

POSTER PRESENTATION

2. INFECTIVE PATHOLOGY

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The management of asymptomatic bacteriuria during the reactivation of CMV infection in renal transplant recipients

KEYWORDS: Kidney transplantation; Cytomegalovirus infections; Bacteriuria

INTRODUCTION

Not even one decade ago, despite advances in selective immunosuppression and refinements in prophylaxis regimen, infections were considered as a major cause of morbidity, graft loss and mortality after solid organ transplantation (1). The risk of infection, particularly opportunistic infection, in the transplant recipients is largely determined by the interactions between epidemiological exposures, the immunosuppression, and antimicrobial prophylaxis. The purpose of this paper was to review the interactions within transplant infective complications as CMV infection and asymptomatic bacteriuria, with possible impact to graft function in kidney transplanted patients.

MATERIAL AND METHODS

We evaluated 60 patients undergoing isolated kidney transplantation during the period from October 1996 till March 1999 in our transplantation center. The immunosuppression was performed as triple or quadruple protocol with ATG induction. Patients received antifungal prophylaxis (parenteral fluconazole and oral nystatin); antiviral prophylaxis (oral ganciclovir 1.5g three times a day for 3 months either with intravenous immunoglobulin or intravenous ganciclovir 2.5mg/kg twice a day during antilymphocyte therapy) and preoperative antibiotic prophylaxis. Acute rejections were treated with steroid boluses dosed 250-500 mg in 3 consecutive days. The asymptomatic bacteriuria was diagnosed as the absence of clinical findings as fever, shivering, or dysuria, but with positive findings in urine analyses, and consecutive urine cultures. The CMV infection detection and monitoring were carried out by standard virological assays of CMV and serology, as well as white blood cell count. This retrospective review was designed with the following relations

between CMV infection and asymptomatic bacteriuria under transplantation conditions (as transplantation type with attaching events as rejection, immunosuppression influence, ATG therapy) and medicament treatment of the infections.

RESULTS

The CMV reactivation was diagnosed in 8 patients (13.3%). Seven of them (87.5%) received triple immunosuppressive therapy and 1 patient (12.5%) managed with quadruple immunosuppression with ATG. In the study population 4 acute rejection episodes were verified. There was no transplant loss or deaths during the follow-up period. The mean interval from transplantation to CMV reactivation was 4.7 months. Reactivation appeared in all monitored patients. In the transplantation group 8 patients were treated for CMV infection; 4 patients (50%) with mild infection and 4 patients with asymptomatic infection. The blood count disorders for the duration of CMV infection were leukocytosis in 3 patients, neutrophilia in 3 patients, and thrombocytopenia in 8 recipients. CMV excretion from urine was observed in 7 (87.5%) infected recipients. In case of a CMV reinfection, ganciclovir was intravenously administered for therapy purposes until resolution of the clinical symptoms or viremia and afterwards continuously by oral application. In the CMV group of 8 patients undergoing ganciclovir administration, the average graft survival was 4 years. No significant correlation was noticed between ATG administration and infection outbreak. Seven patients with CMV infection didn't develop rejection episodes and displayed an irrelevant period between CMV infection outbreak and rejection. *Pseudomonas aeruginosa*, *Enterococcus species*, and *E.colli* were isolated by the urine culture in the transplant recipients as causes of asymptomatic bacteriuria. The urine sediment was quantitatively estimated as positive for proteins, nitrates, leukocytes and bacteria in 5 patients considered to have asymptomatic bacteriuria. Acute maxillary sinusitis, acute mild infections of the upper respiratory tract, and active hepatitis C, each in only one patient respectively, were diagnosed and treated as recidivate infections. In only one female patient the CMV reactivation with asymptomatic bacteriuria with *Enterococcus faecalis* was followed by a mild transplant dysfunction presented by pain in the graft location and worsening of the kidney function parameters (elevation of the serum urea to 9.1mmol/l and creatinine to 148 μmol/l). On the second day of antibiotic, antiviral and antirejection treatment the infective symptoms began to resolve and the function parameters (laboratory findings) normalized.

