

increase in SOD activity in erythrocytes in our study might have occurred to neutralize the excess superoxide anions originating from volatile organic compounds such as benzene, toluene, and thinner. Halifeoglu et al<sup>4</sup> also found increased MDA and SOD activity in a study sample working with paint thinner.<sup>4</sup> The antioxidant system have many components. The antioxidant capacity may give more relevant biological information compared to that obtained by the measurement of individual components, as it considers the cumulative effect of all antioxidants present in plasma and body fluids.

We observed a significant decrease in the concentration of TAC in the paint group's sera compared to control. These findings showed that the other antioxidant defense mechanism is used versus oxidative damage. A plausible explanation could be that the solvent exposure may cause inhibition of enzymes or depletion of substrate molecule (glutathione, GSH and so forth) and an increase in the concentration of ROS. Our data indicate that smoking is not a confounder for the association between solvent exposure and changes in blood parameters. Also, Pinto et al<sup>5</sup> reported that smoking or alcohol intake did not correlate positively with the cytogenetic damage observed in outdoor painters. As a result, elevated MDA levels in the paint group may indicate that increased lipid peroxidation at exposure to long-term organic solvents. Whereas elevated SOD activity in the paint group compared to control, it is shown that the antioxidant system is activated against lipid peroxidation. Beside this, decreased TAC level in the paint group may indicate that another antioxidant system is used. Whichever the case is, our results permit us to conclude that paint workers studied represent a risk group and should be medically followed up with more frequent periodic examinations. These workers should take antioxidants and use gloves and protective equipment.

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## Synchronous occurrence of Philadelphia chromosome-positive chronic myelogenous leukemia and breast cancer

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The synchronous occurrence of non-treatment related Philadelphia chromosome positive (Ph-C+) chronic myelogenous leukemia (CML) and breast cancer (BC), is reported in this communication. The coincidental discovery of CML and BC is described in 2 patients, aged 37 and 39 years, who presented almost in a similar manner, where the diagnosis of chronic uncontrolled phase of CML was made upon working up the patient for radical surgery for a coexisting breast cancer. Both patients were treated with modified radical mastectomy with axillary clearance, which was followed by chemotherapy for both diseases. The first patient subsequently underwent autologous bone marrow transplantation, and is alive and well when last followed up nearly 27 months after the initial diagnosis. The second patient, who has a strong family history of breast cancer, died 18 months after initial diagnosis of uncontrolled metastatic breast cancer to the central nervous system.

A 37-year-old Caucasian, gravida 3, para 3 and otherwise healthy female teacher, was admitted to work her up for a recently diagnosed BC by fine needle aspiration biopsy (FNAB). The mass (in the upper lateral quadrant) was painless and was initially felt while taking a shower and was found to progressively increase in size. The first FNAB carried out 4 weeks after breast mass discovery, was erroneously interpreted as a fibroadenoma. As the mass continued to enlarge, a second FNAB was carried and revealed the definitive presence of adenocarcinoma. Family history for BC was negative. She was scheduled for mastectomy, for which she underwent as part of her work up an admission,

complete blood count (CBC), which incidentally revealed the following incidental findings: hemoglobin 11.0 gm/dl, hematocrit 33%, white blood cell (WBC) 51,750, differential-lymphocytes 2%, segmented neutrophils 35%, bands 16%, metamyelocytes 5%, myelocytes 29%, promyelocytes 3%, blasts 2%, basophils 5%, eosinophils 1%, monocytes 2%, and platelets 374,000. Blood film examination was suggestive of a chronic uncontrolled phase of CML. Physical examination was remarkable (other than the breast mass) only for splenomegaly slightly below the level of the umbilicus. Subsequently, a bone marrow biopsy and aspiration were carried out, and the diagnosis of chronic myeloproliferative disorder most consistent with CML was made. Cytogenetic analysis revealed the presence of Philadelphia chromosome [46XX, t(9;22)(q34;q11.2)] in all of the 15 metaphases that were examined. Florescent in-situ hybridization (F.I.S.H.) for breakpoint cluster region - ABL was positive in 95% of the interphase cells for BCR/ABL translocation. The patient was then worked up by total body skeletal survey, bone isotope scans, mammography for the opposite breast, computed tomographic (CT) scans for the abdomen, pelvis and chest; patient was found to have a homogenously enlarged spleen and BC that was localized to one breast with only few regional lymph nodes enlargement. Modified radical mastectomy with axillary lymph node clearance confirmed the cancer state with 2 lymph node involvement by metastatic cancer. She was later placed on chemotherapy [Tamoxifen and Cyclophosphamide, methotrexate, and fluorouracil (C.A.F. regiment)] and hydroxyurea, for both diseases. Six months later, she underwent autologous bone marrow transplantation at the MD Anderson. She continued her follow-up visits with the local oncology team and continued to be disease free. She was last seen at follow up visit 27 months after the initial diagnosis, and was then disease free.

