CASE REPORT

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Pleural empyema caused by *Salmonella enteritidis* in a patient with non-Hodgkin lymphoma

Empijem pleure prouzrokovan salmonelom enteritidis kod bolesnika sa nehodžkinovim limfomom

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Abstract

Introduction. Extraintestinal manifestations of nontyphoidal salmonellosis are usually seen in patients with cellular immunodeficiency. Pleural empyema caused by nontyphoidal *Salmonella* is very rare clinical presentation of salmonellosis and there are just a few cases described in a literature. We presented a very rare case of pleural empyema caused by *Salmonella enteritidis* in a patient with non-Hodgkin limphoma. **Case report.** A 60-year-old male with low grade B-cell lymphoma, mucosa associated lymphoid tissue (MALT) type in IV clinical degree, manifested with infiltration of stomach, bronchus, pleura and peritoneum was admitted to the hospital. Initially the patient was presented with nonspecific symptoms and signs, suggesting poor general condition. During the hospitalization his pleural fluid became purulent and changes in blood counts were registered with the increase of leukocytes, especially neutrophils. A large number of leukocytes was found by microscopic evaluation of pleural fluid and *Salmonella enteritidis* was isolated by its culture. There were no pathogenic bacteria in stool culture and hemoculture remained sterile. Toxins A and B of *Clostridium difficile* were not detected in stool. The patient was treated by ciprofloxacin and cefrtiaxone for 14 days with drainage of the purulent content, what was followed by the resolution and organization of the pleural fluid. After the stabilization of his general condition, chemotherapy with cyclophosphamide, vincristine, prednisone (COP) was introduced, with complete response. **Conclusion.** Although rare, pleural empyema caused by nontyphoidal *Salmonella* should be considered in patients with severe immunosuppression, because appropriate antimicrobial therapy with surgical measures are very important for the outcome in these patients.

Key words:
empyema, pleural; diagnosis; salmonella enteritidis; lymphoma, non-hodgkin.

Apstrakt

Uvod. Ekstraintestinalne manifestacije netifusnih salmoneloza obično se sreću kod bolesnika sa imunodeficijencijom ćelijskog tipa. Pleuralni empijem prouzrokovan netifusnim salmonelama predstavlja veoma retku kliničku prezentaciju infekcije salmonelama i postoji svega nekoliko ovakvih slučajeva objavljenih u literaturi. Prikazali smo veoma redak slučaj empijema pleure izazvanog sojem *Salmonella enteritidis* kod bolesnika sa nehodžkinovim limfomom. **Prikaz bolesnika.** Šezdesetogodišnji muškarac sa niskogradusnim B-ćelijskim limfomom, tipa limfom limfnog tkiva mukoze (MALT), u IV kliničkom stadijumu, sa inflitracijom želuca, bronha, pleure i peritoneuma, primljen je na bolničko lečenje. U početku se bolest manifestovala nespecifičnim simptomima i znacima i lošim opštim stanjem. Tokom hospitalizacije pleuralna tečnost je postala purulentna, uz promene u krvnoj slici sa leukocitozom i neutrofilijom. Mikroskopskim pregledom pleuralne tečnosti uočen je veliki broj leukocita, a kulturom je izolovana *Salmonella enteritidis*. Koprokulturom nisu izolovane patogene bakterije. Hemokultura je ostala sterilna. Toksini A i B *Clostridium difficile* nisu nađeni u stolici. Bolesnik je lečen ciprofloksacinom i ceftriaksonom uz drenažu purulentnog sadržaja, što je bilo praćeno rezolucijom i organizacijom pleuralne tečnosti. Po stabilizaciji opšteg stanja bolesnika uvedena je hemioterapija po protokolu ciklofosfamid, vinkristin, prednizon (COP), sa kompletnim odgovorom. **Zaključak.** Iako redak, pleuralni empijem prouzrokovan netifusnim salmonelama trebalo bi razmotriti kod bolesnika sa teškom imunodeficijencijom, budući da su adekvatna i pravovremena antimikrobna terapija, uz hirurške mere, veoma važni za ishod lečenja ovih bolesnika.

Ključne reči:
empijem, pleuralni; dijagnoza; salmonella enteritidis; limfom, nehodžkinov.