DISCUSSION

The CMV infection is still found as a common, serious complication of transplantation, that may trigger the organ dysfunction, or lead to severe diseases, which untreated might have a negative course for the graft function (3). In this study we have also reconsidered the recent results (2) on the frequency of urinary tract infections (UTI) as infectious complications after renal transplantation and found a similar incidence of asymptomatic bacteriuria in our recipients. The microbial isolation has revealed the ubiquitous germs for the urinary tract infection. Our experience points out the importance of differentiating the infection from acute rejection. The diagnostic approach reported by Smith et al. facilitates the monitoring of acute rejection and UTI and could provide a strategy for the diagnosis of acute rejection and for its differentiation from UTI. It has also proved the reliability of the serum C-reactive protein level (sCRP) in identifying the renal-transplant dysfunction due to rejection, infection, cyclosporine A nephrotoxicity or acute tubular necrosis (4). Comparing our results to the recent data, it is to notice that the therapy approach we applied prevented the potential bacteriemia. We estimate that antifungal, antiviral prophylaxis is mandatory in the setting of either antilymphocyte induction or rescue therapy and was also effective in reducing the severity of CMV and other infections. Preoperative application of prophylactic antibiotics and administration of nystatin in our patients reduced the incidence of bacterial and fungal infection. Mainly the urine infections were considered as

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numerous infections with no graft threatening course. Yet in only one case we had the CMV infection accompanied with asymptomatic bacteriuria followed by a low grade graft dysfunction. The positive effects of administered antimicrobial prophylaxis and therapy stand out in fast resolution of clinical signs and laboratory findings. Based on the literature data (5) and our study results, we conclude that infective agents monitoring is necessary for an adequate therapy approach providing consecutive better allograft function. The antimicrobial prophylaxis we provided is mandatory in the setting of either the anti-lymphocyte induction or rescue therapy. We concluded that a useful prophylaxis of infections and though-out immunosuppression might contribute to the adequate approach aimed to preserve the graft function.

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Coecal amoeboma: A case report

KEYWORDS: Amebiasis; Large intestine; Pathology

INTRODUCTION

Amebae cause dysentery-bloody diarrhea, intestinal pain and fever; when they attach to the colonic epithelium, lyse colonic epithelial cells, and invade the bowel wall. Ameba proteins that may be involved in tissue invasion include lecithin on the parasite surface, a channel-forming protein that induces pores in the plasma membrane of colonic epithelial cells and lyses them and cysteine proteinases-able to break down proteins of the extracellular matrix (1). Histologically, a fortunate biopsy shows the typical liquefactive inflammation and undermined ulcerations penetrating the colonic submucosa that make the term "Entamoeba histolytica" so appropriate. Careful inspection at high magnification then demonstrates individual, rounded, amebic trophozoites with their bland, round nucleus and perhaps some ingested erythrocytes. The amebae are larger than macrophages, and the cells appear nonhuman. Special stain with PAS aids in the identification of the glycogen-rich Entamoeba, but well-prepared routine stains appear equally useful (2). We report an uncommon lesion - amoeboma, a napkin-like constrictive lesion, which represents a focus of profuse granulation tissue response to the parasites and is sometimes mistaken for a colonic tumor.

MATERIALS AND METHODS

Chief Complaints: A woman 64-years old, from a village at the Vranje region. Eight months ago, she had fever, bloody diarrhea containing mucus, accompanied by lower abdominal pains and cramps relieved by defecation. During the last two months she had fatigue, weakness, iron-deficiency anemia and weight loss. For the last week, the syndrome of intestinal obstruction was marked by abdominal pain and distention, vomiting, obstipation and failure to pass flatus. After the right colectomy at night because of the cecal stenotic tumor, surgical material was sent to pathology.

RESULTS

Macroscopically, coecal occlusive submucosal tumor 6cm in longitudinal diameter, hard and yellow-brown in colour was discovered. On section, gran-

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ulomatous structure was seen. Microscopically, confluent granulomas containing lympho-plasmocytes, monocytes, granulocytes, especially eosinophils, giant cells of foreign body, foamy macrophages, surrounded by dense fibromatous tissue, were found. Amebae had the appearance of macrophages because of their comparable size and large number of vacuoles; the parasites, however, had a smaller nucleus, which contained a large karyosome. Amebae had PAS positive reaction in their cytoplasm. Pathological diagnosis was: coecal amoeboma.