A 39-year-old, gravida 4, para 4, Caucasian female housewife complaining of a retro-areolar hard painless fixed mass with associated nipple ulceration and inversion. The mass which was felt by palpation as "nodular in texture" showed progressive enlargement over the ensuing 4 months becoming almost confluent with associated nipple discharge thought to be related to breast feeding as she was lactating her baby. Subsequently, the patient underwent a FNAB of the mass, which revealed "suspicious for malignant cells". She was scheduled for an excisional biopsy of the mass, during which her admission CBC revealed the following incidental findings: hemoglobin 11.0 gm/dl, hematocrit 33.0%, WBC 49,375, differential-lymphocytes 2%, segmented neutrophils 34%, bands 14%, metamyelocytes 4%, myelocytes 31%,

promyelocytes 3%, blasts 2%, basophils 6%, eosinophils 4%, and platelets 610,000. Blood film examination was suggestive of a chronic uncontrolled phase of CML. A bone marrow biopsy and aspiration confirmed the presence of chronic myeloproliferative disorder, most consistent with CML. Splenic enlargement was documented by both physical examination and by abdominal ultrasound. Cytogenetic evaluation of the bone marrow cells, revealed the presence of Philadelphia chromosome [46XX, t(9;22)(q34;q11.2)] in all the 23 metaphases examined, and 88% of the interphase cells showing BCR/ABL translocation by F.I.S.H. She was worked up with total body and isotope bone scans, chest abdomen and pelvic CT scans, mammography for the opposite breast, and was found to have disease limited to the breast. A modified radical mastectomy with axillary lymph node clearance revealed multifocal infiltrating poorly differentiated ductal adenocarcinoma with metastasis to 23 out of 24 regional lymph nodes. She was subsequently placed on Tamoxifen and adjuvant chemotherapy (C.A.F.) in addition to hydroxyurea. Family history revealed a mother, and a sister who both died of breast cancer at an early age; she died after 18 months of uncontrolled breast cancer metastasis to the brain.

**Pathological findings.** Bone marrow aspiration and biopsy in both patients showed similarly a cellularity of 90-95% (packed marrow), with myeloid predominance (hyperplasia), reticulin content was +1 to +2/+4, the myeloid: erythroid (M:E) ratio is 15-20:1, megakaryocytes are increased with many exhibiting single small nuclei; all myeloid stages of maturation are observed with expansion of the intermediate and late compartments, blasts did not exceed 5%. Coupled with the results of the cytogenetics, the overall picture was diagnostic of a chronic uncontrolled phase of CML. Keratin stains for the bone marrow biopsy samples were negative in both patients. The breast mass in the first patient measured 7.5 cms. Low power view of the tumor showed pushing margins and stellate central fibrosis entrapping foci of necrosis. High power examination showed an in situ comedo intraductal adenocarcinoma component constituted 25%, with the remaining tumor composed of infiltrating poorly differentiated ductal adenocarcinoma without any accompanying lymphovascular invasion. Both estrogen receptors (ER) and progesterone receptors (PR) were positive; with no p53 overexpression; no androgen receptor expression; Keratin (CK-7) positive; Her-2/neu is 0-1/3; and Ki-67 score of 1/3; leukocyte common antigen (LCA) was negative; GCDFP-15 was positive. Two of the 18 regional lymph nodes show microscopic (subcapsular) metastasis. Margins of resection of the mastectomy sample were all free of tumor. The breast mass in the second patient was

