate in a proportion of 10:66 in an aqueous solution (formed from amidotrizoic acid or diatrizoic acid: 3,5-bis-acetamido-2,4,6-triiodobenzoic acid). Urographine 76% 1 ml contains sodium amidotrizoate 0.10 g and meglumine amidotrizoate 0.66 g. Each 20 ml ampoule contains sodium amidotrizoate 2.00 g and meglumine amidotrizoate 13.20 g (370 mg I/ml). According to Roest, the occurrence of an allergic reaction is influenced by the contrast material [13, 14].

Urographine 76% used as a contrast agent since it is more affordable, easy to use, and efficient. Urographine is a water-soluble ionic contrast material with high osmolality that provides a clearer image of the uterine cavity and fallopian tubes. In addition, HSG value will better than using non-ionic (oil-based) contrast with low osmolarity. Furthermore, this material has a five times risk of anaphylactoid reactions compared to nonionic contrast material [15-18].

Anaphylactoid reactions (Anaphylactoid like reactions) may occur during contrast agent usage of HSG examination, therefore, it has to be handled and maintained properly to prevent anaphylactoid reactions [15, 16]. Allergic reactions that occur on HSG examination usually occur due to several reasons, including intravasation of contrast material into blood vessels (especially veins) through vascularity from the endometrium and myometrium due to increased vascular wall permeability. In this case, the contrast administration on HSG was extravascular and it defines that the risk of hypersensitivity reactions due to intravascular entry contrast material was almost absent or rare [13, 14]. Contrast material administered intravenously tend to result in an anaphylactoid reaction 3x more than when administered nonvascular [9, 13-19].

Anaphylactoid reactions occur because systemically iodinate Urographine contrast enters through the venous myometrium plexus and spreads intravenously in the parametrium. Iodinated contrast that enters the intravascular systemically results in the release of histamine

