





**CASE REPORT**

**VERSION 2: PEER REVIEW - APPROVED**

**Blue finger syndrome as a paraneoplastic manifestation: case report [Version 2; Peer Review - Approved]**

**Síndrome de dedo azul como manifestación paraneoplásica: reporte de caso [Versión 2; Revisión por pares - Aprobado]**

Fernando Stalin Freire Villón<sup>1</sup>  , Gabriela Alexandra Narváez Bravo<sup>1</sup>  , Kevin Andrés Tierra Aguirre<sup>1</sup>  , Roberto Albán Espinoza<sup>2</sup>   , Claudia Gabriela Clavijo Rosales<sup>1</sup>  

<sup>1</sup>Universidad Católica de Cuenca. Carrera de Medicina - Campus Cuenca. Cuenca, Ecuador.

<sup>2</sup>Hospital Vicente Corral Moscoso. Cuenca, Ecuador.

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**ABSTRACT**

It is currently known that cancer is a prothrombotic state that alters certain coagulation factors, and due to this presence of malignancy, pro-coagulation factors are secreted that contribute to a state of hypercoagulability that favors metastasis. In addition, there is also evidence of an increased excretion of thrombin, favoring clot formation. We present the clinical case of a 65-year-old man with multiple diseases, who presented with a neurological condition manifested by left facial paralysis, deviation of the labial commissure to the left, in addition to presenting horizontal nystagmus and gait disorders. Physical examination revealed a bluish coloration at the level of the fingers of the right lower extremity, with suspicion of vasculitis in the first instance. After several studies, a diagnosis of prostate cancer was made, bilateral orchiectomy was performed and the following treatments were sent: oncologic, antihypertensive, antidiabetic and oral anticoagulation.

**Key words:** Blue Finger Syndrome; Neoplasm; Neoplasm Manifesting; Thromboembolism; Thrombophilia.

**RESUMEN**

En la actualidad se conoce que el cáncer es un estado protrombótico que alteran ciertos factores de coagulación, y debido a esta presencia de malignidad se secretan factores de pro-coagulación que contribuyen a un estado de hipercoagulabilidad que favorece la metástasis. Además, también se evidencia una mayor excreción de trombina, favoreciendo la formación de coágulos. Se presenta el caso clínico de un hombre de 65 años con múltiples enfermedades, acude por un cuadro neurológico manifestado por parálisis facial izquierda, desviación de la comisura labial hacia la izquierda, además de presentar nistagmus horizontal y trastornos en la marcha. Se evidenció al examen físico una coloración azulada a nivel de los dedos de la extremidad inferior derecha, con sospecha de vasculitis en primera instancia. Posterior a varios estudios se llega al diagnóstico de cáncer de próstata, se realiza orquiectomía bilateral y se envían los siguientes tratamientos: oncológico, antihipertensivos, antidiabético y anticoagulación oral.

**Palabras clave:** Manifestación Neoplásica; Neoplásica; Tromboembolismo; Trombofilia; Síndrome de Dedo Azul.

## INTRODUCTION

Cancer is considered a prothrombotic condition; it means that this medical condition is 15-20% more prone to occur in oncologic patients since coagulation is altered by several mechanisms, mainly increase in fibrinogen, some factors in the coagulation cascade such as V (Leiden), VII (Anti-hemophilic A), IX (Hemophilia B) and X (Stuart); therefore, formation of thrombi may occur, if those thrombi are venous, they are composed of fibrin, and the erythrocytes or arterial thrombi are composed of platelet aggregates, “an imbalance between the coagulant factors, the fibrinolytic system and the platelet function”.<sup>(1,2,3)</sup>

The tissue factor (TF) of the cancerogenic cells causes both local and systemic hypercoagulability conditions. Said factor has an activity that is potentiated by the action of the anionic phospholipids and secretes heparinase, which is the one that degrades the glycosaminoglycans existing in the external matrix of cells, which favors the progression of the tumor and can even cause metastasis. Besides, its action blocks the antithrombotic effect caused by the tissue factor pathway inhibitor (TFPI), which generates more activity of the TF.<sup>(4)</sup>

