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MYELODYSPLASIA SYNDROME CAUSED BY RADIOTHERAPY AND CHEMOTHERAPY

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ABSTRACT

Among the various types of myelodysplastic syndromes (MDS), clonal hematopoietic disorders are closely related. In addition to hypocellular or hypercellular bone, peripheral blood cytopenia is often present, followed by progressive paralysis of myelodysplastic stem cells that are prone to developing acute myeloid leukemias (AMLs). This study is to evaluate Myelodysplasia Syndrome Caused by Radiotherapy and Chemotherapy. The adjusted odds ratio for MDS risk in non-CT patients was 1.51-fold (95 percent confidence interval: 1.25–1.82) greater than the odds ratio in CT patients. A substantial relationship between higher MDS risk and diabetes, stroke, and ischemic heart disease was found in patients who also used alkylating drugs or topoisomerase II inhibitors. Hematological malignancies have been linked to those who have been exposed to ionising radiation by accident, as well as cancer patients who have had radiation therapy. Alkylating medicines, topoisomerase II inhibitors, and antimetabolites, on the other hand, are often mentioned in the literature as causes of CT-induced MDS. Radiation treatment and chemotherapy are both linked to the later development of MDS, according to this population-based nested case–control study. Following cancer therapy, some tumour sites are more prone to the formation of MDS than others. It is possible that RT and CT have a beneficial relationship.

Key words: Antimetabolites, CT Patients, Diabetes.

INTRODUCTION

Our knowledge to date indicates that there has been no countrywide population-based investigation that has assessed treatment-related MDS for cancer in general or for specific individual malignancies. In Taiwan, we conducted research on this topic. It was our goal with this study to establish which initial cancer sites were more prone to the formation of MDS after therapy in cancer survivors, as well as to evaluate whether CT and RT interact. The study was conducted using the Taiwan National Health Insurance (NHI) network. Since 1982, when it became the leading cause of death, cancer was ranked high. Since then, the inconsistency rate has grown steadily, rising in 2011 with 320.65 new cases per 100,000 people. [1] cancer management and health problems related to the onset and treatment of cancer have become very important. [3]

Early detection, better diagnostic procedures, early and effective treatment, increased postoperative follow-up, and the aging population all contribute to people living with cancer longer. [2] In such a situation, MDS is a multidimensional clonal hematopoietic disorder that is closely related to the disease. In acute myeloid leukemia (AML), myeodysplastic stem cells gradually begin to paralyze following hypocellular or hypercellular bone morphology which is deformed and mature. [4,5,6] Chemotherapy (CT) and radiation therapy (RT) before MDS seem to be associated with higher rates of the disease. MDS has been linked to cancer treatment for a variety of cancers, including breast cancer, non-Hodgkin lymphoma, Hodgkin lymphoma, endometrial cancer, cervical cancer, prostate cancer, and brain cancer.

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AIMS AND OBJECTIVES:

To evaluate the Myelodysplasia Syndrome Caused by Radiotherapy and Chemotherapy.

Source of Information on Methods:

Approximately 99 percent of Taiwan's population (N 14 23.74 million) is currently registered in the NHI programme, which has been in place since 1995 and has been administered nationwide. [14] An analysis of retrospective nested case–control data using the National Health Insurance Research Database (NHIRD) Longitudinal Health Insurance Database 2000 (LHID2000). [7,8] National Health Research Institutes creates and maintains LHID2000 (NHRI) data. In 2000, a random sample of 4.5 percent of Taiwanese people was randomly selected from the NHIRD claim site, and data on LHID2000 reflects that segment. As per the National Health Insurance Research Institute (NHRI) of Taiwan, there were no statistically significant differences between LHID2000 and general insurance subscribers in sexual costs, age, or health care. Encryption of patient identification numbers and other personal information ensured complete confidentiality and security. The institutional review board at China Medical University in Central Taiwan, which performed the study, gave its approval (CMU-REC-101-012). [9,10] A diagnosis and procedure code from the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) was used to identify the disorders.

Participants that were chosen at random

Nest-based case management research was performed with LHID2000, and the findings were published. A twenty-year-old or older individual diagnosed with primary cancer by ICD-9-CM 140-195 and 200-208 codes was identified in the Registry for Catastrophic Illness Database as an exposure group, and this excluded all other groups. myeloid leukemia (ICD-9-CM codes 205.0 and 205.10) between January 1, 2000, and December 31, 2011. Case registration in the Disaster Management Register, physician diagnosis, and confirmation reports of pathology or other supporting medical evidence, required; these documents are then officially inspected by the insurance authorities. Patients with a history of MDS before 2000, as well as those with a history of MDS before a cancer diagnosis, were not included in the study. [11,12]

The case patient group was tracked until they were diagnosed with MDS in the years 2000-2011 (ICD-9-CM codes 284.9, 285.0, 205.10, and 205.0), whereas the non-MDS patient group was followed until death. via MDS. The diagnostic date was determined to be the MDS reference date. We randomly selected four people from the non-MDS group who were diagnosed with cancer at the same time as the case group and were usually associated with the case group by age (5 years), gender, age of cancer diagnosis, and the MDS reference year to create a comparison group. [13,14] We included 1265 MDS patients as trial participants and 5057 non-MDS individuals as controls in this study.

