

Non-Traumatic Clostridial Sepsis : A Postmortem Case Report

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Abstract

Clostridial bacteremia, caused by a gram-positive microorganism which proliferates in anaerobic condition is most often seen after surgery or trauma as a complication of heavily contaminated wounds. Occasionally cases of non-traumatic clostridial gas gangrene occurring spontaneously have been reported in the absence of any external wound or trauma, associated with immunosuppression and/or malignancy. This report describes a postmortem case: a 5-year-old boy who presented with synchronous lymphoma and extensive gram-positive bacteremia.

Key words: *Clostridial sepsis, lymphoma.*

Nontravmatik Klostridyal Sepsis: Postmortem Olgu Sunumu

Özet

Anaerobik koşullarda çoğalan bir gram pozitif mikroorganizmanın sebep olduğu klostridyal bakteriyemi, i en sık kontamine olmuş yaraların bir komplikasyonu olarak travma ya da cerrahiden sonra görülür. Herhangi bir dış yaralanma ya da travma olmaksızın, immunsupresyon ve/veya malignitenin eşlik ettiği, spontan nontravmatik klostridial gazlı gangren olguları arasına bildirilmektedir. Bu postmortem olgu sunumunda yaygın gram pozitif bakteriyemi ile birlikte lenfoması olan 5 yaşında erkek çocuk tanımlanmaktadır.

Anahtar Kelimeler: *Klostridyal sepsis, lenfoma*

Gram-positive bacteraemia formed by Clostridium genus occurs in anaerobic condition. The etiological microorganism is Clostridium perfringens in more than 80% of cases (1,2). Most frequently it occurs after surgery or trauma as a complication of heavily contaminated wounds. Occasionally, cases of non-traumatic clostridial gas gangrene occurring spontaneously have been reported in the absence of any external wound or trauma. This entity mostly occurs in cases associated with immunosuppression and/or malignan-

cy, and may cause mortality (4,6,7). In this study, a postmortem case synchronously demonstrating lymphomatous malignancy and gram-positive bacteraemia is presented.

Case

A 5-year-old boy was admitted to the Department of Paediatrics, University of Ankara

Medical School, with a history of swelling in abdomen, a mass in the jaw, toothache and knee pain. On physical examination, he was confused with signs of respiratory distress. He had bilateral exophthalmos, anisokoric pupils with a positive light reflex. Abdomen was tender and distended, and also a mass measuring 16x12 cm in diameter was palpated in the right lower quadrant. On laboratory examination, he had anemia, trombositopenia, and showed sings of uric acid nephropathy. In smears of both lumbar puncture and bone marrow aspiration blastic infiltrations showing features of L3 cells were found. Fine needle aspiration biopsy of abdominal mass also showed similar atypical lymphoid cells. These findings suggested a diagnosis of Burkitt's Lymphoma with leukemic transformation. Immediate supportive treatment was commenced, but the patient failed to respond and died in twenty-four hours after admission.

Postmortem examination: The body had an undefined offensive odour and there were extensive purple-black echymotic areas on the skin. Bilateral exophthalmos and a swelling in both right parotid gland and left submandibular area were seen. Fine needle aspiration biopsy was performed from these two masses giving the feel of crepitation on palpation. Following aspiration where little hemorrhagic fluid was taken both of the masses disappeared. The body was opened by classic "Y" incision. Thoracal cavity contained 400-cc hemorrhagic fluid while 50-cc fluid was present in pericardial cavity. No obvious lesion was seen intrathoracically. When abdomen was opened, an enlarged liver with yellow granular surface filling upper abdomen was seen. The lower abdominal cavity was filled with a large necrotic tumorous mass covering the intestinal surfaces, measuring 15x10x10 cm. There was a perforation site on the mesenteric side of the colonic wall. The mesentery of the colon contained numerous enlarged lymph nodes. The kidneys were also enlarged with lobulated surfaces and the hilum of the left kidney was filled with a necrotic mass. When cranial cavity was opened

hemorrhage was seen on the dura with no other mass lesion.