DISCUSSION AND CONCLUSION

Ameboma is an uncommon, a napkin-like constrictive lesion. It represents a focus of profuse granulation tissue response to the parasites; because that, amoeboma was clinically mistaken for a colonic cancer. The most important histological characteristics for recognizing amoeboma were eosinophilic cell infiltration and amebae morphology.

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Crimean-congo hemorrhagic fever - A case review

KEYWORDS: Crimean-Congo; Hemorrhagic fever virus; Serotyping

INTRODUCTION

Crimean Congo hemorrhagic fever is one of the most severe human viral disease. The disease is endemic in many countries in Asia, Africa, middle East, south and east Europe. The virus which causes Crimean Congo hemorrhagic fever (CCHF) is a *Nairovirus* in the *Bunyaviridae* family (1). Although primarily a zoonosis, sporadic cases and outbreaks of CCHF affect humans. Vector, reservoir is tick *Ixoid*, mostly of the *Hyalomma* genus and the virus is transmitted to humans by the bite of ticks or by the contact with blood or tissues from human patients or infected livestock (1). After an incubation period of 3-12 days, the patient has onset of fever, chills, myalgia, headache, dizziness, tachycardia followed by hemorrhagic state with melaena, haematuria, epistaxis, petechiae, ecchymoses and bleeding from the gums. The mortality rate approximately 30% (with death occurring in the second week of illness) (2).

CLINICAL FEATURES

Female patient in the age of 43, has been hospitalized due to sudden onset of fever, headache, vomiting and abdominal pain. In hospital she became afebrile, but she started vomiting blood, also fresh blood appeared in stool. Laboratory analysis showed anemia, thrombocytopenia, and increased level of serum transaminases. In following clinical course of illness, patient is delirious, adynamic, hypotensive, anuric and with intensive bleeding from gastrointestinal and genital system. Multiple hematomas had been found on her skin, as well as on the parts of skin where medications were applied. During next few days her condition became worse, she is unconscious, anuric, cyanotic, with multiple edema on extremities, large vaginal coagulum and with appearance of hemorrhagic secretion in aspirated fluid from respiratory tract. Three days after admission to hospital due to sudden onset of cardiac arrest, in the spite of medicamentous measures of reanimation, she died.

PATHOLOGIC FEATURES

Severe bleeding from the mucous membranes and internal organs were

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found, particularly emphasized on liver, kidneys, heart, brain and other organs. Noticeable focal hepatocellular necrosis and focal necrosis in both kidneys were also found. Described condition represents the pathological features of distinct hemorrhagic diathesis, which led to shock and death. Widespread hepatocellular necrosis with focal microvesicular steatosis and multiple intracytoplasmatic microvesicular inclusions were the most striking morphological findings. Diffuse necrosis of renal tissue was also found. Recent hemorrhage in lungs, cardiac muscle, glandula suprarenal, spleen and gastric mucosa were found. Lymphoid depletion was detected in lymph nodes. The Polimerase Chain Reaction -PCR (by reverse transcriptase synthesized CCHF virus was used) has been applied in analyzing serum and tissue. Serological testing (A. Pappa, Thessaloniki, Greece) and testing from paraffin molded tissue (SR Zaki, CDC Atlanta, USA) were positive.

DISCUSSION AND CONCLUSION

Pathologic findings at autopsy CCHF, include widespread hemorrhages of skin, mucous membranes, pleura, peritoneum (2). Necrosis is frequent in all organs and tissues, often ischemic by nature. Our autopsy results had similar pathologic findings, and by PCR method we confirmed ethiopathogenesis of this disease.

