LETTER TO THE EDITOR

Diabetes mellitus and cancer in Werner syndrome

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Abstract Onishi et al. recently reported here an association of diabetes mellitus (DM) with neoplasm type in newly identified patients with Werner syndrome (WS), an autosomal recessive cancer predisposition syndrome with features of premature aging that include a high risk of DM (Onishi et al. in Acta Diabetol 49(Suppl 1):259–260, 2012; Epstein et al. in Medicine 45:177–121, 1966). In contrast, we did not detect an association between DM and neoplasm type in an independent WS cohort we assembled to determine the histopathologic spectrum and type-specific risk of neoplasia in WS.

Keywords Werner syndrome · RECQ helicase deficiency · Cancer risk · Diabetes · Cancer epidemiology · Meningioma

To the Editors,

There is growing interest in the association between—and potential causal links between—diabetes mellitus (DM) and neoplasia [1]. Onishi et al. recently reported here an association of DM with neoplasm type in newly identified patients with Werner syndrome (WS), an autosomal recessive cancer predisposition syndrome with features of premature aging that include a high risk of DM [2, 3]. In contrast, we did not detect an association between DM and neoplasm type in an independent WS cohort we assembled to determine the histopathologic spectrum and type-specific risk of neoplasia in WS [4].

Onishi et al. [2] reported 39 neoplasms in 102 WS patients with DM (38.2 %) versus 16 neoplasms in 61 WS patients without DM (26.2 %), and a much higher prevalence of epithelial neoplasms in WS patients with than without DM (16.6 vs. 4.6 %, respectively). They observed no corresponding difference in the prevalence of non-epithelial neoplasms in WS patients with or without DM (21.6 vs. 21.3 %).

Our newly assembled WS cohort allowed us to determine DM prevalence by neoplasm type, though not the prevalence of neoplasia among WS patients with DM. We classified WS patients with DM or abnormal glucose homeostasis as DM positive; as DM minus when DM had been ruled out; or of unknown DM status. A majority of our WS patients with neoplasia were DM positive (119 of 189, or 63 % of patients). Table 1 lists WS patients in our cohort by neoplasm histopathologic type and DM status. The mean age at diagnosis of neoplasia in this cohort was significantly higher for DM-positive than for DM-minus patients with epithelial or non-epithelial neoplasms (47.2 vs. 37.1 years, t test p = 0.0003 and 44.6 vs. 38.7 years, t test p = 0.039, respectively). However, we did not observe an association...
of DM with either epithelial or non-epithelial neoplasms (Pearson’s $\chi^2$ test $p = 0.12$ when we excluded DM-unknown cases and seven DM-positive cases with both neoplasm types; see Table 1 footnote for patient numbers).

Sensitivity analyses demonstrated no association between DM and neoplasm type when we assumed patients with unknown DM status were equally likely to be DM positive or negative ($p = 0.17$). In contrast, there were significant associations between neoplasm type and DM status if we classified all patients of unknown DM status with epithelial neoplasms as DM positive and patients of unknown status with non-epithelial neoplasms as DM negative or vice versa ($p = 0.005$ and $p = 2.6e-9$, respectively). These analyses indicate it is possible to identify associations between neoplasm type and DM in small cohorts if all patients can be reliably classified as DM positive or minus.

Although we could not confirm Onishi et al.’s observations, we did identify two interesting associations between DM and cancer in WS. First, we found an association between DM and multiple neoplasia in our WS cohort as a whole ($p = 0.026$). Second, 3/4 of meningiomas (21 of 27, or 78%) and pancreatic neoplasms (3 of 4, or 75%) in our cohort were in DM-positive patients. Moreover, we found two case reports that describe the resolution of DM in WS patients following surgical removal of meningiomas [5, 6]. While causal links between DM and meningioma remain obscure, there are already plausible links between pancreatic carcinoma and DM both in WS patients as well as in the general population [7].

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Conflict of interest None.

References