MDS is associated with a number of potential comorbidities and treatments.

Diabetes (ICD-9-CM code 250), hypertension (ICD-9-CM codes 401–405), hyperlipidemia (ICD-9-CM code 272), stroke (ICD-9-CM codes 430–438), chronic obstructive pulmonary disease (ICD-9-CM codes 490–496), and alcoholism (ICD-9-CM codes 291, 303, 305.00, 305.01, 305.02, 305.03) were all considered comorbidities (ICD-9-CM codes 571.0, 571.1, and 571.3). [15,16]

We also looked at anti-cancer drugs, such as alkylating agents, topoisomerase II inhibitors, and antimetabolites, all of which have been linked to increased risk of MDS. [13] A possible association between MDS and radiation and chemotherapy were studied prior to the reference date.

Examining the data and conducting a statistical analysis

Comparisons between the MDS group and the non-MDS group were made by comparing the distribution of demographic characteristics, co-morbidities, and initial treatment between the two groups. X2 tests were conducted on phase data, and t tests were conducted on continuous variables. The researchers used the statistical analysis of variables and unconditional variables to calculate orthopedic variables (ORs) and 95 percent confidence intervals (CIs) to link MDS and RT and CT. In a variety of models, diabetes, stroke, coronary heart disease, chronic obstructive pulmonary disease (COPD), alcoholism, and anticancer drugs have all been considered simultaneously. Risks associated with the use of RT and MDT CT were also measured using models. The SAS statistics software for Windows (version 9.3; SAS Institute, Inc., Cary, NC) was used to analyze all studies. A significant 0.05 rate was used for all subjects.

TABLE 1: Patient Demographic Details With Myeloplastic Syndrome

		MYELODYSPLASTIC SYNDROME		
	NO N=5057		YES N=1265	
	N	%	N	%
GENDER				
MEN	2573	50.9	643	50.8
WOMEN	2484	49.1	622	49.2
AGE				

20-49	880	17.4	220	17.4
50-64	1344	26.6	336	26.4
65-74	1283	25.4	321	25.4
>75	1550	30.6	388	30.4
MEAN	65.2	14.8	65.2	14.8
COMORBIDITIES				
DM	851	16.8	254	20.01
HTN	2515	49.8	652	21.5
HYPERLIPIDEMIA	1280	25.3	291	51.3
STROKE	394	7.77	130	10.02
IHD	1283	25.4	391	31
COPD	1977	39.1	550	43.5
ALCHOHOLISM	75	1.48	31	2.4

RESULTS:

Demographic data, baseline comorbidities, and treatment distributions are included in Table for comparison between the MDS and non-MDS populations. Women constituted 50.8 percent of the 1265 patients with MDS, and the majority of them were above the age of 65, according to the study (56.1 percent). [TABLE1] MDS groups and non-MDS groups were 65.2 years old (normal deviation: 14 14.8) and 65.2 (normal deviation: 14 14.8) years, respectively. Diabetes, stroke, ischemic heart disease, chronic obstructive pulmonary disease, alcoholism, the use of alkylating agents, the use of topoisomerase II inhibitor, and the use of antimetabolites were all more common in the MDS group than the non-MDS group. -MDS (all statistically significant; all P 0.05). The MDS group received significantly more RT and CT treatment than the non-MDS group, showing significant differences in treatment outcomes. The results of multivariable logistic regression models for the connection of RT and CT with MDS risk in cancer patients who had radiation and chemotherapy are shown in the table. Our study found a 1.53-fold increase in MDS among cancer patients receiving RT treatment compared to patients who did not receive it, even after accounting for complications such as diabetes, stroke, ischemic heart disease, chronic obstructive pulmonary disease, alcoholism, and anticancer drugs. RT treatment (95% confidence interval: 1.33–1.77). The adjusted odds ratio for MDS risk in non-CT patients was 1.51-fold (95 percent confidence interval: 1.25–1.82) greater than the odds ratio in CT patients. A substantial relationship between higher MDS risk and diabetes, stroke, and ischemic heart disease was found in patients who also used alkylating drugs or topoisomerase II inhibitors.