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Trichinellosis-parasitic disease of humans and animals

KEYWORDS: Trichinosis; Complications; Autopsy; Case report

Trichinellosis is a parasitic infection of humans and some sorts of mammals, caused by helminths from the *Trichinella* group. This is a cosmopolitan disease and the infected pork meat is the main source of the infection. This infectious disease appears sporadically or in the form of a small (family) epidemic. A 67-year old patient was admitted at the Department of Neurology with a heavy headache of the migrenous type, exuberant periorbital swelling, high temperature, myalgia, weakness, vomiting, diarrhoea, hemiplegia, dysphagia and heavy breathing. On the basis of clinical evaluation and laboratory analyses Dexamethason and Tiabendazol were introduced. The general condition deteriorated rapidly and cardiopulmonary insufficiency led to a fatal outcome. Clinically suspected Trichinellosis was confirmed by autopsy. The larvae of Trichinellosis were found in the skeletal, intercostal and diaphragm muscles. There are different types of Trichinellosis - from rudiment, abortive to deadly ones. This was a case of the deadly type of this parasitic disease developing cardiopulmonary insufficiency which caused death in the active stage of the disease.



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Cryptococcus infection - A case report

Giardia lamblia infection - A case report

KEYWORDS: Cryptococcal meningitis; Skin infections; Case report

KEYWORDS: Giardiasis; Gastrectomy; Pathology

Cryptococcus may arise in healthy individuals but more commonly it occurs as an opportunistic infection particularly in patients with leukemia, lymphoma, Hodgkin's disease or AIDS. The disease is caused by *Cryptococcus neoformans*. The lungs are usually the primary sites of localization, but the infection may remain asymptomatic. The most frequent manifestation of cryptococcal infection is meningitis. A case of a 46-year-old male with cryptococcus infection is reported. The patient was hospitalized at the Clinic for Dermatovenerologic Diseases because of the skin lesion on his back consisted of a tumor formation surrounded with several satellite nodes. After diagnosing cryptococcosis, the patient developed cryptococcal meningitis. Despite the application of the therapy the patient died nine months later. During the examinations, the primary cause of the immunodeficient state wasn't found. The patient was TBC, HIV, HV negative and no autoimmune disease was diagnosed. We received a skin biopsy specimen with dimension 3 x 3 x 2 mm. Using the standard histology staining with hematoxylin eosin and alcian blue, we have presented the cryptococcus spores and the surrounding gelatinous capsule. Histology examination exhibited many subepidermally localized PAS positive spores within pseudocystic formations surrounded with numerous multinucleated giant cells and histiocytes. Among these formations a mixed inflammatory infiltrate was present. Alcian blue staining confirmed the thick gelatinous capsule.

The flagellate protozoan *Giardia lamblia* is the commonest intestinal parasite in many of the countries of Europe. Giardiasis may occur in a coeliac disease, following partial gastrectomy and in gastrointestinal immunodeficiency syndromes. The infection may be subclinical or may cause acute or chronic diarrhea, steatorrhea or constipation. Epidemiological evidence points to contaminated water supplies as the vehicle of infection. Many of these patients were infected following a travel abroad and because *Giardia* cysts are not killed by chlorine, *Giardia* is endemic in public water supplies that are not filtered through sand in streams accessed by campers. *Giardia* exists in two forms: (1) a dormant but infectious cysts spread by the fecal - oral route from person to person (as well as from cats, bears and beavers to person), and (2) trophozoites that multiply in the intestinal lumen and cause the disease. *Giardia* trophozoites have two nuclei rather than one, are flagellated, reside in the duodenum rather than the colon, adhere to but do not invade intestinal epithelial cells, and so cause diarrhea rather than dysentery. **Chief complaint:** A 74-years old male who had already undergone Billroth II gastrectomy (induced by duodenal peptic ulcer), was hospitalized to the Clinic of Gastroenterology with the following symptoms: abdominal discomfort, flatulence, diarrhea and steatorrhea. In addition to anemia, the patient had nausea, vomiting and significant weight loss (raising the specter of some hidden malignancy). In the distal part of the resected stomach, a stenosis resembling the stump carcinoma was seen on endoscopy. In biopsies of the gastric mucosa from the stenosis and the surrounding area, trophozoites were most numerous in the zone of foveolar and surface epithelium. Trophozoites were confined to the laminal surface. Adhering to the epithelium, trophozoites mostly appeared as sickle-shaped bodies with their concave surface facing the epithelium. Sectioned coronally, numerous protozoa were pear-shaped, bilaterally symmetrical, from 10 - 21 µm long and 5-15 µm wide and with two large nuclei anteriorly and four pairs of flagella project from the tail, both sides and the center. Viewed from the side, trophozoites appear as arched or angulated structures. Finally, the atrophic gastritis with pyloric metaplasia and with mixed inflammatory infiltrate associated with dense collagen proliferation was observed. The stenosis resulted from fibroplasia in the lamina propria. *Giardia* may block nutrient absorption by covering the surface of the epithelial cells, or by mechanically damaging the microvilli, thus reducing the absorptive area. Antibody-mediated immunity, including secretory IgA, is important in the resistance to *Giardia* because gammaglobulinemic individuals are severely affected by the parasite. Immunity to *Giardia*, however, is limited by the fact that the parasite is able to vary its major surface proteins into antigenically distinct forms. The localization of giardiasis in the gastric mucosa, in our case, can be explained by the former partial gastrectomy.