composed of multiple confluent smaller masses that measure in maximum dimensions 5.5 cms. Sections were initially thought to represent granulocytic sarcoma (owing to the recent recognition of coexisting CML in the patient), but histopathologic examination of the mass revealed infiltrating poorly differentiated ductal adenocarcinoma, with widespread lymphovascular permeation. Examination of the mastectomy sample revealed the presence of multifocal adenocarcinoma in the other breast quadrants, and 23/24 regional lymph nodes show metastatic adenocarcinoma. She was ER and PR positive, her-2/neu 0-1/3. Keratin (CK-7) was positive; LCA was negative. Surgical margins of resection were tumor free.

Improvements in the chemotherapy and radiotherapy regimens administered, or both, as well as immunosuppressive treatment following allogeneic organ transplantation has increased the incidence of secondary hematological malignancies after therapy for primary neoplastic diseases as an important late complication of therapy in cancer patients. The occurrence of "Non-Treatment-related" leukemia on the other hand is exceedingly rare as a second primary and is reported to occur in older individuals (in Western countries).<sup>1</sup> Treatment-related CML, which is indistinguishable from de novo CML and does not appear to have peculiar cytogenetics is a rare event, and its development seems to be associated with chemotherapy, radiotherapy, or immunotherapy.<sup>4</sup> The term synchronously occurring cancers has been used to describe cancers diagnosed simultaneously in the same patient within a 6-month period between the diagnosis of the 2 cancers apart, whereas the term metachronous cancers is used to describe cancers occurring within a period of more than 6 months apart.<sup>2</sup>

In one study on 8428 autopsied cases, the average age of the examined cases was 64 years  $\pm$  2 years, the incidence of multiple primary tumors had an incidence of 0.8%, and 3.6 % of all cancer autopsied cases. First, primary malignant tumors were most common in the hematopoietic system and the cervix, second primary malignant tumors were most common in the lungs and the hematopoietic system.<sup>2</sup> Age has been reported to play a significant role in multiple primary cancers in older individuals in the Western published data only, such a barrier against occurrence has not been confirmed from Middle-Eastern cases. Synchronous occurrence of primary epithelial neoplasm and a primary hematopoietic neoplasm is uncommon, most reported cases cite only the occurrence of BC after the use of chemotherapy for BC (namely, therapy-related). The only single report that clearly described an association between BC and chronic myelomonocytic leukemia (CMML) of the FAB classification, and

not Ph (+ve) CML, was that by Cavanna et al,<sup>3</sup> who discovered the presence of the leukemia (CMML) 2 weeks after the diagnosis of operable breast cancer. Metachronous occurrence of such tumors; on the other hand, is more common where the second malignancy (usually hematopoietic neoplasm), develops due to the effects of chemotherapy, namely, secondary leukemia.<sup>4</sup> Early metachronous is a related term used by some to refer to cancers occurring within a period of 3 years from initial diagnosis of the primary tumor. From the data by Specchia et al,<sup>1</sup> the only epithelial neoplasms occurring simultaneously with de novo CML were those from the lung, prostate, bladder (one case each), and rectal cancer (2 cases); there has been no second malignancies with de novo CML cases reported from their series to arise from the breast. Oncologists know that the composition of chemotherapy, with particular reference to its high proportions of prednisolone, appears to enhance the leukemogenic effects of other chemotherapy agents used. The carcinogenic effects of adjuvant Tamoxifen treatment and radiotherapy for breast cancer are estimated to be in the range of 0.5%. Among 236 cases of hematological malignancies, synchronous solid cancers in the same patient were estimated to be in the range of 3%, none of their patients had BC. Others report a higher frequency of double cancer in the patients with hematopoietic neoplasms being close to 21.5% in patients of the older age group (>65 years), versus 2.6% in the patients of the younger age group.<sup>2,3</sup>

