Primary Brain Tumours and Lipids

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Abstract

The values of many biochemical parameters undergo changes to a certain degree in neoplastic conditions; serum lipids are some of those whose levels may be altered.

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A prospective study to investigate the serum lipid profile of a group of Iraqi patients suffering from primary brain tumours (PBT) and to compare it with healthy volunteers.

This study had been conducted between November 2000 and October 2001. Patients were evaluated by full medical history to exclude any existing systemic disease that may affect the parameters to be diagnosed, particularly diabetes, liver disease, renal disease and chronic drug intake, otherwise the patient would have been excluded from the study.

One hundred and seven patients harboring clinically and histologically diagnosed PBT, qualified for the study. Their age ranged between 2-75 years, 56 males and 51 females. Blood samples were collected after 10-12 hours of fasting that had followed a light dinner the night before; the serum lipids were analysed using the enzymatic method.

Forty age- and sex matched normal subjects were used as controls.

The present study demonstrated a variable changes among circulating lipids; a highly significant increase in serum cholesterol of patients was noticed in comparison to that of normal subjects; the same finding was observed in serum LDL. On the other hand, a high decrease in serum HDL and TG was observed.

The levels of the most common serum lipids do change in patients with PBT. Brain tumour cells may manufacture their requirements from lipids. Our results are in agreement with the findings of few other researchers investigating lipids in neoplastic conditions. It is recommended that further studies similar to the present study to be conducted on a larger scale in order to find whether therapeutic measures may need to be implemented to correct such abnormalities that may have untoward consequences on patients health.

Introduction

Brain tumor is a mass of unnecessary, and often abnormal growth of tissue found inside the skull [1,2]. There are two categories of brain tumors [3-12]: primary brain tumors (PBT), which originate in the brain and they represent about 1% of all cancers and 2.5% of all cancer deaths, and metastatic (secondary) brain tumours [13], which represent approximately 25% of all cancer. Patients develop metastatic brain tumors when cancer cells from other parts of the body, such as the lungs, kidneys, breasts[14] and skin spread to the brain. [7].

The first category, PBT, could be classified into [1,8-10]:

Benign brain tumors, e.g., meningioma, craniopharyngioma, ependymoma, schwannoma, and epidermoid cyst.

Malignant brain tumors, e.g., glioma, medulloblastoma , pineoblastoma, and chondrosarcoma. Patients with malignant brain tumors develop cognitive and personality changes related to the area of the brain that the tumor invades, and most experience progressive neurological decline as their disease progresses [11-13].

Lipids

Lipids are important dietary constituents although lipids have many functions [14-51], two of the most important are energy storage and membrane structure. Lipids serve other functions, including being precursors for steroids and bile acids, and thermal insulation (triacylglycerols).

Cholesterol [1,2] is a lipid with very low solubility in water, the very high solubility of cholesterol in blood is due to the presence of proteins called plasma lipoproteins (mainly LDL and VLDL) that have the ability to bind and thereby solubilise large amounts of cholesterol .Cholesterol is widely distributed in all cells of the body, but particularly in nervous tissue.[1,2] Cholesterol plays a number of important roles [1-8], that are beyond the scope of this article, however, it is especially abundant in the myelinated structures of the brain and central nervous system.

Serum lipids, also, include triglycerides [15, 21], fatty acid esters of glycerol, each containing three different fatty acids; triglycerides [1,2] are the predominant lipids in chylomicrons and VLDL . Lipoproteins [16], another constituent of serum lipids, are of multi-component complexes of protein and lipids of characteristic density, molecular

weight, size and chemical composition; there are five main classes of Lipoproteins. [18]

Patients and methods

This study had been conducted between November 2000 and October 2001 at both THK and NH in Baghdad. Patients were evaluated by full medical history to exclude any existing systemic disease that may affect the parameters to be diagnosed, particularly diabetes, liver disease, renal disease and chronic drug intake, other wise the patient was excluded from the study.

One hundred and seven patients diagnosed clinically and histologically as harboring PBT qualified for the study; their age ranged between 2-75 years, 56 males and 51 females.

Out of the 107 patients suffering form primary brain tumors with an age range 2-75 years (mean 35, the standard SD ± 19), 56 were males (52.3%), and 51 were females (47.6%). The most affected age group was 31-40 years (17.75%), 89% of the patients were under the age of 60 years (Table I).

