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Prevalence and Causes of Pyogenic Liver Abscess in Patients with Diabetes Mellitus

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Abstract The article presents an analysis of the epidemiological aspects of liver abscess occurring against the background of diabetes mellitus, highlights general information on the prevalence and causes of pyogenic liver abscess. Data on the frequency of development and treatment outcomes of focal purulent-destructive liver damage in various regions of the world are presented. The main etiological factors depending on the population are also considered. The analysis of the literature data indicates that the relevance of systematization of adequate diagnosis and treatment tactics in this category of patients remains.

Keywords Pyogenic liver abscess, Diabetes mellitus, Puncture-drainage interventions, Purulent infection

1. Introduction

Pyogenic liver abscess (PLA), which is a purulent infection of the liver parenchyma, remains a pathological condition associated with mortality and is reported in China and around the world, especially in Asia. The incidence of PLA varies worldwide and continues to increase annually [2,5,22]. PLA is reported worldwide, but its frequency varies significantly between countries (from 8 to 22 patients per 1,000,000 people) [28]. The incidence of PLA in Asia is higher than in Western countries, with the highest rate in Taiwan, China [26, 32]. In Taiwan, the annual incidence of PLA among all ages gradually increased from 10.83 to 15.45 cases per 100,000 people from 2000 to 2011 [11]. In northeast China, a large population-based retrospective study reported an incidence of 5.7 cases per 100,000 people [13]. In the USA, a large study described an incidence of 3.59 cases per 100,000 people. PLA accompanies many diseases. These diseases are important risk factors and include diabetes mellitus (DM), malignancies, cholangitis, urinary tract diseases, pneumonia, cardiovascular diseases, autoimmune diseases and malnutrition [15]. In recent years, patients with PLA and concomitant DM have become more common in this hospital, and previous case reports show that DM leads to an increased risk of PLA [31]. Tian LT et al. provided a comprehensive perspective on PLAs [32], but are there differences between patients with PLA with and without concomitant diabetes, especially in Southern China. Regional differences in the use of new technologies have led to the fact that the death rate remains high. A review by Chan KS et al. Of the 16 articles, the PLA showed a mortality rate from 0% to 15.7% (11 articles) [9].

At the beginning of the 20th century, the most common route of infection with PLA was portal phlebitis, often secondary to acute appendicitis, and the overall mortality rate reached 80%. However, the various pathways of infection described since then include biliary tract concretions, portal vein, hepatic artery, cryptogenic pathway, and neighboring infections [4,20]. Some studies have reported that DM is a risk factor for PLA [32]. Recent studies have shown that changes in the biliary tract (including acute cholecystitis, common bile duct stones, chronic pancreatitis and tumor obstruction of the biliary tract) are the main route of infection with PLA [19,23]. The number of cases of cryptogenic liver abscess is increasing, and Thomas McNeil et al. no predisposing conditions (cryptogenic) were found in 14 (18%) patients in their cohort [21].

The clinical manifestations of PLA are nonspecific. The main symptoms are fever and chills, and there may also be pain in the right hypochondrium/discomfort in the epigastrium, but sometimes the symptoms are unclear. Early diagnoses of PLA mainly depend on imaging studies. B-ultrasound is the first method of choice, followed by computed tomography (CT) of the abdominal cavity and magnetic resonance imaging (MRI). Risk factors for PLA include age, male gender, diabetes mellitus, gallstones, immunodeficiency, and the use of proton pump inhibitors [1,14,28]. And the pathogens associated with PLA are mainly gram-negative bacilli, but there are reports of mixed infections of streptococcus and anaerobic bacteria.

Ultrasound is the first tool for examining liver abscesses, since it is simple and accurate and does not lead to radiation exposure, it must be performed by experienced specialists.

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Ultrasound is simple and non-invasive, and it displays the shape, size, number, location, dilution and separation of abscesses in real time. Although the specificity of ultrasound can reach more than 85%, there are deviations in the observations of air cavities and separation of abscesses. CT specificity is above 95%, and liver abscesses with a diameter of about 0.5 cm are clearly detected. Diagnostic criteria for atypical liver abscesses in CT examinations may be "petal symptom" and "cluster symptom" and other indirect signs of problems with the biliary tract. Some studies have shown that for K. pneumoniae-associated liver abscesses, the most common visualizing manifestations are right-lobed single abscesses in the liver parenchyma with indistinct boundaries, which are mostly solid and multicameral, and with air volumes in the abscess, which are significantly larger than the commonly observed liver abscesses not associated with K. Pneumoniae [33]. The specificity and sensitivity of an MRI scan are not as clear, but the "ring target mark" on an CT scan is an important key to the diagnosis of a liver abscess.