By way of the TF complex of factor VII, it joins the phospholipids existing in the platelet membrane, where they proceed to activate factor X, thus initiating the formation of thrombin at the rate of factor II (prothrombin). As there is excess thrombin, a hypercoagulative condition is generated, it causes the activation of the platelet pathway together with factors V and VIII (VonWillebrand), resulting in more production of thrombin to this system.<sup>(4)</sup>

In certain cases, there are irregular coagulation values in these patients, such as the increase in factor VII a, as well as the thrombin-antithrombin complex, coagulation initiation factor, and factors II and VIII. Besides, there is a decrease in certain anticoagulative proteins that are C and S. Finally, we can stress that these anomalies are not a factor to predict more risks of developing thrombosis.<sup>(4)</sup>

The blue finger syndrome is characterized by having a purplish or bluish coloration on one or more fingers, it is a manifestation that can be triggered by multiple vascular diseases such as thrombosis, embolism, serious vasoconstriction, vascular bed disease or any freezing condition, and it may even be present as an expression of systemic diseases.<sup>(5,6,7)</sup>

The following article will cover the relationship existing between prostate cancer and the paraneoplastic blue finger manifestation as its expression by way of presenting the following case.

## CLINICAL CASE

A male 60-year-old patient with a pathological history of type 2 diabetes mellitus (DM2) five years ago, under treatment with dapagliflozin 10mg/day, high blood pressure (HBP) under treatment with losartan 50mg/day and chronic renal disease (CRD) under treatment with furosemide 40mg/day.

We went to the emergency service and said that four days before his being hospitalized and without any apparent cause, he had symptoms of palpebrate ptosis together with alteration of his cognitive condition; 24 hours later, there were disorders when walking, nausea resulting in vomit on three occasions in a moderate amount of food.

The physical examination showed pale sclera, left palpebrate ptosis, deviation of the commissure of the lips towards the left, dry oral mucosae, rhythmic r1-r2 heart increased in tone and intensity. The left thoracoabdominal region made up of several purple lesions being, approximately 20 cm x 10cm.

There was dermatosis disseminated onto the trunk and lower limbs and consisting in palpable purple erythematous lesions that did not disappear when applying acupressure (Figure 1), so there was a suspected small vessel alteration. Tests and renal ultrasounds were performed on the patient, which showed an inflammatory process of the left kidney and complex enteric cysts.



**Figure 1.** Dermatitis on the right lower limb consists in palpable purplish erythematous lesions that do not disappear when applying acupressure.

Due to the presence of the cyst, tumor marker screening was performed and it showed an elevation of total

PSA so prostatic ultrasound was requested and it showed diagnostic signs of prostate cancer. When expanding the tests for staging, cancer was found to be in stage IV due to the presence of metastatic lung nodules + retroperitoneal mediastinal lymph nodes and left axilla + blastic lesions in lumbar vertebrae, pelvis and femur.

The patient is currently receiving oncologic treatment and oral anticoagulation and is clinically stable. Treatment of his hormonal pressure began with leuprolide acetate plus bicalutamide until an orchiectomy was performed. After surgery, the oncology service will continue his treatment.

Besides, anticoagulation treatment for thrombophilia began with rivaroxaban and hormonal treatment with levothyroxine 25 mg orally without eating for two weeks, followed by 50 micrograms orally without eating.

## DISCUSSION

It was determined that the blue finger syndrome appeared because of the occlusion of a superficial vein due to the presence of a thrombus at its level; said expression appeared on the fingers of the right lower limb, also the presence of an ischemic vascular process found through computerized axial tomography (CAT), this symptom being the first clinical manifestation the patient had.

As the causes for the thrombotic process, others, such as vasculitis, were discarded, and high levels of PSA were not found, which, together with other tests, resulted in a diagnosis of stage IV prostate cancer.