Forty age- and sex-matched normal subjects were used as controls.

The duration of the disease ranged from <1-<9 years. The majority of the patients (57.94%) presented within less than 1-year from the onset of their symptoms.

About 10 mls venous blood was drawn aseptically into sterile test tube following 10 to 12 hours of fasting.

Cholesterol kit, HDL cholesterol kit and Triglycerides kit were obtained from BioMerieux – France.

Assays were done within one week to one month of collection at the laboratories of THK, NH, and the Medical Research Centre (MRC) of The College of Medicine, Al-Nahrain University

Results

Out of the 107 patients suffering form primary brain tumors with an age range 2-75 years (mean 35, the standard SD ± 19), 56 were males (52.3%), and 51 were females (47.6%). The most affected age group was 31-40 years (17.75%), 89% of the patients were under the age of 60 years.

Histological typing of PBT in this study included: 75 gliomas ("benign", grades I and II, and "anaplastic" malignant grades III and IV) and 32 meningiomas (benign)

The highest percentage of the pathological grading was grade IV (34%), followed by grade III (27%).

Table (1): Mean Lipid profile concentration in serum of PBT patients and normal subjects.

Lipid profile	Patient serum mean ± SD (g/l)	Normal serum mean ± SD (g/l)	P value
Cholesterol	4.7887 ± 0.9525	2.4080 ± 0.1060	<0.01
HDL	0.1256 ± 0.0636	0.3010 ± 0.0940	<0.01
LDL	4.4309 ± 0.9720	1.6700 ± 0.7510	<0.01
VLDL	0.2692 ± 0.1154	0.3600 ± 0.8520	<0.01
TG	1.0813 ± 0.5827	1.6108 ± 0.6920	<0.01

Discussion

Exploring the biochemical profile of patients of various disease conditions, remains an interesting and valuable processes, and may be even an essential step, in the investigation of those diseases

Although there are many factors that are associated with blood lipid profile levels such as age, obesity, exercise, pregnancy, smoking, alcohol consumption, coffee consumption, emotional factors, race, seasonal variation, diabetes mellitus, liver disease, renal disease, hypothyroidism, oestrogen and progesterone hormones, and dietary factors [19], also, in patients with acquired immune-deficiency syndrome (AIDS), especially when associated with severe wasting and diarrhea, a poor prognosis [120], however, the present study has stretched throughout a whole year including only PBT patients and healthy volunteers from both sexes.

Abramson et al found that the mean cholesterol value of the cases with brain tumours was 22 mg/dl higher than that of the controls. This difference was statistically significant (P = 0.007). Controlling for weight, region of birth, season of year, social class, medications and length of hospitalization before the measurement of cholesterol did not reduce the cholesterol difference, and in some instances increased it. [121]

Reduced blood cholesterol levels were reported in patients with a variety of malignant peripheral tumors [97-99]. This fact is likely related to increased cholesterol demand by proliferating tumor cells [122], or to nutritional status [123], though others think that the abnormality is a common feature of both hematological and solid tumors and is not entirely explained by poor nutrition [124]

The present study demonstrated a variable changes among circulating lipids (Table 2). A highly significant increase in serum cholesterol of patients was noticed in comparison to that of normal subjects, the same finding was observed in serum LDL. On the other hand, a high decrease in serum HDL and TG was observed . Our results are in agreement with the findings reported by Al-Mubsen [125], who found the same observations (for cholesterol, LDL and HDL) in serum of patients with malignant ascites. Elevated LDL was also noticed by Spiegel and colleagues [126] in serum of 25 patients with acute leukemia. The increase in cholesterol and LDL levels may be due to provision of excess energy to tumor cells [79]. Several studies have shown that in human systems, alterations of

membrane lipid occur in certain malignant cells, and altered cholesterol metabolism can accompany markedly increased low-density lipoprotein receptors in these cells [30-31]. It has been suggested that these lipid alterations may be due to intrinsic cell proliferation or malignant transformation [30,32].

