

Severe Transient Leukopenia following Hysterosalpingography

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Key Words

Leukopenia · Hysterosalpingogram · Conray 280 · Iothalamate

Abstract

Severe anaphylaxis to contrast media used in hysterosalpingography is very rare. Leukopenia may sometimes be seen in severe anaphylaxis associated with shock. This case report is about an atypical presentation of anaphylaxis following the injection of Conray 280 for hysterosalpingography. The patient had severe leukopenia without other associated features of anaphylaxis that resolved spontaneously after 48 h. This type of reaction to Conray 280 has not been reported before.

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Introduction

Hysterosalpingogram is a common investigation performed to assess patency of tubes in infertile couples. Water-soluble contrast agents are preferred to oil-based agents due to their lower incidence of inflammation. Major complications from hysterosalpingography are very rare and mostly consist of pelvic infections. The incidence of such infections is reported to be higher in patients with tubal pathology. Anaphylaxis following hys-

terosolpingography is very rare and has been reported only three times in the literature [2–4].

We report a case of severe transient leukopenia following the use of iothalamate meglumine (Conray 280) for hysterosalpingography. We believe this is an atypical late anaphylactic reaction to iothalamate meglumine.

Case Report

A 28-year-old female had a hysterosalpingogram with Conray 280 for secondary infertility. She has had one previous normal delivery and two miscarriages in the past. The procedure was completed uneventfully and showed normal uterine contours and spillage of dye from both tubes. She left the hospital after an hour of observation.

She had a background history of polycystic ovarian syndrome for which she was taking metformin 1,500 mg daily. There was no other medical or surgical history of relevance especially of allergies. High vaginal swabs done prior to the procedure showed only normal vaginal flora. There was no evidence of chlamydial or gonococcal infection in the cervical swab test.

About 4 h after the hysterosalpingogram, she was admitted to the emergency department with severe epigastric pain, nausea and one episode of vomiting.

Examination revealed the patient to be in distress due to pain. Her pulse was 80/min and blood pressure was 100/54. She was shivering and had a temperature of 38.1°C. She did not have any rashes, urticaria or breathing difficulty.

Examination of the abdomen revealed tenderness in the right upper quadrant and epigastrium. There were no signs of peritonitis on clinical examination. Pelvic examination did not reveal

Table 1. Blood results starting two months before the incident up to 48 h after admission

	Normal range	2 months previously	At admission	3 h after admission	24 h after admission	48 h after admission
Hb, g/dl	12–15	15.1	14.7	12.4	12.3	13
WBC, $\times 10^9/l$	4.0–11.0	7.2	1.0	2.9	3.2	3.8
Platelets, $\times 10^9/l$	150–400	197	162	153	146	131
RBC, $\times 10^{12}/l$	3.8–5.1	5.05	4.97	4.23	4.16	4.4
Hematocrit	0.37–0.47	0.44	0.44	0.37	0.36	0.38
N, $\times 10^9/l$	2.0–7.5	5	0.83	2.84	6.82	2.21
L, $\times 10^9/l$	1.3–3.5	1.79	0.13	0.07	0.28	1.21
M, $\times 10^9/l$	0.2–0.8	0.27	0	0.01	0.05	0.27
E, $\times 10^9/l$	0.04–0.44	0.1	0.01	0.01	0.02	0.06
B, $\times 10^9/l$	0.0–0.1	0.01	0	0	0	0
CRP	<5		<2		19	6
Amylase, IU/l	30–100		<30			
Tryptase, $\mu g/l$	2–14		3.26			

Hb = Haemoglobin; WBC = white blood count; RBC = red blood count; N= neutrophils; L = lymphocytes; M = monocytes; E = eosinophils; B = basophils; CRP = C reactive protein.

any tenderness or masses. In particular there was no discharge of note and there was no cervical motion tenderness.

Blood cultures were taken along with other investigations.

She was administered 1 g of paracetamol and 60 mg of codeine phosphate for analgesia and was immediately started on intravenous antibiotics (cefuroxime and metronidazole).

Later, she developed shortness of breath and generalised tenderness over the abdomen.

Full blood count on admission showed severe leukopenia and peripheral smear showed shift to the right with minimal immature forms. The full blood count gradually improved after about 3 h of admission. She was treated conservatively with paracetamol and codeine phosphate for pain and antibiotics for any possible infection. Her abdominal symptoms resolved within a couple of hours after admission and clinically, she showed good improvement. The leukopenia continued to improve gradually and was within normal limits after 48 h (table 1). She was discharged home after 48 h when blood picture improved and completed a 5-day course of oral augmentin (amocycillin/clavulanate). Microbial culture results including blood, urine and genital swabs were negative for bacterial infections and Chlamydia. All other investigations including abdominal and chest X-rays and tryptase levels were normal. Serum levels of tryptase are raised in severe anaphylaxis due to increased mast cell activation and it is recommended in the diagnostic work up of suspected cases of severe anaphylaxis.

Discussion

Water-based agents are preferred for hysterosalpingogram as they cause less peritoneal inflammation than oil-based agents [5].

Conray 280 is one such ionic agent with high osmolar properties. Each milliliter contains 45.6% iothalamate acid, an iodine-based agent, which is the main ingredient. High osmolar agents are preferred because their slow-moving properties give more detail of the tube on imaging. The main procedure-related symptoms reported are abdominal pain, shakiness, faintness, nausea and sensation of heat or cold. These are minor symptoms that settle spontaneously [6]. Abdominal pain from hysterosalpingography can be due to a combination of instrumentation and peritoneal irritation by the contrast media. Bilaterally blocked tubes may also cause pain as the dye may be injected with greater pressure resulting in extravasation and subsequent pain.

Iothalamate is a safe agent and no major complications have been reported with its use in hysterosalpingography. It is, however, known to cause inflammation of the tubes and this has been confirmed in animal studies [7, 8]. Most patients complain of moderate to severe degree of abdominal discomfort after the procedure, which is most likely to be due to the inflammatory reaction in the pelvic peritoneum [9].

We performed a thorough literature search using PUBMED and EMBASE with the following search words: iothalamate, iothalamate meglumine, anaphylaxis, Conray and hysterosalpingography. Our literature search did not show any similar case reports of leukopenia related to hysterosalpingography.

Leukopenia can be caused by a variety of conditions. These include drugs toxicity, chemotherapeutic agents, bone marrow failure, liver failure and splenic sequestration.

Studies on severe anaphylaxis associated with shock have shown neutropenia [10, 11].

Although we do not know the exact cause of leukopenia in this case, we believe it is more likely to be due to a late allergic reaction. The late reaction may be due to the slow absorption through the pelvic peritoneum, which further led to a 'consumption leukopenia'. There are very few case reports on anaphylaxis related to hysterosalpingography. In two of them the reaction occurred within 10 min and in the other it occurred after one hour. They all had symptoms and signs of anaphylaxis including urticaria and shock requiring specific treatment [2, 4]. Our

case was different to these presentations as she presented about 4 h later and there were no symptoms or signs of anaphylaxis. Although our patient had a single episode of elevated temperature at the time of admission, we do not think there was enough evidence to support an infectious aetiology because of two reasons. Firstly, such kind of infection would be very severe and would not show improvement in blood picture 3 h after admission. Secondly and more importantly, all cultures were negative.

Late reactions are extremely rare. There is only one previous published case report where a reaction occurred after 1 h [4]. We observe patients for about an hour after the procedure for anaphylactic symptoms before discharge. From our experience we feel that patients should be warned about late symptoms before discharge so that they can seek medical help if needed.

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