As reported by Ameletal.<sup>(7)</sup> thromboembolism in patients with cancer occurs due to several factors, including malignant neoplasm and the release of procoagulative factors as well as comorbidities and complications in therapeutic interventions. Usually, there are increased values of thrombin and fibrin formation, which can trigger a hypercoagulability condition resulting in phenomena of angiogenesis, motility and tissue invasion, which allows further tumoral development and quick metastasis before generating clinical manifestations of possible thrombosis.

Malignant neoplasias have been associated with vascular thrombosis since 1865. Trousseau made known the relation to migratory thrombophlebitis in persons having cancer. Nowadays, Arrieta et al.<sup>(8)</sup> report that this association occurs because of the interaction among the tumor, prophylactic measures, risk factors and certain biomarkers. So the diagnosis for vascular thrombosis does not differ between patients with cancer and those who do not have it.

## CONCLUSIONS

It is concluded that cancer is a prothrombotic condition; therefore, in the case presented herein, the patient had a bluish coloration on the fingers of his right lower limb because neoplasia alters certain coagulation factors. Due to the presence of malignity, pro-coagulation factors contributing both to this hypercoagulability condition and to prostate cancer resulting in metastasis were secreted; in addition, more thrombin is excreted, too, thus favoring the formation of coagula.

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#### INFORMED CONSENT

Informed consent was obtained from the patient for the performance of this paper.

#### FUNDING

None.

#### CONFLICT OF INTEREST

None.

#### AUTHOR'S CONTRIBUTION

*Conceptualization:* Fernando Stalin Freire Villón, Gabriela Alexandra Narváez Bravo, Kevin Andrés Tierra Aguirre, Roberto Albán Espinoza, Claudia Clavijo Rosales.

*Research:* Fernando Stalin Freire Villón, Gabriela Alexandra Narváez Bravo, Kevin Andrés Tierra Aguirre, Roberto Albán Espinoza, Claudia Clavijo Rosales.

*Methodology:* Fernando Stalin Freire Villón, Gabriela Alexandra Narváez Bravo, Kevin Andrés Tierra Aguirre, Roberto Albán Espinoza, Claudia Clavijo Rosales.

*Project management:* Fernando Stalin Freire Villón, Gabriela Narváez, Gabriela Alexandra Narváez Bravo, Kevin Andrés Tierra Aguirre, Roberto Albán Espinoza, Claudia Clavijo Rosales.

*Original drafting and editing:* Fernando Stalin Freire Villón, Gabriela Alexandra Narváez Bravo, Kevin Andrés Tierra Aguirre, Roberto Albán Espinoza, Claudia Clavijo Rosales.

*Writing-revision and editing:* Fernando Stalin Freire Villón, Gabriela Alexandra Narváez Bravo, Kevin Andrés Tierra Aguirre, Roberto Albán Espinoza, Claudia Clavijo Rosales.

## SECTION NOT TRANSLATED

**Note:** In order to avoid misinterpretation or misunderstanding of the reviewers' and/or editors' comments, this section was not translated.

## OBSERVATIONS DERIVED FROM PEER REVIEW, PUBLISHING PROCESS AND AUTHOR'S RESPONSE

### *Observaciones de la Revisión por Pares:*

**Revisor 1/1:** Dr. Luis Alberto Pérez Ramírez, Universidad de Ciencias Médicas de Holguín (Cuba)

Las observaciones del revisor se realizaron en forma de comentarios, por lo que se han colocado los párrafos o frases donde se han colocado los comentarios con la finalidad de contextualizar la observación.

1. El resumen se escogió una forma no estructurado por la modalidad de presentación del manuscrito, pero recomendaría que no excediera las 150 palabras.
2. En vez de la palabra PATOLOGÍA usaría el término ENFERMEDAD para describir una afección médica; evitar la repetición de este conector.
3. La expresión “Se va con” no es la terminología médica adecuada, recomiendo sustituirla.
4. Ordenar las palabras clave alfabéticamente y revisar la palabra PARANEOPLASIA no aparece en los descriptores en Ciencias de Salud.

### *Respuesta a los revisores por parte de los autores:*

Los autores no emitieron carta de respuesta a los revisores y/o editor, sin embargo, aceptaron las recomendaciones y se realizaron las correcciones necesarias.