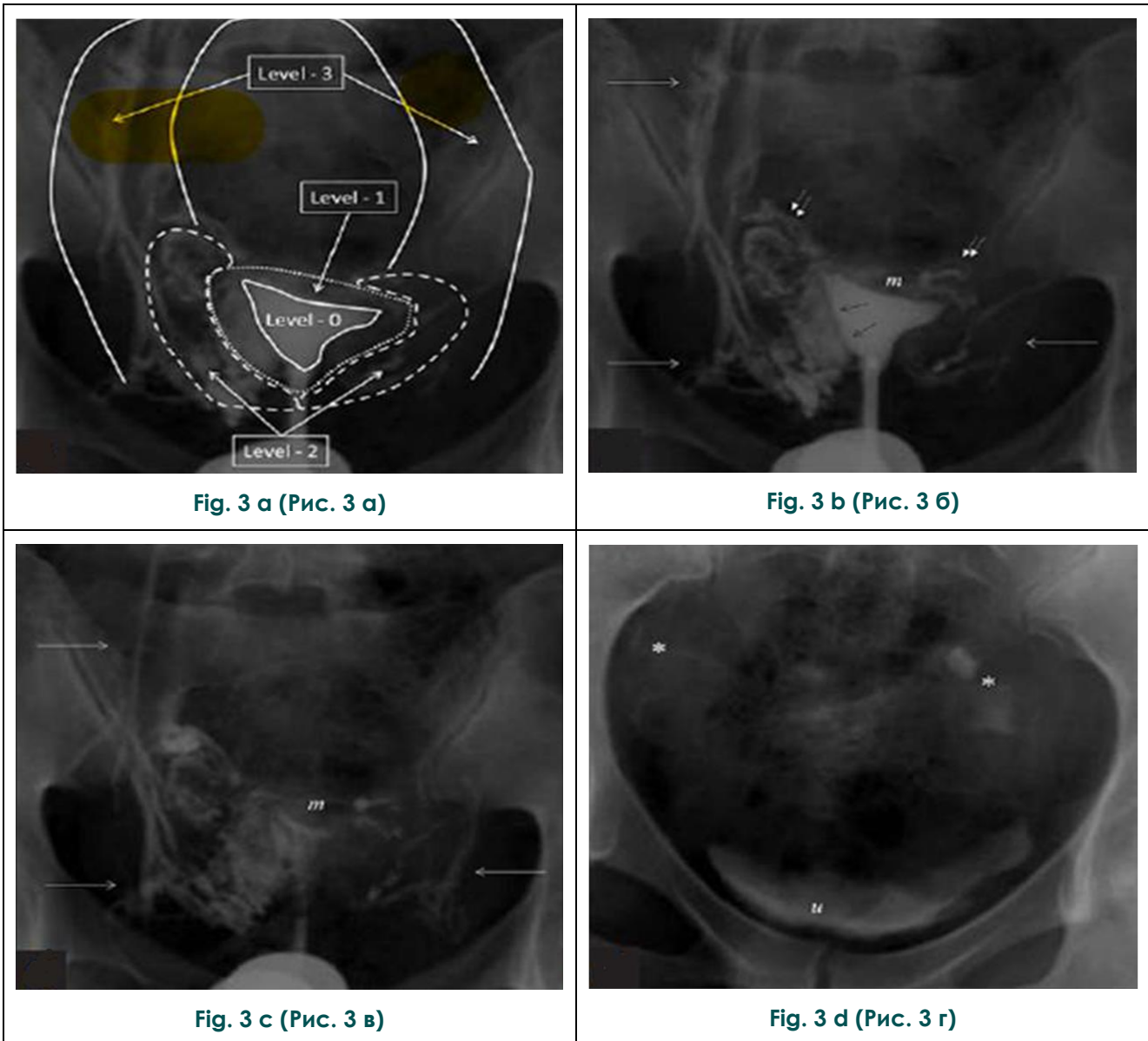


Fig. 3 а (Рис. 3 а)

Fig. 3 б (Рис. 3 б)

Fig. 3 в (Рис. 3 в)

Fig. 3 д (Рис. 3 г)

**Fig. 3. Hysterosalpingography.**

Schematic display of the intravasation severity score based on regional landmarks for intravasation:

a – Level 0: endometrium (absent); Level 1: myometrium (mild); Level 2: parametrium (medium), and Level 3: para iliac (severe).

b-d – A 24-year-old woman with a uterine arcuate. The picture shows severe (Level 3) intravasation in the internal iliac vein that occurs immediately (thin arrow), endometrial protrusions (black arrows), increased myometrium (m), and patents tubes (double arrows) with localized peritoneal spills (\*), and protruding urine visualization of the bladder (u) [2].

**Рис. 3. Гистеросальпингография.**

Схематическое изображение оценки степени тяжести интравазации на основе региональных ориентиров:

а – уровень 0: эндометрий (отсутствует); уровень 1: миометрий (легкий); уровень 2: параметрий (средний) и уровень 3: околоподвздошный (тяжелый).

б-г – Женщина, 24 лет, седловидная матка. На снимках визуализируется выраженная интравазация (уровень 3) во внутреннюю подвздошную вену, которая возникла немедленно (тонкая стрелка), выпячивания эндометрия (черные стрелки), утолщение миометрия (m), проходимые трубы (двойные стрелки) с локализованными перитонеальными затеками (\*), контрастирование в области мочевого пузыря (u) [2].

from mast cells and basophil leucocytes directly. Histamine is the most important mediator to trigger an anaphylactoid reaction that can directly activate the A1.2 tentative pathway of the complement system [3, 15, 17].

Some references mention that the intravasation of contrast material into the vein on HSG examination tends to anaphylactic reactions or greater hypersensitivity reactions. Intravasation severity scores are divided into four levels: Level 0, no intravasation; Level 1, mild intravasation limited to myometrium; Level 2, moderate intravasation in the slow-moving parametrial-adnexal vein; and Level 3, extending intravasation from myometrial-parametrial to the paracaval vein. To facilitate the division of intravenous contrast intravasation levels is divided into four levels, namely: (0) endometrial level, (1) myometrium, (2) parametrial, and (3) parailiaca vein (fig. 3) [2, 3, 5, 9].

Based on clinical symptoms, this case is an example of a moderate level of allergy. The subject occurred swelling of the palpebral (eyes area), a feeling of shortness of breath, and dry throat, all were the symptoms of hypersensitivity reaction. Furthermore, the subject's HSG features including type I (immediate) hypersensitivity reaction or anaphylactoid reaction. Type 1 hypersensitivity reactions which are also called rapid reactions or anaphylactic reactions, or allergic reactions occur as soon as the body is exposed to an allergen. In type I reactions, allergens that enter the body cause an immune response in the form of IgE production and allergic diseases such as allergic rhinitis, asthma, and atopic dermatitis.

Type I hypersensitivity reactions are divided into 2, namely allergies and pseudo-allergy (anaphylactoid). Pseudo allergy/anaphylactoid in this case is a common systemic reaction that involves the release of a

mediator by mast cells that occurs not via IgE. During a pseudo allergic reaction, the drug does not function as an antigen, but the drug has the ability by its chemical or pharmacological properties to stimulate direct release/activation of inflammatory mediators from mast cells, basophils, or other body tissues. This reaction does not require prior exposure to irritation. Anaphylactoid reactions can be induced antimicrobial, protein, contrast with iodine, penicillin, muscle relaxants, etc. In this subject, oral antihistamines were prescribed, namely Chlorpheniramine Maleate (CTM) 1 tablet (4 mg) and anti-inflammatory/corticosteroid, namely Prednisone 10 mg (2 tablets) to take orally. These drugs are used to inhibit the release or activation of inflammatory mediators and allergic reactions.

The level of allergy to contrast material after HSG procedure based on clinical symptoms and level of contrast intravasation in this subject case was a moderate level, namely level two and including type I hypersensitivity.

#### Conclusion.

Before the HSG examination, it is important to pay attention to the subject's clinical symptoms such as vaginal discharge, drug allergy, infection record, and other contraindications. We need to pay attention to abnormalities in the genital organs externally as well as inspeculo.

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