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Introduction

Nontyphoidal *Salmonella* is widely spread in nature and usually presents as gastroenteritis in immunocompetent persons [1]. However, in immunocompromised patients, extraintestinal manifestations are possible, especially in patients with cellular immunodeficiency. For the last two decades the prevalence of nontyphoid salmonellosis has been increasing [2, 3]. The most important risk factors for extraintestinal salmonellosis are: extremes of age, malignancy, HIV infection, diabetes mellitus, sickle cell disease and therapeutic immunosupression [1, 2]. About 5% of symptomatic salmonellosis develop bacteriemia while less than 1% are focal infections like osteomyelitis, soft tissue infection, urinary tract infections or endocarditis [1]. Pleural empyema caused by non-typhoid *Salmonella* is an extremely rare condition and there are just a few cases described in the literature [4–6].

We presented a very rare case of pleural empyema caused by *Salmonella enteritidis* in a patient with non-Hodgkin lymphoma.

Case report

A 60-years-old male was admitted to the Clinic for Gastroenterology and Hepatology of the Military Medical Academy (MMA) in Belgrade on December 15 2013, because of swelling of the abdomen, sensation of early filling, noticed six months earlier, and intensified in the last three months, and were followed by extensive night sweating, lost of weight, fatigue and dyspnea. The patient was dismissed in good condition, he used no contaminated food, and there was no diarrheal illness in his surroundings, nor in himself.

At admission the patient was pale, dyspnoic with impaired respiratory sound on the left, silent cardiac sounds and systolic murmurs of the aortic confluence. The patient was normotensive with abdominal distension due to a large volume of ascites.

Laboratory data at admission were (as follows): red blood cells (RBC) 5.78 × 10^{12}/L (reference range 4.50–6.50 × 10^{12}/L), white blood cells (WBC) 10.6 × 10^{9}/L (reference range 4.00–11.00 × 10^{9}/L), neutrophils (Ne) 72.4% (reference range 40–74%), platelets (PLT) 578 × 10^{9}/L (reference range 160–370 × 10^{9}/L), glucosae 4.8 mmol/L (reference range 4.1–5.9 mmol/L), urea 4.4 mmol/L (reference range 2.5–7.5 mmol/L), creatinine 58 mmol/L (reference range 62–115 mmol/L), proteins 60 g/L (60–83 g/L), albumins 32 g/L (reference range 32–50 g/L), bilirubin 10 mmol/L (reference range 0–18 mmol/L), Na^{+} 140 mmol/L (reference range 136–145 mmol/L), K^{+} 5.2 mmol/L (reference range 3.5–5.1 mmol/L), Ca^{2+} 2.56 mmol/L (reference range 2.10–5.60 mmol/L), aspartate aminotransferase (AST) 33 U/L (reference range 0–37 U/L), alanine aminotransferase (ALT) 39 U/L (reference range 20–65 U/L), lactate dehydrogenase (LDH) 392 U/L (reference range 85–227 U/L), gama glutamyl transpeptidase (GGT) 147 U/L (reference range 0–73 U/L), alkaline phosphatase (ALP) 591 U/L (reference range 90–360 U/L), INR 0.97 (reference range 0.9–1.2), serum ascites albumin gradient (SAAG) 12 g/L; in ascites: albumins 20 g/L, LDH 392 U/L, GGT 147 U/L, ALP 591 U/L.

Chest radiography showed a pleural effusion in organisation on the left. A liver cyst 3 cm in diameter, was diagnosed on abdominal echotomography. On chest and abdominal multislice computed tomography (MSCT) massive pleural effusions on the left and smaller effusion on the right with compressive atelectasis were registred. The liver was enlarged, 17 cm in diameter, with massive ascites and the gastric thickened wall up to 19 mm (Figure 1).

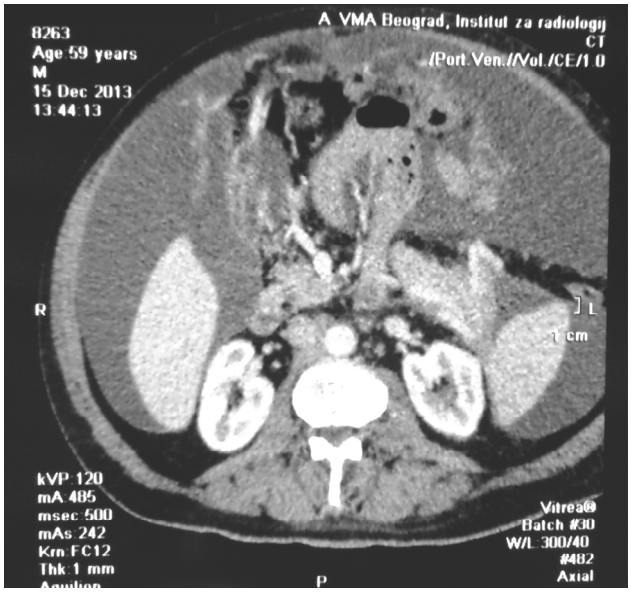

Fig. 1 – Multislice computed tomography of the abdomen revealed ascites in a patient with non-Hodgkin lymphoma.

