



Unexplained Puerperal Fever

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Abstract

There are numerous infectious and non-infectious causes of fever in the postpartum period. We present a case of a 30-year-old secundipara with puerperal fever which persisted despite initial broad-spectrum antibiotic therapy. Chest X-ray was eventually taken and showed perihilar infiltrates that were subsequently diagnosed to be enlarged lymph nodes due to Hodgkin lymphoma. The case highlights the importance of constructing a thorough differential diagnosis when managing women with fever in the postpartum period. This is especially important when therapy for most common infectious etiologies has not been successful.

Introduction

There are several possible causes for fever following childbirth that are either infectious (infection of laparotomy or episiotomy wounds, endometritis, mastitis, infection of the urinary tract, respiratory system or skin) or non-infectious (dehydration, tissue damage, breast engorgement, thromboembolic complications, malignancies, connective tissue disease) [1,2]. Infectious causes should be considered first and managed aggressively, since puerperal sepsis continues to be an important cause of direct maternal mortality both in high- as well as in low-income countries [3]. However, a broad differential diagnosis should be constructed, and non-infectious causes should also be pursued, especially when fever persists in spite of initial antibiotic therapy. We present a case which highlights the importance of considering non-infectious etiologies of puerperal fever after unsuccessful antibiotic treatment.

Case Presentation

A 30-year-old secundipara with no known illnesses had Caesarean section at week 40 because of her previous Caesarean section. During pregnancy, she had gained only 3 kg (78→81 kg), she once had sinusitis and received antibiotics. From the beginning of the second trimester onwards she had a dry irritating cough, a few days before the delivery she noticed darker urine and had a burning sensation during micturition. During delivery her Body Temperature (BT) was 37.7°C. The postpartum period in the hospital was uneventful, with the exception of anemia, Hemoglobin (Hb) 94 g/L. She was discharged 4 days after delivery reporting no problems.

Eight days after delivery she was referred to the outpatient clinic due to wound infection. She reported feeling well. Admission status: BT 37.5°C, normal breast and lochia, abdomen insensitive on palpation. There was a minor dehiscence (1 cm) and a retained clip in the right corner of the laparotomy wound. We removed the clips, cleaned the wound and changed the dressing. Patient was discharged with instructions.

Twelve days after the delivery she came to the clinic because of a headache and for generally feeling unwell. She reported high BT for 1 week and a slightly foul-smelling lochia. She was breastfeeding without difficulty. **Admission status:** BT 38.4°C, blood pressure 123/78 mmHg, pulse 108/min, breasts were normal; there were no signs of wound inflammation.

Gynecological status: foul-smelling lochia.

Working diagnosis: mild endometritis. We introduced per oral Amoxicillin/Clavulanic Acid 1000 mg/12 h for 1 week.

Fifteen days after the delivery she returned to the outpatient clinic for persistent malaise, loss of appetite, and a slight cough. She reported no problems with micturition or bowel movements. At home BT was 38°C. On admission she was sub febrile, BT 37.4°C. The wound was healed. Breasts were soft, without redness.

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Figure 1: Chest X-ray—mediastinal tumor mass.

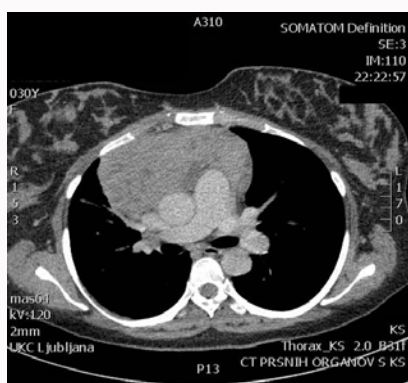


Figure 2: Thoracic CT scan: Mediastinal tumor mass.

Gynecological status: uterus contracted, insensitive on palpation. Vaginal ultrasound: minimally mixed echogenicity in the uterine cavity, not suspicious of endometritis or retained placental tissue. The patient was hospitalized at the Department of Perinatology Intensive Perinatal Medicine Unit for additional diagnostics.

Course of Treatment

Laboratory findings on admission: \uparrow CRP 215 mg/l, \downarrow Hb 93 g/l, \downarrow Fe 1.4 μ mol/l, \uparrow Platelets $727 \times 10^9/l$; in DBC \uparrow neutrophils 82.2%, \uparrow lymphocytes $0.72 \times 10^9/l$ or 8%.

We consulted an infection disease specialist and decided on a chest X-ray, where a 13 cm large semi-circular thickening was visible in the right perihilar anterior region. The radiologist advised a thoracic CT that showed: a large, 12 cm \times 6 cm \times 11 cm, heterogeneous, well-restricted, solid formation with numerous necrotic areas in the anterior mediastinum, not infiltrating into adjacent structures but slightly compressing the vena cava superior and enlarged lymph nodes at the aortic arch, upper mediastinum and supraclavicular in front of the sternocleidomastoid muscle.