Macroscopical findings: The liver was sponge-like containing multiple cystic cavities on the cut surface. Irregular yellow-white small areas were present in corteges of both kidneys, and also an irregular infiltrating lesion was seen in the left renal hilum. The cut surface of the tumorous mass originated from the intestinal wall had a sponge-like appearance and infiltrated the mesentery causing adhesions between intestinal loops. In the cut surfaces of the brain, multiple cysts similar to the ones in the liver were presented, particularly in the white matter surrounding the lateral ventricles (Fig. 1). Other organs looked macroscopically normal.

Microscopical findings: The light microscopic examination revealed a diffuse lymphoma consisting of small non-cleaved atypical lymphoid cells with L3 morphology infiltrating the intestinal wall, suggesting Burkitt's Lymphoma. Although this tumour was located in the intestinal wall, many organs or tissues



Figure 1: In the cut surface of the brain, multipl cysts were presented (arrows) particularly in the white matter surrounding the lateral ventricles.

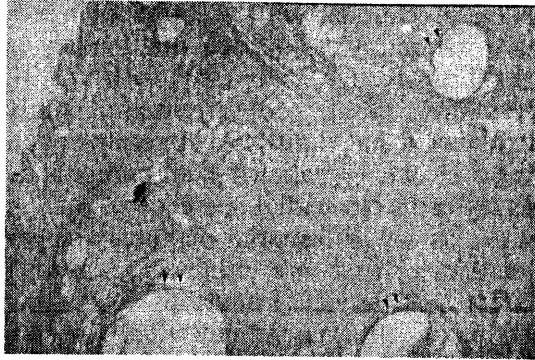


Figure 2: Burkitt's lymphoma infiltrating duodenal wall with gas-filled cysts (arrowheads) within the tumor tissue (HEEx40).including kidneys, intraabdominal and left renal lymph nodes, gall bladder, dura, pancreas and thymus were also infiltrated.

Another most important histologic finding was gas-filled multiple cysts, which were lined by groups of bacilli found in all of the organs including the tumour tissue (Fig.2), except testicles with no inflammatory reaction surrounding the cystic spaces. In addition to

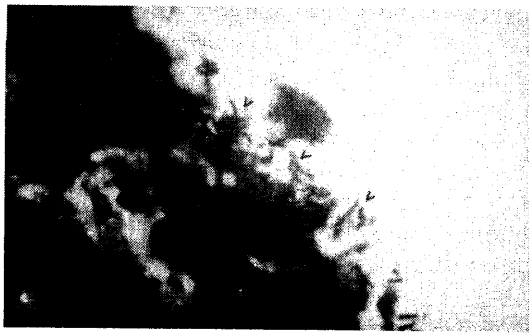


Figure 3: Gram positive rods (arrowheads) with no obvious spores lining the cyst walls (Gram stain;oil immersion).

these findings, cytological examination of the fine needle aspirations of both right parotid lodge and left submandibular area showed small non-cleaved lymphoid cells. Immunohistochemical study of the paraffin blocks revealed membranous positive staining of the tumour cells with CD45 (NCL-LCA; 1:20), CD20 (Zymed 18-0088; 1:50) and CD10 (NCL-CD10-270; 1:30) confirming B cell immunophenotype, and also CD3 (Dako-M7193; 1:50) was negative. On microbiological

consultation, gram stain showed gram-positive rods lined gas-filled cysts, with no obvious spores (Fig.3), suggesting Clostridial bacteremia.

Discussion

Macroscopical and microscopical findings of our postmortem case revealed abdominal Burkitt's Lymphoma causing perforation on the intestinal wall. A second pathologic feature was a gram-positive basil septicemia caused possibly by an anaerobic clostridium group. Clostridia were considered as the responsible organisms because of many findings consistent with clostridium septicemia including purple-black discoloration of the skin, offensive odour of the body, cystic changes without inflammatory reaction in many tissues, and also gram positive staining.

The Clostridium genus comprises anaerobic, gram-positive and spore-forming bacilli widely distributed in nature, being responsible for various histotoxic clostridial syndromes, which are caused by specific toxins (e.g. enteric diseases, neurological syndromes, soft tissue infections) (1,2). *C.perfringens*, the most frequent clinical isolate, was the first described member of this genus (2). It is found in soil and normal intestinal flora of humans and animals (1-3). It has a distinctive box-car appearance on gram stain of clinical material. It is immotile and its spores are rarely seen in clinical specimens or in culture (2). *C.septicum*, on the other hand, is a motile and spore-forming rod, a feature distinguishing it from *C.perfringens* (6).