On esophagogastroduodenoscopy many irregular, partially affiliated ulcerations in stomach were seen. Low grade B-cell lymphoma of the marginal zone was proved by its pathohistological examination. Bronchial infiltration for the left lower lobe was seen on bronchoscopy, whose histopathological examination proved the same type of lymphoma. Malignant lymphoma cells were also found by cytological examination of pleural and peritoneal fluid. Drainage of the thoracic cavity was made. Methylprednisolone in a dose of 1 mg/kg was started and the patient was transferred to the Clinic for Haematology of MMA on December 29, 2013. Just after the admission the patient had large-volume diarrhoea and fever. The patient received a short course of metronidazole until the arrival of microbiological analyses. In laboratory findings, the increase in the number of WBC was noticed up to 21.18 × 10^{9}/L, with the predominance of granulocytes (Ne 19.8 × 10^{9}/L). In the same time the pleural fluid became purulent (Figure 2), and microscopic evaluation showed a large number of polymorphonuclear leucocytes. Its bacteriological culture was positive for *Salmonella enteritidis*. Hemoculture remained sterile. Pathogenic bacteria were not isolated by stool culture. Stool was, also, negative for toxins A and B of *Clostridium difficile*.

The patient was treated by pareteral antimicrobial therapy, ciprofloxacin and ceftriaxone, simultaneously, according to the antibiogram, during 14 days, with drainage, that was followed by resolution and organisation of the pleural effusion. In further course the patient was pale, adynamic,

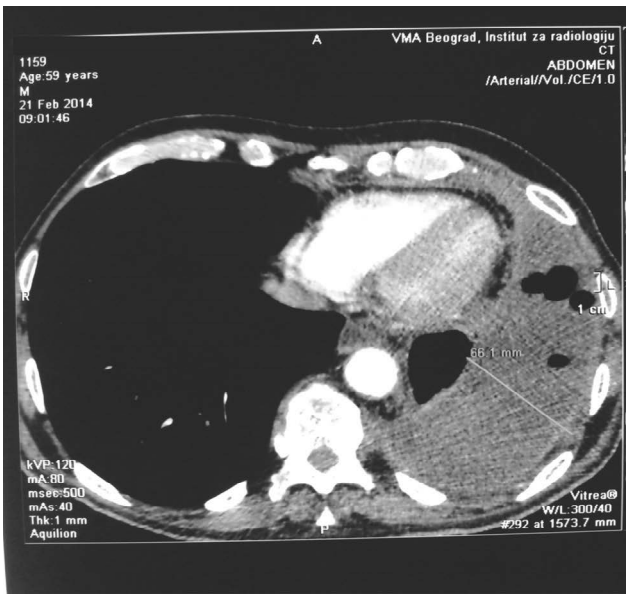

Fig. 2 – Empyema of the pleura in a patient with non-Hodgkin lymphoma detected using chest multislice computed tomography.

with deterioration of general condition, with radiographic picture indicating perforation of the hollow organ. On chest and abdomen MSCT, signs of pneumoperitoneum were found (Figure 3a). The surgeon decided not to operate the patient because of his poor general condition, but to go on with wide spectrum antimicrobal therapy (meropenem, metronidazole and fluconazole), supportive measures and drainage. After stabilisation of general condition, chemotherapy with cyclophosphamide, vincristine, prednisone (COP) was introduced. The patient recieved eight cycles of chemotherapy, with complete response. During chemotherapy there were no infectious complications, no neutropenia in our patient.

therapeutical procedures, the number of immunocompromised persons has increased. That is the reason for the incidence of extraintestinal nontyphoidal *Salmonella* infection to incease, also. Most of the patients with pleuropulmonary salmonellosis have additional lung or pleural disease [4, 5, 7]. Although, the presented patient was severely immunocompromised by his disseminated malignant disease and immunosuppressive treatment, he had also local immunosuppression, because of his infiltrated bronchus and pleura. Combination of systemic and local immunosuppression could be the explanation for this rare form of disease [8].