The use of percutaneous aspiration under ultrasound control followed by continuous catheter drainage along with parenteral antibacterial therapy has shown a high level of success. Since 1953, intravenous administration of antibiotics after puncture and drainage of a liver abscess has become a classic method of treating bacterial liver abscesses [6,24,27,34,35]. Indications for puncture or catheter drainage are: 1) liver abscess with ineffective drug treatment or constant increase in body temperature; (2) liver abscess with wall formation and dilution, which tends to mature; (3) abscess with a diameter of 3-5 cm, which can be punctured and drained, and an abscess with a diameter of more than 5 cm, which can be drained with a tube; (4) abscess liver in patients with normal coagulation function and intolerance to surgery. For abscesses larger than 10 cm, two drainage tubes can be installed at different angles to facilitate complete drainage and, if necessary, rinse the purulent cavity [3]. Meta-analysis reported a success rate of 77.8% of percutaneous needle aspiration (PNA) cases and 96.1% of percutaneous catheter drainage (PCD) cases. PNA or PCD achieved clinical remission in a shorter time than antibiotic therapy alone. PCD is the first choice for the treatment of liver abscesses, because not only it is simple and cheap, but also because even with multiple liver abscesses that are difficult to treat, the treatment success rate exceeds 90% [8]. Ahmed S et al. I found that PCD is safe and sufficient even for patients with giant PLA [7]. The drainage tubes were removed after the patient's laboratory examination and clinical parameters returned to normal, the drainage fluid diuresis was less than 5 ml/day, and the imaging results confirmed that the diameter of the purulent cavity after drainage was less than 2 cm.

In the Nie S study, (2023) [25] microbiological productivity, including pus and blood cultures, was 72.6% (77/106), which is similar to the results of the Singapore study [29]. The main isolates were K. Pneumoniae (42 cases 54.5%) and E. Coli (27 cases 35.1%). Over the past three decades, K. Pneumoniae has become the main pathogen and the sole leading cause of PLA in South and East Asia, including India, Korea, Singapore, Hong Kong, mainland China and Taiwan. In a nationwide prospective study of PLA in Korea, K. Pneumoniae was the main etiological organism [23]. Highly invasive K. Pneumoniae strains possess genes responsible for the phenotype of increased mucosal viscosity associated with serotypes K1 and K2. These highly invasive strains of K. Pneumoniae can cause colonization of the intestine in healthy people, which can lead to pathogenesis by opportunistic microorganisms after the resulting changes in the composition of the microbiota, especially a decrease in the number of lactobacilli [10]. When this occurs during bacterial translocation, pathogens can circulate in the liver through the portal vein, causing liver abscesses. After colonization of the gastrointestinal tract of K. Pneumoniae as a result of environmental exposure or fecal-oral transmission, bacteria can cross the intestinal barrier and enter the liver. Asian populations may be predisposed to colonization of the intestine by highly toxic strains of K. pneumoniae, which may explain the high prevalence of K. Pneumoniae in patients with NOA in Asia. E. Coli is the most common causative agent of liver biliary tract abscess, accounting for 20-35% of patients infected with E. coli alone [30], followed by K. Pneumoniae. This may be the main reason for the differences in etiology between Asia and Europe. The main pathogen found in Europe was E. coli, which accounts for 60% of PLA.

Lee CH, et al. (2021) [17] retrospectively analyzed data on patients with PLA who were hospitalized between 2005 and 2018 at three tertiary level hospitals in Jeonbuk Province, South Korea. Long-term hospital stay was defined as the length of hospital stay of more than 21 days. The study included 648 patients (406 men and 242 women) diagnosed with pyogenic liver abscess. The average maximum diameter of the liver abscess was 5.4±2.6 cm, 74.9% of the lesions were single. The three groups were divided according to the maximum diameter of the abscess. Laboratory indicators indicated a more pronounced inflammatory condition and a higher incidence of complications and extrahepatic manifestations as the size of the abscess increased. The frequency of percutaneous catheter drainage, multiple drainage and rescue procedures, as well as the duration of drainage were also higher in the group with a large liver abscess. It should be noted that the duration of hospitalization and hospital-acquired mortality were significantly higher in the group with a large liver abscess. Multifactorial analysis showed that diabetes mellitus, hypoalbuminemia, high baseline levels of highly sensitive C-reactive protein (hf-CRP) and procalcitonin, as well as a large maximum abscess diameter were independent factors associated with prolonged hospital stay. With regard to hospital mortality, acute renal failure upon admission and the maximum diameter of the abscess were independent factors associated with hospital mortality. The large maximum diameter of the liver abscess at admission indicated prolonged hospitalization and an unfavorable prognosis. More aggressive treatment strategies with careful monitoring are justified in patients with large liver abscesses.

