Letter

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Letter to the editor: What about cholesterol as a novel biomarker for bladder and kidney cancer diagnosis and surveillance? In memory of my dad Sossio Mormile

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To the editor:

Low serum cholesterol levels have recently been associated with risk for bladder cancer (BC) and kidney cancer (KC) [1]. However, it is still unknown whether low serum cholesterol levels can affect the incidence of urologic cancers [1]. Mechanism linking hypocholesterolemia to a worse outcome in BC and KC is intriguing and has been heavily investigated but still not well defined [1]. Currently, there is an ongoing debate on the prognostic significance of serum cholesterol level in cancer [2]. Disturbances in the lipid profile have long been involved in cancer development [2]. Some studies have demonstrated an inverse association between low serum cholesterol and cancer mortality [2]. Higher serum total cholesterol levels appear to be protective for overall survival in cancer patients [2]. Total cholesterol level has been identified as an independent risk factor for reduced mortality in cancer patients [2]. It has been observed that patients with higher total cholesterol levels before cancer diagnosis show better overall survival or disease-free survival in comparison to patients with lower levels [2]. The pro-inflammatory Interleukin-6 (IL-6) has been recognized to exert a significant impact on circulating lipid profile [3]. Inflammation has been documented to reduce circulating lipid levels through induction of IL-6 [3]. IL-6 has been shown to influence lipid metabolism in humans [3]. IL-6 has been proved to cause a decrease in serum total cholesterol [3]. Concordantly, blockade of IL-6 appears to increase blood levels of total cholesterol [3]. IL-6 appears to be a significant prognostic predictor for several cancer types including BC and KC [4,5]. IL-6 has been connected with tumorigenicity and prognosis in BC [4]. IL-6 appears to be overexpressed in BC specimens compared with non-malignant bladder tissues [4]. Increased expression of IL-6 has been significantly linked to a lower complete response rate after treatment, a higher clinical stage, and a shorter survival period, implying that IL-6 determination may be useful in predicting BC prognosis [4]. Conversely, bladder tumor growth and its invasive capability appear to be attenuated when IL-6 is blocked [4]. IL-6 and its signaling pathways have also been implicated in increasing the risk for KC development [5]. IL-6 has been described as a potential marker in KC patients with a negative impact on nephrectomy, quality of life, and treatment [5]. Concordantly, IL-6 inhibition has been proposed as a promising therapeutic target for KC [5]. Taken together, I hypothesize that low serum cholesterol levels may relate to an increased risk of developing BC and KC as a result of the underlying up-regulation of IL-6 gene expression which

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accompanies the onset and relapse of BC and KC. I suppose that lower levels of serum cholesterol without drugs and diet or even due to an apparent increased effect of drugs at recommended doses, may be an insidious and indirect sign for onset or relapse of KD and BC before the clinical symptoms. Research studies are needed to assess whether cholesterol may represent a non-invasive biomarker in clinical practice for early diagnosis, disease monitoring, and management response in BC and KC.

CONFLICTS OF INTEREST

The author has nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Raffaella Mormile. Data acquisition: Raffaella Mormile. Statistical analysis: Raffaella Mormile. Data analysis and interpretation: Raffaella Mormile. Drafting of the manuscript: Raffaella Mormile. Critical revision of the manuscript: Raffaella Mormile. Obtaining funding: Raffaella Mormile. Administrative, technical, or material support: Raffaella Mormile. Supervision: Raffaella Mormile. Approval of the final manuscript: Raffaella Mormile

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