Septic Thrombophlebitis in The Upper Limb Secondary to Folliculitis in The Hand

Case Report

María Cortes Avilés-Martínez[1], Alejandro María Muñoz-Morillas[2], Rubén Cordero-Bernabé[3] and Ignacio Marañés-Antoñanzas[3]

[1] *Servicio de Medicina Interna del Complejo Hospitalario Universitario de Albacete*
[2] *Medicina Familiar y Comunitaria en Hellín (Albacete)*
[3] *Servicio de Medicina Interna del Hospital de Hellín (Albacete)*

Reception date of the manuscript: 18/January/2023
Acceptance date of the manuscript: 16/May/2023
Publication date: 01/August/2023
DOI: 10.5281/zenodo.10534608

Abstract—Septic Thrombophlebitis in The Upper Limb Secondary to Folliculitis in The Hand
Deep vein thrombosis of the upper extremities is a rare disease and that does not mean we can forget about it, since it can cause important complications such as septic thrombophlebitis. We present the case of a 54-year-old patient with an initial pustular lesion in the right hand of 15 days of evolution, appearing in the last 3 days inflammation and pain, from the wrist to the axillary region, following the venous path of the arm, being compatible with a thrombophlebitis and confirmed with Doppler ultrasound. Empirical intravenous antibiotic therapy and anticoagulation with heparin were initiated, presenting clinical improvement. However, 3 days later, small, non-suppurative nodular lesions appeared following the venous course. The patient was discharged with oral antibiotic therapy and anticoagulation with heparin. In the first review, after observing a new nodular lesion with persistent phlebitic cord, antibiotic therapy was restarted for a week. After that, the nodules on her forearm had practically resolved, but those on her wrist and arm fluctuated, drained, obtaining negative cultures. In the subsequent review, the nodular lesions had been filled again, and due to elevated acute phase reactants, the patient was readmitted, undergoing new drainage and intravenous antibiotic therapy. In control Doppler ultrasound, thrombophlebitis persists, maintaining heparin. The patient showed clinical improvement, so she was discharged to her home to continue oral antibiotic therapy for 7 days and then discontinued, resulting in remission of the nodular lesions. Finally, a month later, she had complete resolution of the phlebitis, discontinuing heparin. **Rev Med Clin 2023;7(2):e01082307019**

Keywords—Thrombophlebitis, Folliculitis, Upper limb

Resumen—Tromboflebitis Séptica en Miebro Superior Secundaria a Foliculitis en Mano
La trombosis venosa profunda de las extremidades superiores es una enfermedad poco frecuente y no por ello podemos olvidarnos de ella, ya que puede causar complicaciones importantes como la tromboflebitis séptica. Presentamos el caso de una paciente de 54 años con una lesión pustulosa inicial en mano derecha de 15 días de evolución, apareciendo en los últimos 3 días inflamación y dolor, desde muñeca hasta región axilar, siguiendo el trayecto venoso del brazo, siendo compatible con una tromboflebitis y confirmándose con ecografía doppler. Se inició antibioterapia empírica intravenosa y anticoagulación con heparina presentando mejoría clínica. Sin embargo, 3 días después aparecieron unas lesiones nodulares pequeñas, no supurativas siguiendo el trayecto venoso. La paciente se fue de alta con antibioterapia oral y anticoagulación con heparina. En la primera revisión, tras observar una nueva lesión nodular con persistencia de cordón flebítico, se reinició antibioterapia durante una semana. Tras ello, los nódulos del antebrazo prácticamente se habían solucionado, pero los de la muñeca y brazo fluctuaban, drenándose, obteniendo cultivos negativos. En la revisión posterior, las lesiones nodulares se habían vuelto a rellenar, y ante elevación de reactantes de fase aguda, la paciente reingresa, realizándose nuevo drenaje y antibioterapia intravenosa. En ecografía doppler de control, persiste tromboflebitis, manteniéndose heparina. La paciente presenta mejoría clínica, por lo que se procede a su alta a domicilio para continuar antibioterapia oral 7 días y suspendiéndose, objetivándose una remisión de las lesiones nodulares. Finalmente, un mes después, presenta una resolución completa de la flebitis, suspendiendo heparina.
Rev Med Clin 2023;7(2):e01082307019