2. Materials and Methods

In a retrospective study, Du Z, et al. (2020) [12] examined patients who were diagnosed with predominantly PLA at the First Affiliated Hospital of Xi'an Jiaotong University between January 2011 and January 2018. All PLA diagnoses were based on clinical features, imaging results, and laboratory tests of blood and purulent cultures. This study included 227 patients. Patients were first divided into two groups based on diagnoses with or without diabetes, and then patients with diabetes were further divided into two subgroups, groups with good and poor glycemic control. All patients with type II DM had a clear history of diabetes upon admission, and none of them were diagnosed after admission. DM patients with HbA1c levels <7% in the good control group and ≥ 7% in the poor control group were identified.

Chen SC, et al. (2005) investigated the clinical characteristics, outcome, and prognostic factors associated with mortality in patients with liver abscess caused by Escherichia coli. The data of 72 patients aged 18 years and older, who were diagnosed with liver abscess caused by E. coli in two medical centers in Taiwan between July 1996 and June 2002, were retrospectively analyzed. The total mortality rate was 26.4%. Most E. coli liver abscesses were solitary, affected the right lobe of the liver and included polymicrobial infections. The cause of liver abscess was the biliary system in 48 patients (66.7%). The most common concomitant diseases were DM (30.6%) and background malignancies (30.6%). Metastatic infection was detected in 4 patients (5.6%). Multifactorial analysis showed that the main malignant neoplasm (p=0.034), deep hypoalbuminemia (<2.5 g/dl) (p=0.008) and multiple abscesses (p=0.004) were the most significant prognostic factors of mortality. The predominant cause of liver abscess caused by E. coli was diseases of the biliary tract.

Meddings L, et al. [22] assessed the incidence of PLA and assessed the predictors of mortality in several population-based studies in North America. A nationwide sample of inpatient patients was used to identify all patients discharged for PLA (ICD-9 572.0) between 1994 and 2005. A multiparametric logistic regression analysis was performed to determine whether mortality was related to patient and hospital characteristics, including comorbidities, interventions, and bacterial cultures. The annual incidence of PLA among the U.S. population was determined and temporal changes were estimated using generalized linear regression models. As a result, 17,787 discharges with a total incidence of 3.6 PLA (95% confidence interval (CI): 3.5-3.7) per 100,000 population were identified. From 1994 to 2005, the average annual percentage increase in morbidity was 4.1% (95% CI:3.4-4.8; P<0.0001). Hospital mortality was 5.6% (95% CI:5.3-6.0). Mortality was associated with older age (65-84 vs. 18-34: odds ratio (OR) = 2,28 (1,48-3,51)); Medicaid (OR=1.74 (1.36-2.23)) and Medicare (OR=1.48 (1.18-1.85) compared to private insurance; concomitant diseases such as cirrhosis, chronic kidney failure and cancer. Patients who underwent percutaneous liver drainage had lower mortality, whereas surgical drainage and endoscopic retrograde cholangiopancreatography were not associated with mortality. The most frequently reported bacterial infections were Streptococcus species (29.5%) and Escherichia coli (18.1%). Patients with bacteremia or septicemia had an increased risk of death. The incidence of PLA is increasing and is associated with significant mortality, which is associated with several modifiable risk factors.