Gas gangrene or clostridial myonecrosis is a rare infection characterized by rapidly progressive, life threatening skeletal muscle necrosis with systemic toxicity (2,3). *C.perfringens* is the most frequent pathogen accounting for approximately 80% of cases with positive cultures (2). Other clostridial species such as *C.novyi* (10-40%), *C.septicum* (5-20%), and also *C.histolyticum*, *C.fallax*, *C.bifermentans* may also be responsible for gas gangrene. In some cases, there are several types of clostridium at the infected

sites, and also other multiple species of bacteria (such as *E.coli*, *Enterobacter*, *Enterococci*) may accomplish them (2,3). α -Toxin is the most important of all, which accounts for the dramatic systemic consequences of gas gangrene (2). Gas gangrene often occurs after trauma or surgery of intestinal or biliary tract, and occasionally may occur spontaneously (2,3). Spontaneous gas gangrene or non-traumatic clostridial myonecrosis has been defined in the absence of any external wound or trauma. This entity occurs most often in association with a haematological or colonic malignancy, and generally either *C.perfringens* or *C.septicum* is the responsible microorganism (3-5,9). Kaiser et al. (4) documented 23 cases of non-traumatic clostridial myonecrosis associated with benign or malignant gastrointestinal diseases (i.e. adenocarcinoma or leukemic/ lymphomatous infiltration) presenting ulcerative areas. In 80% of these patients, the malignancy was found incidentally on additional examination or at autopsy. The primary source of the organism is probably mucosal ulceration or perforation of the intestinal tract (3,4). In addition, septic abortion, gangrenous cholecystitis and diabetes mellitus may facilitate non-traumatic clostridial myonecrosis (4). In our case, a similar intestinal perforation was determined. Larson et al. (6) noted that the infection of *C. septicum* is likely associated with malignancy or immunosuppression, and it occurs spontaneously without trauma in contrast to *C.perfringens* infections. The patients with *C.septicum* had a higher incidence of myonecrosis and a higher mortality compared with the other clostridial species. Also clinical observations suggested an opportunistic role for *C.septicum* in patients with either malignancy or immunosuppression (6,7). Johnson et al. (8) reported that humoral responses to α -toxin during *C.septicum* infection could be related to the host's clinical condition and immune status. They also noted that *C.septicum* infection might display a clinical status ranging from uncomplicated bacteraemia to myonecrosis and gas gangrene. According to some published cases, sur-

vival of patients with *C.septicum* infection having an associated malignancy is ranging from 35% to 50% (5,9). Rampling et al. (10) reported a study explaining that *C.difficile* infection developed in twenty patients with malignancy as different clostridial specie.

In the differential diagnosis of gas gangrene, there are other gas forming deep soft tissue infections including crepitant cellulitis, streptococcal fasciitis, necrotising fasciitis due to mixed aerobic-anaerobic infections and necrotising cellulitis. Extensive gas formation and only minor or no systemic toxicity signs are found in crepitant cellulitis (2). Generally, non-clostridial crepitant cellulitis develops at the infected region together with several other types of bacteria including of *E.coli*, *Klebsiella*, *Bacteroides*, *Peptostreptococcus*, and various streptococci (3).

In the presented case, bacteraemia was characterized by extensive cystic change lined by bacilli in various organs and tissues except testicles. There was no inflammatory reaction surrounding the cystic spaces. Although microbiologic cultures could not be performed, gram stain revealed gram-positive rods with no obvious spores, suggesting a diagnosis of clostridium genus. According to the related literature, *C.septicum* is a spore-forming agent, and it is the most common lethal organism in the cases of malignancy, whereas in our case no spores were observed. In our case, anaerobic condition seemed to have developed by the abdominal tumour infiltrating the intestinal wall forming large necrotic areas and causing perforation of the intestinal wall.

In summary, the presented autopsy case is important to indicate that clostridial infection should be considered as an etiological cause when clinical suspicion is present and necessary diagnostic tests should be performed for diagnosis.

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