Palabras clave—Tromboflebitis, Foliculitis, Miembro superior

INTRODUCTION

Upper extremity deep vein thrombosis is a rare disease, but it should be carefully considered in patients with isolated unilateral inflammation of the upper extremities because of its potential to cause devastating complications and sequelae, such as pulmonary embolism and septic thrombophlebitis, the latter being the most common protagonist of our case. The increasingly frequent use of Doppler ultrasound has made it possible to distinguish thrombophlebitis from phlebitis by confirming the presence or absence of thrombi within a vein, being able to offer better targeted early treatment and avoid the complications that it can cause.[1–4]

CASE REPORT

A 54-year-old woman attended the emergency department due to a pustular lesion in the right hand. As personal antecedents, the following stand out: intolerance to clavulanic acid, smoker of 10 cigarettes a day, hypothyroidism in replacement treatment, seronegative HLA-B27 bilateral sacroiliitis without immunosuppressive treatment, only with first-step analgesics under monitoring by Internal Medicine, asthma with on-demand treatment and depressive syndrome. As chronic treatment, she was taking levothyroxine 112 mcg/24h, venlafaxine retard 75mg/24h, omeprazole 20mg/24h, lorazepam 1mg/24h, alprazolam 0.5mg/12h, and hydropherol 0.266mg/month.

She went to the emergency department due to a pustular lesion on the back of the proximal interphalangeal joint of the second finger of her right hand for 15 days, with discharge of purulent material and without impairment of mobility. In the last 3 days, she has associated inflammation and pain on the inner part of the arm, from the wrist to the axillary region, compatible with the venous path of the right arm. Absence of measured fever.

As for the physical examination, she presented a good general condition, conscious and oriented, normal colored, normal hydrated and normal perfused. Blood pressure: 125/85 mmHg, heart rate: 112 bpm, temperature: 36ºC, oxygen saturation: 98% basal. He presented a superficial wound of 0.5 cm in diameter in the right upper limb with desquamation in the proximal interphalangeal area of the 2nd finger, without exudate, on an erythematous base that extends towards the venous tract, which is inflamed, indurated and hot, from the wrist to the axillary region being palpable a venous cord, which is painful on palpation.

Analytically, leukocytosis of 11,300/uL stands out with 7,200/uL neutrophils, C-reactive protein of 3.1mg/dl (normal range 0-1), biochemistry without alterations and in coagulation, a slight decrease in prothrombin time of 10.70 seconds (normal range 11.50-13-50). A venous Doppler ultrasound of the right upper limb was performed, where echogenic material was observed inside the cephalic vein of the forearm, without color or spectral Doppler flow inside it, as well as thickening of the skin and subcutaneous cell tissue. These were findings related to thrombophlebitis (Figure 1, 2).

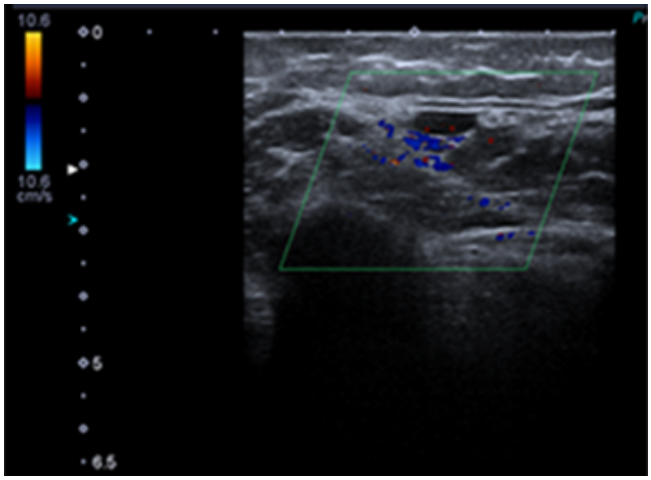

Figure 1: Echogenic material inside the cephalic vein of the forearm without Doppler flow inside.

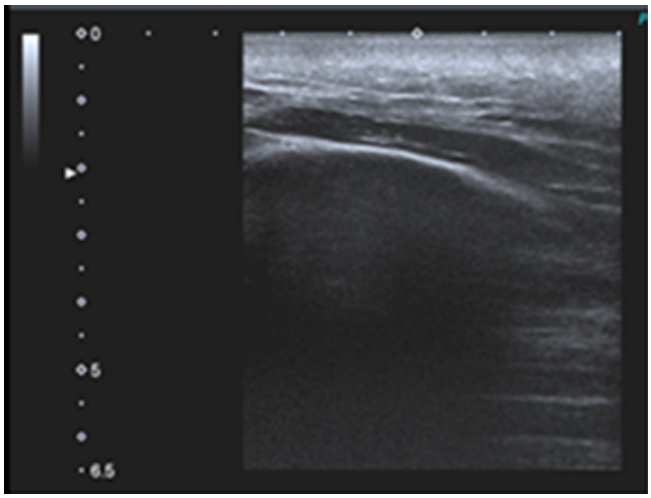

Figure 2: Longitudinal section of the cephalic vein with echogenic material inside.