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Leishmaniasis (kala-azar) of the bone marrow

KEYWORDS: Leishmaniasis; Bone marrow; Pathology

Visceral leishmaniasis is an uncommon infection in our country except in some parts of Montenegro where is endemic. Atypical clinical presentation of leishmaniasis with generalized lymphadenopathy, hepatosplenomegaly and pancytopenia accompanied by systemic symptoms may imitate a lymphoma. The bone marrow aspirate is very useful and sometimes necessary for establishing the diagnosis. In cases with hypocellular and packed marrow or secondary myelofibrosis bone marrow, trephine biopsy is necessary for the diagnosis. We analyzed 12 patients in whom the diagnosis of visceral leishmaniasis was obtained by a histopathological examination of the bone marrow trephine biopsy. All specimens were stained with H&E, Giemsa stain, PAS and methematin silver method. In 5 specimens the additional immunocytochemical methods were performed to determine the type and clonality of lymphoid infiltrates. The bone marrow was hypercellular in all, 75% (60%-100%). The dominant change was hyperplasia of all three hematopoietic lineages with a minimal left shift and eosinophilia. There was an increase of lymphoid cells, more than 20% of all bone marrow cells, with plasmacytosis (5%-15%). Interstitial infiltration was far more common; in one case lymphoid infiltration was nodular. In 4 specimens atypical large B cells were seen but they were polyclonal. *Leishmania donovani* were seen in macrophages and between the hematopoietic cells. The organisms were PAS-. Giemsa stain demonstrated a small paranuclear basophilic body, known as kinetoplast giving the organism a characteristic "double dot" appearance. Detailed morphological analysis together with histochemical staining are necessary for the diagnosis of kala-azar. The immunocytochemical analysis is sometimes useful in establishing the nature of lymphoid infiltrates.

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Viral hemorrhagic fevers (Hantavirus-pulmonal and renal syndrome)

KEYWORDS: Hantavirus; Hemorrhagic fever; Renal syndrome; Pulmonary syndrome

Hemorrhagic fevers are febrile diseases which are characterized by disturbed blood coagulation and disorders within the vascular system. They are caused by RNA viruses of the Bunyaviridae. These are the zoonotic diseases transmitted to humans from rodents via the infected urine, saliva and respiration. Hantaan virus Seoul, Hanta virus Dobrava/Belgrade, Hanta virus Puumala virus produce the syndrome of hemorrhagic fever with renal failure (HFRS). A patient at the age of 44, admitted at the Clinic for Infective Diseases for the reasons of: myalgia, tachypnea, high temperature, anxiousness, malaise, vomiting and oliguria. Trough inspection, subconjunctival suffusion, hemorrhagic rash distributed on thighs, hematomas and ascites were found. Ultrasonography proved ascites and pointed to the enlargement of the kidneys. Catheterization was performed; but the patient's general condition became worse with the signs of the hemorrhagic syndrome, ending lethally. On the autopsy, the morphologic changes, such as hemorrhages involving all tissues, most likely resembling the hemorrhagic fever (Hantaan virus infection was proved from blood samples, postmortally). The diagnosis was established on the basis of serologic findings at the Institute for Immunology and Virology - Torlac, in the laboratory for hemorrhagic fevers. The very diagnosis of the HVI was set through serologic tests for the particular viral kind, but for the reason of a low incidence of this particular disease, unfortunately, in the majority of the cases the true nature of the disease can be determined only after autopsy.