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Letter to the Editor

Revisiting the meaning of Trousseau sign and syndrome

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We read with interest the cases series by Kanno et al. [1] of Trousseau syndrome in six women with metastatic cervical cancer complicated by cerebral infarction secondary to nonbacterial thrombotic endocarditis (NBTE), detected by transesophageal echocardiography (TEE) in four patients. The authors identified a short temporal relationship (up to 6 months) between the diagnosis of cerebral infarction and death [1]. Kanno et al. [1] used the term "Trousseau syndrome" when referring to cerebral infarction caused by cancer-induced arterial thrombosis or NBTE. We traced the origin of the term "Trousseau syndrome" to better understand its appropriate use in the medical lexicon.

Similar to Kanno et al. [1] findings in cervical cancer, Trousseau in 1868 recognized the association between uterine cancer and venous thrombosis in women during the later course of the disease [2]:

> *Patients of this description, on the last stage of their disease, present the symptoms of cachexia, and then, all at once, the inferior extremities become swollen, soon after which the saphea and crual veins can be felt to be hardened: in such cases it is found on examination after death, that their hard condition is owning to cruoric or intra-vascular fibrinous clots [p. 287].*

Trousseau was credited for recognizing the association between cancer and superficial and deep venous thrombosis, specifically, phlegmasia alba dolens [2]:

> *I have long been struck with the frequency with which cancerous patients are affected with painful oedema in the superior or inferior extremities,* ***whether one or other was the seat of cancer****. This frequent occurrence of phlegmasia alba dolens with an appreciable cancerous tumor, led me to the inquiry whether a relationship of cause and effect did not exist between the two, and whether the phlegmasia was not the consequence of the cancerous cachexia. I have since that period had an opportunity of observing other cases of painful oedema, in which, at the autopsy, I found visceral cancer, but in which during life, there was no appreciable cancerous tumor; and in which there existed a cachexia referable neither to the tubercular diathesis, the puerperal state nor chlorosis. I have thus been led to the occlusion, that when there is a cachectic state not attributable to tuberculous diathesis not to the puerperal state, there is most probably a cancerous tumor in some organ [p. 287].*

Author Contributions

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The correlation between cancer and venous thrombosis originally observed by Trousseau has been appropriately named Trousseau's sign. Trousseau also noted that patients with latent tetany exhibited a characteristic position of the hand and feet when a bandage is applied compressing the limb (carpopedal spasm) [3]. Therefore, it is appropriate to specify this form as "Trousseau sign of tetany" to differentiate it from the former "Trousseau's sign of malignancy." Additionally, this is one of the few instances where using an eponym's possessive form is appropriate since Trousseau died from gastric cancer occurring in the setting of venous thrombosis, the same disease he described in prior patients [2]. We believe that the term "sign" best describes this phenomenon as it requires the use of reasoning and judgment to infer its significance. Signs are helpful when present, as they provide physicians with information about the underlying disease. If a symptom possesses the attributes of sign, inferring that a conclusion can be drawn from its presence, it become a sign. If no inference can be made, then it remains a symptom.

Sproul in 1938 [4], conducted 4,258 consecutive autopsy studies and identified arterial, venous and cardiac thrombi in 617 patients, of which carcinoma constituted nearly half of all events. The term "Trousseau symptom" was first coined by Pieragnoli in 1956 [5] to refer to arterial and venous thrombosis occurring in visceral cancer. Sack et al. [6] in 1977 is frequently credited for being the first to use the term "Trousseau syndrome" to describe the spectrum of arterial and venous disorders occurring in patients with cancer, including venous thromboembolic disease, migratory thrombophlebitis, NBTE, chronic disseminated intravascular coagulopathy, arterial emboli, and microangiopathic hemolytic anemia [1,4,6,7]. Our review suggests that they used the term Trousseau syndrome exclusively to refer to the venous thrombotic and migratory thrombophlebitic events separately from the arterial conditions occurring in patients with cancer. The conditions commonly grouped under the term Trousseau syndrome represent diseases, not symptoms, and thus do not constitute a syndrome, a collection of various signs and symptoms. Hence, it would be a misnomer to name them as such. This represents more than semantics, as medical terminology must be consistent and precisely articulated. To our knowledge, there is no evidence that Trousseau himself reported arterial thrombotic events (e.g., stroke or cerebral infarctions) in cancer patients. Therefore, it would be incorrect to attribute these events to this eponym.

We recommend that the term "cancer-associated thrombosis" should be used to describe the broad spectrum of thrombotic events occurring in cancer patients. Specifically, "cancer-associated arterial thrombosis" or "cancer-induced arterial thrombosis" should be used to describe thromboembolic conditions involving the arterial side of the circulation in cancer patients. This definition is descriptive and encompasses the full range of arterial thrombotic events that can occur in cancer patient. We also support Johnson's suggestions that a basic clinic description is appropriate due to the inconsistent and confusing terminology with Trousseau syndrome [8].

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