Differential diagnosis: thymoma, lymphoma.

A repeated thorough clinical examination revealed a palpable enlarged supraclavicular lymph node, which was extirpated and sent for a histopathological examination; the results pointed to a classic nodular sclerosing Hodgkin lymphoma. Following staging examination (PET/CT) the lymphoma was classified as stage II or III. B.X (there was a questionable focus in front of the splenic hilum that was accumulating isotope, but less intensely than other positive

localizations).

The patient was transferred to the Institute of Oncology (IO). BEACOPP escalated chemotherapy (Bleomycin, Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine) was initiated. During the course of treatment, the patient required several transfusions of blood derivatives (erythrocytes, platelets), and prophylaxis with low molecular weight heparin was introduced due to the compression and fusion of the superior vena cava and brachiocephalic vein. She received a total of six cycles of the aforementioned therapy, where the last two cycles were in reduced doses due to side effects of the therapy. As early as cycle three, a chest X-ray showed a narrowing of the mediastinum, which indirectly indicated a good treatment effect. After cycle six, she underwent a PET/CT, which indicated a complete metabolic response consistent with complete remission. The patient was then followed up regularly, with no clinical signs of disease recurrence. Control CT scans are due later in 2019.

Discussion

Lymphomas are clonal diseases that result from malignant transformation and uncontrolled growth of a lymphatic cell type B, T, or natural killer cells in lymphatic organs. They are divided into Hodgkin lymphoma, which occurs more frequently between the ages of 15 and 34 and after the age of 50, and non-Hodgkin lymphomas, whose incidence increases with age [4,5].

Epidemiology of Hodgkin lymphoma specifically, but also cancer in pregnancy/postpartum in general, is not well studied, since most national registries usually do not combine information on both cancer diagnosis and obstetric data. This is also true for the Cancer Registry of Republic of Slovenia [6], making it impossible to accurately state the incidence of Hodgkin lymphoma in pregnancy in our country. Nevertheless, since Hodgkin lymphoma in women occur predominantly in childbearing age; it can be assumed that it represents an important proportion of all malignancies diagnosed during pregnancy or shortly after delivery. Available epidemiological data support this. According to the International Network on Cancer, Infertility, and Pregnancy, lymphomas are the second most common malignancy in pregnancy/puerperium (13 % of all cancers in pregnancy/puerperium) second only to breast cancer (35% of all cancers in pregnancy/puerperium) [7].

The disease is manifested by enlarged lymph nodes, which are usually painless on palpation. They are most commonly found in the neck, supraclavicular, axillary and inguinal regions [4,5,8]. Lymph nodes in the mediastinum are often enlarged, which can cause a dry irritating cough, shortness of breath, and superior vena cava syndrome. If present in the abdominal cavity it can be manifested by abdominal pain, constipation and difficult micturition. An enlarged spleen can cause pain under the left rib arch. General or B symptoms are also common: unexplained fever, night sweats, and unintentional weight loss. Hodgkin's lymphoma is also often accompanied by itchy skin [4,5,8].

Diagnosis is made by histologic examination of the affected lymph node, and disease staging is determined by imaging [2]. Depending on the number and localization of the affected lymph nodes or organs the disease is staged into I-IV [8].

Two chemotherapy regimens are most common modes of treatment, i.e. ABVD (Doxorubicin, Bleomycin, Vinblastine and

Dacarbazine, Corticosteroids) and high-dose therapy escalated BEACOPP. Imaging tests are repeated during treatment and after completion of chemotherapy to evaluate the effect of the treatment. However, radiation therapy (depending on the baseline stage) is indicated to complete the treatment depending on the outcome at the end of chemotherapy [5,8]. After the completion of specific treatment, patients with HL are in a follow-up scheme for another 5 years at the IO. In the event of recovery, they are then referred to their GP for follow-up.

Conclusion

In the second week after a Caesarean section and after exclusion of the most common puerperal infections, the puerpera with persistent malaise and fever underwent imaging diagnostics which revealed a mediastinal mass and an enlarged lymph node in the neck, which was extirpated. Hodgkin's lymphoma was confirmed histopathologically. The patient was admitted for oncological treatment and received appropriate chemotherapy.

The main problem encountered in the course of treatment of the patient was the non-existent clinical pathway for referral of women with suspected malignancy during pregnancy and in the postpartum period between the UMCL Department of Perinatology and Institute of Oncology, which unfortunately is increasingly needed.

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