SHORT COMMUNICATION

DRUG - INDUCED HYPERALKALINEPHOSPHATASEMIA, A ONE YEAR RETROSPECTIVE STUDY IN KING CHULALONGKORN MEMORIAL HOSPITAL

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ABSTRACT

An increase in serum alkaline phosphatase (ALP) level is frequently associated with a variety of diseases. Such disorders as extrahepatic bile obstruction, intrahepatic cholestasis, infiltrative liver disease, hepatitis and drug induced disorder are mentioned. This study was done in order to determine the prevalence of drug induced markedly elevated serum ALP among Thai hospitalized patients. A review was made of medical records of inpatients with high ALP levels above 1,000 IU/L in King Chulalongkorn Memorial Hospital, Thailand from January 1998 to December 1998. During the one-year period, a total of 203 hospitalized patients with serum ALP levels over 1,000 IU/L were identified. Of these 203 cases, 163 had got the definitive diagnosis. In interest, only 3 cases with diagnosis of drug induced hyperalkalinephosphatasemia were identified (allopurinol in 2 cases and diphenylhydantoin in 1 case). The average serum ALP in these cases was equal to 4,023.0 $\pm$ 3,493.6 IU/L. Drug induced toxicity is a rare cause of hyperalkalinephosphatasemia in the hospitalized patients. The relative percentage of drug-induced hyperalkalinephosphatasemia was equal to 1.47 %. Comparing to the total ALP tests performed in the setting in the study period, the low prevalence as 1: 10,000 was observed. Nevertheless, each case of drug-induced hyperalkalinephosphatasemia seems to be severe and can be overlooked.

Key words : hyperalkalinephosphatasemia, drug-induced, Thai patients

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ภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงจากยา การศึกษาย้อนหลังในช่วงเวลา 1 ปี ณ โรงพยาบาลจุฬาลงกรณ์

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บทคัดย่อ

ภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงเกิดได้จากหลายสาเหตุ เช่น การอุดตันของท่อน้ำดีนอกตับ และในตับ โรคของเนื้อตับ ตับอักเสบ รวมถึงตับถูกทำลายจากยา ได้ทำการศึกษานี้เพื่อหาความชุกของภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงจากยาในกลุ่มผู้ป่วยชาวไทย โดยการทบทวนเวชระเบียนของผู้ป่วยในโรงพยาบาลจุฬาลงกรณ์ที่มีผลการตรวจพบระดับเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงกว่า 1,000 IU/L ในช่วงปีพุทธศักราช 2541 ในช่วงปีที่ทำการศึกษาพบผู้ป่วยที่มีภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงเข้าเกณฑ์ 203 ราย โดยมี 163 รายที่สืบค้นการวินิจฉัยขั้นสุดท้ายได้ พบว่ามี 3 รายที่มีภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงจากยา (allopurinol 2 ราย และ diphenylhydantoin 1 ราย) ค่าเฉลี่ยของเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดของผู้ป่วยกลุ่มนี้เท่ากับ 4,023.0 ± 3,493.6 IU/L ภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงจากยาพบได้ไม่บ่อย ค่าร้อยละสัมพัทธ์ของภาวะนี้ต่อภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูงจากยาโดยรวมเท่ากับ 1.47% และเมื่อเทียบกับการส่งตรวจระดับเอนไซม์อัลคาไลน์ฟอสฟาเตสทั้งหมดในช่วงดังกล่าวพบความชุกของภาวะที่ศึกษาเท่ากับ 1: 10,000

คำสำคัญ : ภาวะเอนไซม์อัลคาไลน์ฟอสฟาเตสในเลือดสูง, ฤทธิ์แทรกแซงจากยา, ผู้ป่วยชาวไทย

INTRODUCTION

Alkaline phosphatase (ALP; EC 3.1.3.1) comprises a group of enzymes that catalyze the hydrolysis of phosphate esters in an alkaline environment, generating an organic radical and inorganic phosphate[1]. An increase in serum ALP level is frequently associated with a variety of diseases. Such disorders as extrahepatic bile obstruction, intrahepatic cholestasis, infiltrative liver disease, hepatitis and drug induced disorder are mentioned[1-3]. Unfortunately, the elevation of ALP less than three times the normal level is considered non specific and insufficient to provide a definite diagnosis[1-3].

In order to determine the prevalence of drug induced markedly elevated serum ALP among Thai hospitalized patients, a review was made of medical records of individuals in whom an ALP level was equal to or greater than 1,000 IU/L during a one-year period in a Thai tertiary hospital.

MATERIALS AND METHODS

This study was performed as a retrospective study. A retrospective case review was made on hospitalized patients who had an ALP level equal to or greater than 1,000 IU/L (Boerhinger Manheim, normal 98-279 IU/L) at the Department of Laboratory Medicine, King Chulalongkorn Memorial Hospital, Bangkok, Thailand. This study focused on a one-year period, from January 1998 to December 1998. The review of the patients' medical records during this period included 203 hyperalkalinephosphatasemic cases with a conclusive diagnosis for further analysis. The data from the discharge summary of these patients were then recorded including their age as well as the final diagnosis. The casess without final diagnosis were excluded.

Descriptive statistics were used in analyzing the patient characteristics and laboratory parameters of each group. All the statistical analyses in this study were made using SPSS 7.0 for Windows Program.

RESULTS

During the one-year period, a total of 203 hospitalized patients with serum ALP levels over 1,000 IU/L were identified. Of these 203 cases, 163 had got the definitive diagnosis (Table 1). In interest, only 3 cases with diagnosis of drug induced hyperalkaline-phosphatasemia were identified (allopurinol in 2 cases and diphenylhydantoin in 1 case). The average serum ALP in these cases was equal to 4,023.0 ± 3,493.6 IU/L (Table 2).

Table 1. Characteristics of included 163 subjects.

Parameters	Characteristics
Age (years)	
Range	21-93
Mean	52.3 ± 15.5
sex	
male	88
female	75

Table 2. Drug-induced hyperalkalinephosphatasemia in the series.

No.	sex	Age (years)	Drug	Seum ALP (IU/L)*	Serum bilirubin (mg %)**	Liver biopsy	Recovery after discontinuation
1	Female	53	Allopurinol	8,057	40.5	no	yes
2	Female	53	Allopurinol	2,014	20.4	no	yes
3	Male	50	Diphenylhydantoin	1,998	19.7	no	yes

* normal value 98 – 279 IU/L
** normal value 0 – 1 mg%

DISCUSSION

A number of diseases are related to the elevation of serum ALP[1], therefore, a study of the etiologies of high serum ALP can be useful in diagnosis. According to a recent report, drug induced toxicity is rarely a cause of hyperalkalinephosphatasemia in the hospitalized patients[3]. The relative percentage of drug-induced hyperalkalinephosphatasemia was equal to 1.47 %. Comparing to the total ALP tests performed in the setting in the study period, the low prevalence as 1: 10,000 was observed.

However, each case of drug-induced hyperalkalinephosphatasemia seems to be severe and was overlooked. In our series, a case with serum ALP as high as 8,057 IU/L was identified. However, on follow up, all patients' serum ALP returned to normal limit within a few months after discontinuation of the drug administration. Indeed, hepatocellular necrosis and a mixed hepatocellular and cholestatic pattern have been previously reported with allopurinol therapy[4]. The mechanism of hepatic injury seems to be that of hypersen-sitivity with a relatively fixed induction period, development of fever with rash and peripheral eosinophilia as well as the findings of tissue eosinophilia and noncaseating granuloma on liver biopsy. Likewise, the patterns of liver damage have also been described in cases with phenytoin toxicity[5].

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