Li W, Chen H, (2018) [18] compared purulent liver abscesses in patients with and without diabetes mellitus: a retrospective study of 246 cases. The patients were in the teaching hospital from January 2012 to December 2016. The patients were divided into two groups depending on comorbidity with DM. The DM group was further divided into two subgroups according to the HbA1c concentration to find out whether glycemic control affects the clinical characteristics of patients with PLA with DM. X^2, Fisher's exact test and t-test were used to analyze and evaluate the differences between the two groups. 246 patients with PLA were identified, 90 (36.6%) of them had concomitant DM. Patients with DM were older, had higher levels of alkaline phosphatase and γ-glutamyltransferase, hypertension, weight loss, single abscess, combined antibacterial therapy with carbapenems and Klebsiella pneumoniae in blood cultures, but less often a history of abdominal surgery and Escherichia coli in their pus cultures. When patients with DM were compared with patients without DM, each of these differences was significant (p<0.05). Patients with PLA diabetes with poor glycemic control had a significantly higher proportion of fever and abscess of both lobes (P<0.05). Patients with PLA with DM are older, have more serious complications, higher prevalence of cardiovascular diseases, more widespread use of combined antibiotic therapy with carbapenem and the predominant causative agent K. pneumoniae, but these patients had fewer abdominal surgeries and fewer E. coli. infections. In addition, poorly controlled glycemia in DM patients with PLA is associated with a high incidence of fever and abscess of both lobes.

3. Results and Discussions

Serraino C, et al. [28] conducted a retrospective descriptive series of cases in one center, evaluating demographic characteristics, clinical manifestation models, etiological factors, microbiological etiology, and management of patients receiving PLA between 2000 and 2016. About 109 patients were identified. The majority of patients had fever (73%); pain in the right hypochondrium in 63.3%, vomiting and nausea in 28.4%. The most common laboratory anomaly among the included indicators was an increase in the level of C-reactive protein and fibrinogen in the blood in 98% and 93.9% of cases, respectively. Ultrasound of the abdominal cavity was a diagnostic study in 42.4% of cases; CT and MRI were performed in 51.1 and 3.3% of cases, respectively. The most common identified microorganism was E. coli (26.5%), followed by streptococcus (13.2%). Early antibiotic treatment

was initiated in all patients, and different approaches were required in 66.7% of cases. Needle aspiration of PLA was performed in 13 patients (11%) under the control of ultrasound or CT, and percutaneous drainage of the abscess was performed in 72 patients (67%). PLA is a diagnostically difficult problem due to its non-specific characteristics. The revealed microbiological result was a typical European spectrum with a predominance of Escherichia coli infections. Once identified, percutaneous drainage and antibiotic treatment are the mainstay of PLA treatment.

Ko MC, et al. (2019) [16] studied the age- and sex-related morbidity and relative risk of PLA in patients with DM2 type, and also assessed the combined effect of DM2 and other clinical risk factors for PLA on the incidence of PLA. The subjects of the study included 613,921 patients with DM2 and 614,613 control patients identified in 2000, who were followed up to the end of 2010. The Cox regression model was used to calculate the risk ratio (HR) and 95% (CI) of PLA with respect to DM2. During the 11-year follow-up, 5,336 patients with DM2 and 1,850 people from the control group were hospitalized for PLA, which accounts for a cumulative incidence of 0.87% and 0.30%, respectively. DM2 was significantly associated with an increased risk of PLA (HR 2.88; 95% CI 2.73-3.04). It was found that age and gender can significantly change the relationship between DM2 and PLA, with a higher heart rate observed in male patients and under the age of 45 years. Biliary tract diseases (HR, 8.60; 95% CI, 7.87-9.40) and cirrhosis of the liver (HR, 7.52; 95% CI, 6.58-8.59) can significantly increase the risk of PLA in patients with DM2. The increased risk of PLA in DM2 was higher in men and younger patients. Careful management of biliary tract diseases and liver cirrhosis can also help reduce the incidence of PLA in patients with DM2.

4. Conclusions

It is extremely important to accurately understand the extent of the current diabetes status; monitor its dynamics; and provide appropriate and timely interventions, tools and educational programs both to prevent or slow the development of diabetes and to help people with diabetes. Diabetes continues to be a serious threat to public health, affecting one in seven adults. However, a significant part of the adult population does not control their disease. It is extremely important to constantly monitor this situation with data representative of the country and develop a program for the prevention of diabetes and related comorbidities in order to achieve the country's urgent aim.

Difficulties in interpreting the clinical picture, the results of laboratory and instrumental research methods, especially against the background of diabetes mellitus, can cause late diagnosis, untimely start of treatment, the development of severe complications and, as a result, an unfavorable outcome of the disease. Therefore, further research and the search for new methods of treating liver abscesses in patients with type 2 diabetes mellitus are of great theoretical and practical importance.

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