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The Comparison of Pre-Diagnostic and Diagnostic Thrombocyte Levels in Pancreatic and Biliary Tract Cancers

Pankreas ve Safra Yolları Kanserlerinde Tanı Öncesi ve Tanı Anındaki Trombosit Düzeylerinin Karşılaştırılması

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ÖZ

Amaç: Trombositlerin tümör büyümesi ve metastatik yayılımdaki rolü, uzak vücut bölgelerinde trombüs oluşumu ve embolizasyon ile yayılan tümör fragmanlarının keşfinden sonra tanımlandı. Çoğu kanserin de trombositoz ile ilişkili olduğu bildirildi. Özellikle meme, akciğer, kolon, mide, renal hücreli kanser ve jinekolojik kanserlerin trombositoz durumunda genel sağkalımı (OS) kısalttığı gösterildi.Bu çalışmada biliyer ve pankreas kanserlerinin trombosit düzeylerinin tanıya kadar geçen süredeki değişimi değerlendirilmeye çalışıldı.
Gereç ve Yöntem: Afyonkarahisar Sağlık Bilimleri Üniversitesi Tıbbi Onkoloji Anabilim Dalı'nın 2012-2018 yılları arasındaki pankreas kanserli hasta kayıtları geriye dönük olarak incelendi. Tanıdan 6 ay veya daha önce tam kan sayımı olan hastalar çalışmaya dahil edildi.Tam kan sayımına ulaşılamayan, yeterli dosya verisi olmayan veya takipleri olmayan hastalar ve ikinci bir kanseri olan hastalar çalışmaya dahil edilmedi.
Bulgular: On yedi pankreas, 17 safra yolu ve 8 safra kesesi adenokarsinomundan oluşan çalışmaya tıbbi kayıtların eksiksiz olarak değerlendirilmesi sonucunda toplam 42 hasta dahil edildi. Ortalama (medyan) trombosit seviyeleri ön tanı ve tanı gruplarında sırasıyla 239000 (230000) ve 260000 (251000) idi. Önceki kan testi ile tanı arasındaki ortalama süre 15.9 aydı. Tanı öncesi ve tanısal trombosit düzeyleri arasında istatistiksel olarak anlamlı olmayan bir fark vardı. (p=0.08) Tanıya kadar geçen süre ile trombosit düzeylerinin arttığı görüldü. Trombosit düzeyleri tanı anında ve tanı öncesi 400000 cut-off ile kategorize edildiğinde gruplar arasında anlamlı fark saptandı (p=0,04).
Sonuç: Bu çalışmada pankreatikobiliyer tümör tanısı ile trombosit seviyelerinde yükselme saptadık. Trombosit seviyeleri bu durumun bir göstergesi olabilir, ancak normal aralıklarda değişiklik göstermesi tanısal değerini azaltmaktadır.
Anahtar Kelimeler: Pankreas kanseri, trombosit seviyeleri, erken tanı

ABSTRACT

Aim: The role of thrombocytes in tumor growth and metastatic spread was defined after the discovery of tumor fragments disseminated with thrombi brake off and embolization in distant body sites. Most cancers reported being related with thrombocytosis. In this study, we try to evaluate the variation of thrombocyte levels of biliary and pancreatic cancers in time to diagnosis.
Material and Methods: The patient records of Afyonkarahisar Health Sciences University Department of Medical Oncology between 2012 and 2018 were retrospectively analyzed. The patients who have 6 months or prior CBC before the diagnosis included in the study.
Results: A total number of 42 patients included in the study which was composed by 17 pancreatic, 17 biliary tract and 8 gallbladder adenocarcinomas after the complete evaluation of medical records. The mean (median) thrombocyte levels were 239000 (230000) and 260000 (251000) in pre-diagnostic and diagnostic groups respectively. The mean time between the prior blood test and diagnosis were 15.9 months. There was a statistically non-significant difference between pre-diagnostic and diagnostic thrombocyte levels. (p=0.08) The correlation was positive which determines thrombocyte levels increase with the time to diagnosis. When the thrombocyte levels categorized with the cut-off 400000 in the time of diagnosis and before diagnosis, there is a significant difference between groups. (p=0.04)
Conclusion: In this study, we found an elevation in the thrombocyte levels through the diagnosis of pancreaticobiliary tumors. The thrombocyte levels may be an indicator for this condition, but the alteration in normal ranges through the diagnosis makes it an unpractical marker.
Key words: Pancreatic cancer, thrombocyte levels, early diagnosis

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INTRODUCTION

The cancer-thrombocyte relationship is well known for a long time. The relationship was first described with the title ''massive increase of platelets'' in patients with cancer. This hypothesis was confirmed and improved by Theodor Billroth (1,2). The thrombocytosis have role in prognosis and increased thromboembolic events in especially gastrointestinal malignancies (3). The role of thrombocytes in tumor growth and metastatic spread was defined after the discovery of tumor fragments disseminated with thrombi brake off and embolization in distant body sites. Most cancers reported being related with thrombocytosis. Especially breast, lung, colon, gastric, renal cell and gynecological cancers were described to be shortened overall survival (OS) in case of thrombocytosis. In the US, thrombocytosis considered to be an adverse factor in at least %50 percent of all cancer-related deaths (4). Although in most cancer types thrombocytosis confirmed to be an adverse factor, pancreatic or periampullary cancers are controversial. The increased thrombocytosis levels speculated to be both adverse and favorable prognostic factor (5-7). The thrombocytosis cancer relationship is hypothesized via multiple mechanisms. The destruction of the interstitial tissue by matrix metalloproteinase-9 (MMP-9) and increased levels of vascular endothelial growth factor (VEGF) is responsible for the enhanced mobilization and production of thrombocytes (8-10).