DISCUSSION:

This human-based case management study found that overall cancer treatment, whether radiation or chemotherapy, could significantly increase the chances of developing MDS in the future. According to the findings of the cancer study, patients with cancer of the stomach, colon, liver, breast, endometrial, prostate, and radiated kidneys were at higher risk of developing MDS. MDS has been shown to be more common in patients with lung cancer, endometrial cancer, and cervical cancer than in most people. Different patterns of MDS risk are seen in three different types of anti-cancer drugs between different tumors. Radiation therapy and computed tomography (CT) have a combined beneficial effect on the environment of MDS, according to further research. MDS is a common condition. About 20,000 cases of MDS were diagnosed in the United States in 2008, according to the National Cancer Institute, about 10 percent of those cases were linked to treatment. 15 In Taiwan, 454 cases of MDS were diagnosed in 2008, according to our National Health Insurance website. The French-American-British Cooperative Group has created a classification system based on laboratory data that is freely accessible for the first time. 16 The presence or absence of ring formed sideroblasts, antagonistic anemia (RAEBs), refractory anemia (RAEBs in transformation), and chronic myelomonocytic leukemia show up in each of the five categories. MDS has low prognosis, the majority of patients progressing to the AML antagonist within a few months after diagnosis.

Depending on the kind of cancer, a person's median survival period might range from months to years:

[17] Therapeutic MDS is a rare but catastrophic long-term effect of cytotoxic drugs in primary diseases. As reported in the literature, traditional cancer treatment works by causing severe damage to the DNA, which limits cell growth and initiates cell death pathways. Because RT and CT do not only target cancer cells, they may also cause changes in healthy cells. When these cells live and contribute to the genes that control the proliferation and secretion of hemopoietic stem and precursor cells, aberrant myeloid cell clone may form (HSPCs). [13]

Hematological malignancies have been linked to those who have been exposed to ionising radiation by accident, as well as cancer patients who have had radiation therapy. [18–20] Alkylating medicines, topoisomerase II inhibitors, and antimetabolites, on the other hand, are often

mentioned in the literature as causes of CT-induced MDS. [13,15] Alkylating agents are a type of anti-cancer drug that works in the treatment of almost all cancers, including lung cancer. 13 According to CDC, alkylating agents are the most common cause of treatment-related MDS. The condition was first diagnosed in Hodgkin's disease, but it has spread since then. The 15 MDS produced by topoisomerase II inhibitors usually detect quickly (within 1-3 years) and lead to moderate genetic mutations, as well as the 11q23 gene involved. most of the time. [21,22]

Exposure to alkylating chemicals, on the other hand, causes the disease to appear later (between 5–10 years) and causes chromosomal imbalances, which often damage chromosomes 5 and 7. [23,24] Radiation-induced effects and chromosomal abnormalities are equal in magnitude and severity to those reported after exposure to alkylating agents, according to a specific study. 25 Another class of cytostatic drugs, in addition to antimetabolites, has been linked to the development of therapeutic myeloid neoplasms. [13, 26]

CONCLUSION

Radiation therapy and chemotherapy are both linked to the latest developments of the MDS, according to this human-based case management study. Following cancer treatment, some tumor sites are more prone to MDS formation than others. It is possible that RT and CT have a good working relationship. In order to confirm our findings, we will need to do more research. Physicians should evaluate the long-term risks of CT and RT, which include the development of chronic illness, according to research findings (MDS). However, this data is unquestionable with well-established benefits of RT and CT in cancer prevention, far outweighing the risk of MDS.