According to the literature, the most frequent serotypes of *Salmonella* isolated from pleural empyema are: *Salmonella typhimurium*, *Salmonella cholerasuis* and *Salmonella paratyphi*, while in just a few cases was isolated *Salmonella enteritidis* [9]. In most patiens the causative bacteria is isolated from stool, blood and pleural empyema. The way by which salmonella reaches the pleural fluid from intestinal tract can be haematogenous or *per continuitatem*. In the presented patient *Salmonella* was not isolated from blood, but it did not exlude hematogenous dissemination *via* transitory bacteriemia. In that case reticuloendothelial system coud be the source of *Salmonella* [5]. Although the causative agent was not detected in stool, we did not exlude acute salmonellosis, because the appearance of fever and diarrhea were time-related with the appearance of pleural empyema. Since we suspected microperforation of upper intestinal tract, direct spreading through diaphragm was also possible. Because the patient had thoracic drainage, before the contents became purulent, external aquisition was not to be excluded [10].

The most frequent clinical symptoms and signs of pleural empyema are fever, cough, dyspnea and pleuritic pain [11]. Clinical characteristics of our patients were non-specific, because they were masked by his poor general condition and the main illness.

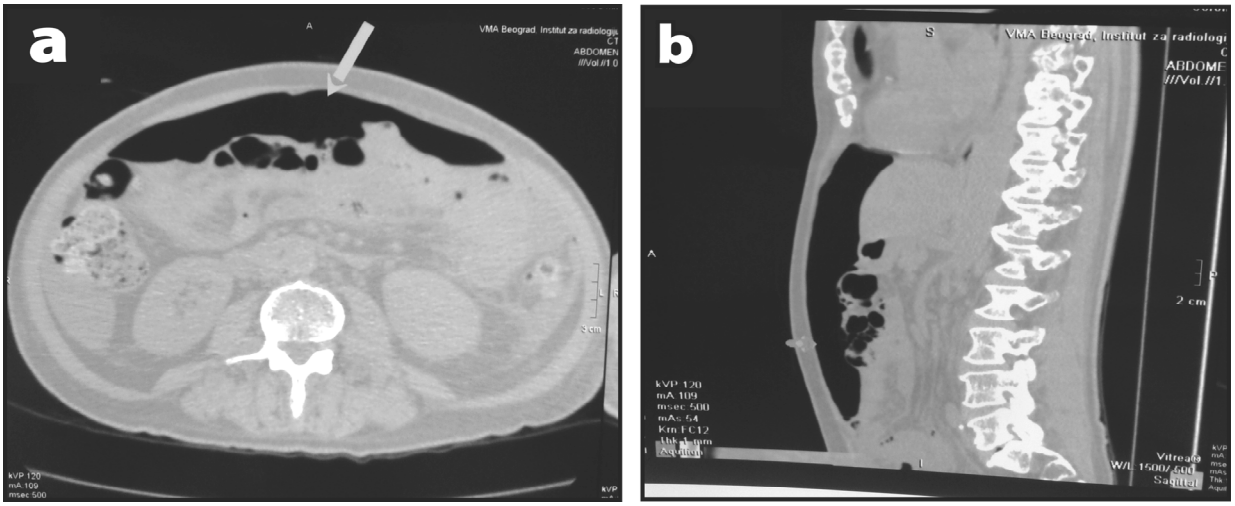

Fig. 3 – Pneumoperitoneum in a patient with non-Hodgkin lymphoma on a) transveral and b) longitudinal section of chest and abdominal multislice computed tomography.

Discussion

This case is an extreme rare form of extraintestinal nontyphoidal salmonellosis in a person with impaired cellular immunity. With the development of new diagnostic and

Most of the authors are consistent that treatment should include antimicrobial therapy and evacuation of pleural empyema by thoracocentesis, open drainage or pleural decortication [11]. Most *Salmonella* respond well to ciprofloxacin and third-generation cephalosporins [4]. The presented patient had a two-

week course of antimicrobial therapy with ciprofloxacin and cefriaxone, followed by open drainage of the thoracic cavity, followed by regression of empyema, despite the advanced disease. Dual antimicrobial therapy was introduced before the results of antibiogram were seen and it was continued after the antibiogram arrival, due to specificity of the affected area and patients poor general condition.

The most important predictive factors for the outcome are: age over 60, the presence of underlying disease and apropriate antimicrobial therapy [9]. The presented patient had more negative predictive factors for the outcome, but he survived with the help of appropriate and early antimicrobial therapy and the other supportive measures.

Conclusion

Althoug rare, nontyphoidal *Salmonella* should be considered as possible etiological factor of pleural empyema in patients with celullar immunodeficiencies, especially if a patient has underlying pulmonary disease. Namely, apropriate antmicrobial therapy with surgical measures can improve the outcome in these patients.

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