After recognizing possible cancer thrombocytosis relationship, the idea of a predictive tool for cancer early diagnosis was composed. The thrombocytosis was found to be 1.5-2% in over 40 years old age population who are applying primary care consultant (11-13). There are conflicting results about the predictive value of thrombocytosis in different cancer types. In primary care studies while thrombocytosis had a predictive effect in the lung, renal uterine and colorectal cancers, it was not relevant in pancreatic, breast and ovarian cancers (12-19). These case-control studies made UK national guideline revisions and thrombocytosis in primary care confirmed to be suspicion of the lung, esophagogastric and uterine cancers (20).

In this study, we try to evaluate the variation of thrombocyte levels of biliary and pancreatic cancers in time to diagnosis.

MATERIAL and METHODS

Study Participants

The patient records of Afyonkarahisar Health Sciences University Department of Medical Oncology between 2012 and 2018 were retrospectively analyzed. From a total number of 5328 patient records 197 pancreaticobiliary cancers were found. There were 115 pancreatic and 82 biliary tract adenocarcinomas. These patients' medical records were evaluated for prior complete blood counts (CBC). The patients who have 6 months or prior CBC before the diagnosis included in the study. The patients whose application reason or comorbidities (hematological or solid organ malignancies, infections, iron deficiency anemia etc) related with thrombocytosis, were excluded. Also, the CBC tests at the time of diagnosis were evaluated for secondary thrombocytosis etiology (Surgery, infection...) After the complete evaluation of medical records, a total number of 42 patients included in the study which was composed by 17 pancreatic, 17 biliary tract and 8 gallbladder adenocarcinomas.

Ethics

The study protocol was approved by the local ethics committee of Afyonkarahisar Health Sciences University. (13.05.2022 dated and 2022/6-284 numbered)

Statistics

The statistical analysis of the study performed with SPSS software (Statistical Package for the Social Sciences, version 22.0, SPSS Inc, Chicago, IL). The Kolmogorov–Smirnov test was used to determine whether data conformed to a normal distribution. Descriptive data are presented as either means or median for continuous variables, frequencies and percentages are reported for categorical variables. Pearson X2 test is used to assessing the associations in categorical variables. Paired Sample T-Test was used to evaluate the relationship between prior and diagnostic thrombocyte levels.

RESULTS

A total number of 42 patients included in the study which was composed by 17 pancreatic, 17 biliary tract and 8 gallbladder adenocarcinomas after the complete evaluation of medical records. The median ages of patients were 63, 60 and 67 in pancreatic, biliary tract and gallbladder cancers respectively. There were 20 males and 22 females in the study. The mean (median) thrombocyte levels were 239000 (230000) and 260000 (251000) in pre-diagnostic and diagnostic groups respectively. The descriptive statistics were shown in Table-1. The mean time between the prior blood test and diagnosis were 15.9 months. There was a statistically non-significant difference between pre-diagnostic and diagnostic thrombocyte levels. (p=0.08) The correlation was positive which determines thrombocyte levels increase with the time to diagnosis. When the thrombocyte levels categorized with the cut-off 400000 in the time of diagnosis and before diagnosis, there is a significant difference between groups. There were 0 (0%) and 4 (9%) patients in pre-diagnosis and di-

agnosis group respectively, who have thrombocytes over 400000. (p=0.04)

DISCUSSION

In this study, we found a significant raise in thrombocyte levels with the time to diagnosis in pancreaticobiliary cancers. There were case-control studies in primary care which showed pre-diagnostic thrombocyte levels may be a predictive tool in some cancer types. Bailey et al.(21) investigated the relationship between the elevated levels of thrombocytes and different types of cancers. In this study elevated levels of thrombocytes relates to lung and colorectal cancers. In contrast to this information breast and prostate cancers had an inverse relationship in the general population. However, related to this paper there was thrombocytosis have minimal positive predictive value for early cancer diagnosis. In large population based study the increased thrombocyte levels found only five percent of the disease group. There is still need an identifying factor for the big part of the population for early diagnosis (21). In a primary care study which was evaluating the predictive factors for pancreatic cancer, the elements except jaundice reported to have no role (18). The three database studies evaluating this phenomenon in England showed no relationship between thrombocytosis and later cancer diagnosis (15,17,18). Although there multiple negative studies, there are some studies showing difference between benign and malign disease in terms of thrombocytosis. In a study, comparing benign and malign lung nodules, there was a six-fold difference between groups (22). There some recent data which show some clinical factor may affect the disease and treatment outcome especially in renal cancers. The increased efficacy of combination treatment in intermediate and poor prognostic group may show a potential in different cancer types with the developing drugs including pancreatic cancers (23).

CONCLUSION

New studies may be needed to evaluate the utility of thrombocytosis for diagnosis and prognosis.

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