Intravenous antibiotic therapy is started with ceftriaxone 2 grams every 24 hours and clindamycin 600 mg every 8 hours for 3 days, along with anticoagulation with enoxaparin 60 mg every 12 hours, presenting a decrease in edema and a drop in local temperature, but with the appearance of small nodular lesions between 1 and 1.5 cm in diameter, with rash, not suppurative following the venous path. In subsequent analytical controls, she presented a decrease in leukocytes, being discharged 5,500/uL with 3,100 neutrophils/uL, but persisting C-reactive protein of 3.5 mg/dl (normal range: 0-1) with normal procalcitonin. At discharge, clindamycin 300 mg every 6h orally was prescribed for 7 more days and tinzaparin sodium at anticoagulant doses 10,500 IU every 24h (Figure 3).

Contact data: María Cortes Avilés-Martínez, Avenida España nº 10 Bajo A, Albacete. CP: 02002, Phone number: (+34) 639 79 49 87, maricortesaviles@gmail.com

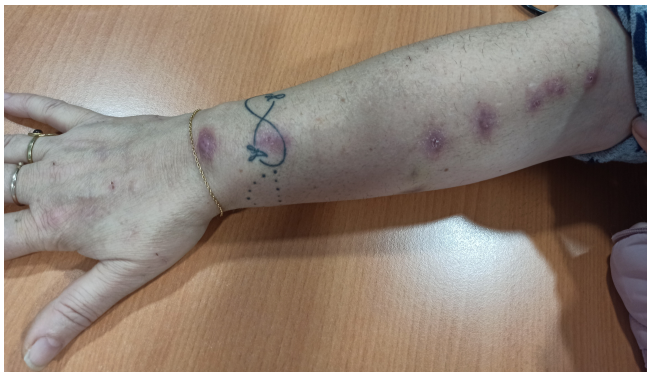

Figure 3: Nodular lesions between 1 and 1.5 cm in diameter, with rash, following the venous path.

Ten days later, the patient came for a check-up, having finished antibiotic therapy and continuing with heparin. She presents a new lesion in the second finger of the right hand and a phlebitic cord persists on the inner side of the arm from the wrist to the middle of the inner biceps, with increased local temperature and pain on palpation. The nodular lesions on the arm that she presented on admission had not changed since discharge, neither in size nor in characteristics. Analytically, there was an elevation in the liver profile, with GOT 37 U/L (normal range: 10-34), GPT 69 U/L (normal range: 10-49), GGT 359 U/L (normal range: 10-38), lactate dehydrogenase 438 U/L (normal range: 208-378), without accompanying digestive symptoms, which is interpreted as secondary to pharmacological toxicity. In addition, a moderately elevated sedimentation rate persists 87 mm (normal range: 0-15). Given the persistence of the symptoms, oral antibiotic therapy with ciprofloxacin and clindamycin was reintroduced, and the heparin was changed to fondaparinux 7.5 mg every 24 hours.

One week after the new treatment regimen, the nodules on the forearm had practically resolved, finding those on the wrist and arm softer, fluctuating and with the possibility of drainage, so these nodules were drained in the consultation, obtaining serohematic material, which was sent for culture, the results of which were negative (including aerobic and anaerobic cultures, in Lowenstein and Ziehl-Nielsen staining).

The following week, she returned to the consultation, presenting a new filling of the nodular lesions that had been drained the previous week. Given a not entirely favorable evolution, a new admission for intravenous treatment is proposed, rotating the antibiotic, prescribing ceftriaxone 2g/24h and metronizadol 500mg/8h. Venous Doppler ultrasound was repeated, in which a persistence of echogenic material was observed inside the cephalic vein of the forearm, with some palpable segments with greater intravenous echogenic content, in addition to thickening of the skin and increased echogenicity of the subcutaneous cell tissue, findings still related to thrombophlebitis. Treatment with fondaparinux and intravenous antibiotic therapy was maintained for 7 days, with progressive clinical and analytical improvement, with a decrease in the swelling of the right arm, as well as the phlebitic cord and nodular lesions, for which the patient was discharged with cefditorene 400mg/12h, metronidazole 500mg/8h and fondaparinux.