REFERENCES

1. Pollack LA, Rowland JH, Crammer C, *et al*. Introduction: charting the landscape of cancer survivors' health-related outcomes and care. *Cancer*. 115, 2009, 4265–4269.
2. Choi M, Craft B, Geraci SA, *et al*. Surveillance and monitoring of adult cancer survivors. *Am J Med*. 124, 2011, 598–601.
3. Cazzola M, Malcovati L. Myelodysplastic syndromes – coping with ineffective hematopoiesis. *N Engl J Med.* 352, 2005, 536–538.
4. Besa EC. Myelodysplastic syndromes (refractory anemia). A perspective of the biologic, clinical, and therapeutic issues. *Med Clin North Am*. 76, 1992, 599–617.
5. Germing U, Kobbe G, Haas R, *et al*. Myelodysplastic syndromes: diagnosis, prognosis, and treatment. *Dtsch Arztebl Int*. 110, 2013, 783–790.
6. Kaplan HG, Malmgren JA, Atwood MK, *et al*. Increased incidence of myelodysplastic syndrome and acute myeloid leukemia following breast cancer treatment with radiation alone or combined with chemotherapy: a registry cohort analysis 1990–2005. *BMC Cancer*. 11, 2011, 260.
7. Cole M, Strair R, *et al*. Acute myelogenous leukemia and myelodysplasia secondary to breast cancer treatment: case studies and literature review. *Am J Med Sci*. 339, 2010, 36–40.
8. Leone G, Pagano L, Ben-Yehuda D, *et al*. Therapy-related leukemia and myelodysplasia: susceptibility and incidence. *Haematologica*. 92, 2007, 1389–1398.
9. Bonin SR, Lanciano RM, Smith MR, *et al*. Treatment-related myelodysplastic syndrome following abdominopelvic radiotherapy for endometrial cancer. *Gynecol Oncol*. 57, 1995, 430–432.
10. Mukherjee S, Reddy CA, Ciezki JP, *et al*. Risk for developing myelodysplastic syndromes in prostate cancer patients definitively treated with radiation. *J Natl Cancer Inst*. 106, 2014, djt462.
11. Sugiyama K, Kurisu K, Arita K, *et al*. Myelodyeplastic syndrome following therapy for brain tumor – two case reports. *Neurol Med Chir (Tokyo).* 42, 2002, 170–174.
12. Sill H, Olipitz W, Zebisch A, *et al*. Therapy-related myeloid neoplasms: pathobiology and clinical characteristics. *Br J Pharmacol.* 162, 2011, 792–805.
13. Cheng TM. Taiwan's National Health Insurance system: high value for the dollar. In Okma, K.G.H. and Crivelli, L. ed. Six Countries, Six Reform Models: The Health Reform Experience of Israel, the Netherlands, New Zealand, Singapore, Switzerland and Taiwan. New Jersey: World Scientific, 2009, 71-204.
14. Graubert T. Therapy-related myelodysplastic syndrome: models and genetics. *Biol Blood Marrow Transplant*. 16, 2010, S45–S47.
15. Bennett JM, Catovsky D, Daniel MT, *et al*. Proposals for the classification of the myelodysplastic syndromes. *Br J Haematol*. 51, 1982, 189–199.
16. Grossi A, Liumbruno GM, *et al*. New drugs in the treatment of myelodysplastic syndromes: are they changing the role of transfusion support? *Blood Transfus*. 6, 2008, 191–198.
17. Iwanaga M, Hsu WL, Soda M, *et al*. Risk of myelodysplastic syndromes in people exposed to ionizing radiation: a retrospective cohort study of Nagasaki atomic bomb survivors. *J Clin Oncol*. 29, 2011, 428–434.
18. Ojha RP, Fischbach LA, Zhou Y, *et al*. Acute myeloid leukemia incidence following radiation therapy for localized or locally advanced prostate adenocarcinoma. *Cancer Epidemiol*. 34, 2010, 274– 278.

19. Le Deley MC, Suzan F, Cutuli B, *et al*. Anthracyclines, mitoxantrone, radiotherapy, and granulocyte colony-stimulating factor: risk factors for leukemia and myelodysplastic syndrome after breast cancer. *J Clin Oncol*. 25, 2007, 292–300.
20. Warlick ED, Smith BD, *et al*. Myelodysplastic syndromes: review of pathophysiology and current novel treatment approaches. *Curr Cancer Drug Targets*. 7, 2007, 541–558.
21. Pedersen-Bjergaard J, Philip P, Larsen SO, *et al*. Therapy-related myelodysplasia and acute myeloid leukemia. Cytogenetic characteristics of 115 consecutive cases and risk in seven cohorts of patients treated intensively for malignant diseases in the Copenhagen series. *Leukemia*. 7, 1993, 1975–1986.
22. Rund D, Ben Yehuda D, *et al*. Therapy-related leukemia and myelodysplasia: evolving concepts of pathogenesis and treatment. Hematology. 9, 2004, 179–187.
23. Pedersen-Bjergaard J, Andersen MK, Christiansen DH, *et al*. Genetic pathways in therapy-related myelodysplasia and acute myeloid leukemia. *Blood*. 99, 2002, 1909–1912.
24. Moloney WC. Radiogenic leukemia revisited. *Blood.* 70, 1987, 905– 908.
25. Leleu X, Soumerai J, Roccaro A, *et al*. Increased incidence of transformation and myelodysplasia/acute leukemia in patients with Waldenstrom macroglobulinemia treated with nucleoside analogs. *J Clin Oncol.* 27, 2009, 250–255.
26. Kaplan H, Malmgren J, De Roos AJ, *et al*. Risk of myelodysplastic syndrome and acute myeloid leukemia post radiation treatment for breast cancer: a population-based study. *Breast Cancer Res Treat*. 137, 2013, 863–867.