The finding in this study of a statistically significant increase in serum cholesterol concentration of PBT patients (4.7887 ± 0.9575 g/l) seen when compared with that of normal serum (2.400 ± 0.5060 g/l), as shown in table 1, is in keeping with that of Al-Rawi et al who found a higher serum cholesterol values compared to those with peripheral tumours and healthy controls [33]; similar results were found by other authors. Reduced blood cholesterol levels were reported in patients with a variety of malignant peripheral tumors [34-37]. This fact is likely related to increased cholesterol demand by proliferating tumor cells [34], or to nutritional status [36], though others think that the abnormality is a common feature of both hematological and solid tumors and is not entirely explained by poor nutrition [38]. The question arises whether this 'tumor-associated ypocholesterolaemia occurs also in patients with brain tumors, and, if it does not, whether its absence can be related to the location of the tumors [34]. Grieb et al have compared fasting serum total cholesterol levels among three groups of patients: 52 patients with gliomas, 56 patients with symptomatic metastatic brain tumors, and 50 patients harboring malignant tumors of peripheral location but showing no clinical signs of brain metastases. Patients in the last group, despite being on an average more age-advanced, had lower total serum cholesterol levels than either the patients with gliomas, or the patients with brain metastases. No difference in the cholesterol levels was found between the two latter groups, and a majority of these patients had borderline or elevated cholesterol levels. This apparent absence of 'tumor-associated hypocholesterolaemia in brain tumor patients may be related to either brain tumors' ability to synthesize cholesterol de novo and their reduced dependence on peripheral cholesterol supply, the existence of brain tumor-blood barrier, effect of medications used to counteract brain edema and seizures, or a combination of these factors [34].

In this study, the decrease in serum TG concentration of patients was highly significant in comparison to normal group (1.0813 ± 0.5821 versus 1.6100 ± .06900 g/l) as observed in table 1.

A highly significant decrease in the level of lipoprotein (HDL) in serum of primary brain tumor patients was observed, when compared with normal serum (Table 1); it is well known that HDL have protective roles in vascular diseases. This finding may warrant further expanded study.

The increase in lipoprotein (LDL) concentration in serum of PBT patients (4.4309 ± 0.9720 g/l) in comparison to normal serum (1.6200 ± 0.3510 g/l) was significant ($p < 0.01$) as seen table 1.

Interestingly, in the setting of experimental human malignant glioma cell lines treatment, researchers have found that the use of the cholesterol-lowering agents, such as the competitive HMG-CoA reductase inhibitor Lovastatin, led to DNA degradation into nucleosome-sized fragments characteristic of apoptosis [39]. They concluded that HMG-CoA reductase inhibitors, such as Lovastatin, merit further investigation as potential therapeutic agents for the treatment of malignant gliomas [39].

Conclusions

This study has shown that levels of the most common serum lipids do, significantly, change in patients with PBT. There is great need for a larger similar study to be performed in order to find whether therapeutic measures may need to be implemented to correct such abnormalities that may have untoward consequences on the health of PBT victims.

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الخلاصة

تتغيّر كثير من المؤشّرات الكيموحياتية في كثير من حالات الأورام؛ و من هذه المركّبات هي الشحوم. يهدف البحث الى دراسة مستويات الشحوم لدى مجموعة من المصابين بأورام الدماغ الأولية و مقارنتها بمجموعة السيطرة.

شملت الدراسة 107 مرضى مصابين بأورام الدماغ الأولية الحميدة و الخبيثة في المستشفى التعليمي بالكاظمية و مستشفى جراحة الجملة العصبية ببغداد و 40 شخصا من الأصحاء كمجموعة سيطرة. تمّ أخذ عينات من الدم الوريدي بعد حوالى 10-12 ساعة من عدم تناول الطعام؛ تمّ تحليل الدم في مختبرات المستشفيين المذكورين بالطرق الأنزيمية.

أظهرت النتائج ارتفاعا واضحا في الكوليستيرول و الشحوم الزلالية المنخفضة الكثافة لدى المرضى بقيمة احصائيةعالية قياسا على مجموعة السيطرة و انخفاضا في مستويات الشحوم الزلالية عالية الكثافة و ثلاثية الكليسيرايد أيضا لدى المرضى.

من المحتمل جدا أن تصنع خلايا أورام الدماغ ماتحتاجه من الشحوم وأن هؤلاء المرضى يحتاجون للأدوية المخفّضة لشحوم الدم.