Although full karyotype was carried out for both patients, no other chromosomal abnormality was detected in both patients, other than that of Philadelphia chromosome. Ideally, a thorough search for specific gene abnormalities should have been undertaken, but that was not arranged at the time of patient management by the oncology team. Such synchronous de-novo malignancies most likely have to deal with genetic aberrations, although this was not substantiated in our study. Logically one presumes that BC related antigens might have been detected in these 2 patients, but as mentioned earlier these studies were not arranged for. Region of deletion on chromosome 22q13 as one of the reported allelic losses has been reported to occur in BC. Similarly, loss of the distal segment distal to M-bcr in a Philadelphia chromosome positive CML (or loss of heterozygosity at chromosome 9p(19), or allelic loss at 9p221-22, smallest common region in the vicinity of the CDKN2 gene in sporadic BC.<sup>5</sup> Finally, one of the major cytological differential diagnoses in this setting of a poorly differentiated neoplasm in the presence of leukemia is granulocytic sarcoma, especially, if the sample is either qualitatively or quantitatively inadequate and if other difficulties existed in the sample



interpretation, due to the therapeutic implications, which are variable in both disease states.

In conclusion, the simultaneous occurrence non-therapy related Philadelphia chromosome negative, CML, and BC in 2 female patients has been reported. The BC was identified earlier than the knowledge that simultaneously present CML was present in these patients, which was discovered incidentally upon working the patients up for breast cancer radical surgery.

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## Prevalence of risk factors of coronary heart disease among diabetic patients in Medina city

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Diabetes mellitus (DM) is a common, complex, serious, and costly disease. Nevertheless, it can affect any part or organ of the body, and coronary artery diseases are major contributors to morbidity. Thus, diabetic patients have a high incidence of silent myocardial infarction, and patients with diabetes type II have 2-3 fold more chances for atheroma related diseases.<sup>1,2</sup> The overall prevalence of DM obtained from an epidemiological national study was 23.7%

in Saudi Arabia. The prevalence in males and females was 26.2% and 21.5% ( $p < 0.00001$ ). The calculated age-adjusted prevalence for the Saudi population for the year 2000 is 21.9%. Diabetes mellitus was more prevalent among Saudis living in urban areas (25.5%) compared to rural Saudis (19.5%) ( $p < 0.00001$ ),<sup>3</sup> and is expected to increase in the near future. In the Kingdom, DM was a major cause of morbidity in the last 2 decades; apparently due to sudden changes in lifestyle, due to economic development, urbanization and competitive lifestyle, and the same has been observed in the city of Medina. Two studies from Primary Health Care centers in Riyadh, showed that the prevalence of overweight ranges from 35-40.8%, and obesity from 36.5-46%.<sup>4,5</sup> Diabetes mellitus is a major health problem in the Kingdom of Saudi Arabia and its implications has to be studied, especially risk factors of coronary heart disease (CHD) in order to reduce the mortality rate of silent killer among Saudi population.

In a retrospective cross-sectional survey, conducted in 2004, and approved by an ethics committee for research in the Saudi Council for Health Specialties, Riyadh as part of postgraduate dissertation requirement, 262 randomly selected files were reviewed at the mini clinics at primary health care units selected randomly from the city of Medina, Saudi Arabia. Of the 262 files, 251 (95.8%) were included in the study as they fulfilled the inclusion criteria of Saudi nationality and not missing a follow-up appointment for 6 months. They all were diabetics (type I & II) and compared with regard to their control of blood glucose level. The Epi-Info version 6 was used to develop a spread data sheet and analysis. The chi-square and student t-tests were used for data analysis for categorical variables. The level of significance was set at 0.05, and estimated power of study was 80%. The study included 171 (68.1%) males and 80 (31.8%) females, the majority of which were in the age group of 50 years ( $50.23 \pm 14.62$  years). Moreover, the majority (80%) was type II diabetic, and almost 50% had the disease for 2-9 years, while almost 79% were either overweight or obese (Table 1).

This study shows that obesity and overweight are highly prevalent among diabetic patients. The overall prevalence of overweight was 37%, and the rate among men was significantly higher than women. The overall prevalence of obesity was 40.2%, and the rate among women was higher than men. These results can be compared with the results of other studies; especially the results of a study conducted in the South West area of the Kingdom, which indicated a high percentage of coronary artery disease (CAD) risk factors, namely: hypercholesterolemia (31%); DM (30%); hypertension (13.8%); family history of CAD (6%); and obesity (45%). The estimated progression of coronary artery