In the next check-up in the consultation, 7 days after hospital discharge, the patient presented improvement with no signs of inflammation and with nodular lesions in remission, for which reason oral antibiotic therapy was withdrawn and low-molecular-weight heparin was maintained. One month later, the patient presented a complete resolution of the phlebitic cord, as well as the nodular lesions, therefore heparin was discontinued.

Discussion

Deep vein thrombosis of the upper extremities is a rare disease, but it must be taken into account and detected early due to its potential to cause significant complications and sequelae, including septic thrombophlebitis, as we wanted to reflect with this clinical case.[1–4]

Most patients, in addition to presenting typical findings associated with venous inflammation and thrombosis, are accompanied by high fever, tenderness along the course of the vein, fluctuation and/or purulent drainage, and erythema that extends significantly further beyond the margin of the vein.[5–9] Some patients may have associated hypoxemia, dyspnea, and chest pain due to pulmonary septic emboli. Septic pulmonary embolism is rare, but cases have been reported in this regard and should be taken into account.[10]

Septic thrombophlebitis (STP) can occur spontaneously, however, most cases involving superficial peripheral veins are due to skin wounds with adjacent localized infection, venipuncture performed for phlebotomy, or intravenous injection. In some cases, intravenous catheters, such as peripherally inserted central catheter (PICC) lines, may be the initial culprit in the peripheral vein, as well as deep veins, such as the superior vena cava. With the inferior vena cava or superior vena cava, septic thrombophlebitis occurs more frequently as a consequence of an indwelling catheter.[10]

Other conditions, such as Lemierre's syndrome, pilethrombophlebitis (septic portal vein thrombosis), septic thrombophlebitis of the dural sinuses and pelvic veins, often result from invasive infection of a nearby nonvascular structure. For example, STP of the pelvic veins may be due to endometritis, pelvic inflammatory disease, intra-abdominal infections, abdominal surgery, childbirth, or septic abortion. Lemierre's syndrome, which is thrombophlebitis of the internal jugular vein, is most often caused by pharyngitis but may be secondary to dental infection. STP of the dural sinus may be due to an ear, nose, or throat infection, such as mastoiditis, otitis media, or even meningitis.[10]

The current incidence of catheter-associated peripheral STP is estimated to be 0.5 cases of bloodstream infections per 1000 days of a peripherally inserted intravenous device. For non-tunneled, non-medicated central venous catheters, the incidence is estimated to be 2.7 per 1000 intravenous

device days. In burn patients it has been reported that approximately 4.2% experience peripheral STP. Deep STP not associated with a catheter is seen much less frequently.[10]

Although the exact pathophysiological mechanism of STP is not fully understood, it is believed that it initially begins with a rupture of the endovascular wall, leading to thrombus formation. This disruption of the vein wall may be due to an endovascular device, such as a peripheral line or a central line. However, it can also be due to a pre-existing hypercoagulable state, such as in cancer patients. Once a thrombus is present, invasion by a microorganism may result from rupture of the skin or an adjacent structure. Once an organism has entered the vein, it proliferates and can further increase thrombus formation and inflammation. The most common organism involved is *Staphylococcus aureus*. However, other microorganisms have been implicated, such as viruses, parasitics and fungi, and even polymicrobials. Other common germs are those of the streptococcal species, anaerobes and gram-negative organisms.[10]

Once septic thrombophlebitis occurs, various complications related to hematogenous bacterial spread and septic thromboembolism may develop, including endocarditis, septic arthritis, and even septic uveitis.[10]

Patient-related factors that confer increased risk of peripheral venous thrombophlebitis are female gender, immunosuppressed states, intercurrent diseases such as infectious processes, comorbidities such as diabetes mellitus that is associated with endothelial dysfunction and is an inflammatory state, hematological malignancies , lymphoreticular, disseminated and solid tumors; previous thrombophlebitis, burns and elevated hemoglobin levels, since hemoglobin levels of 12.5 g/dL to 13.9 g/dL have a higher risk compared to hemoglobin < 10.5 g/dL.[11] In our case, the only factor that could be related to an increased risk of thrombophlebitis is a history of seronegative bilateral sacroiliitis, but since the patient is not receiving any immunosuppressive treatment, we do not believe that it could have favored the development of septic thrombophlebitis.[11]

The presence of intercurrent diseases is a contributing factor to the development of thrombophlebitis. Intercurrent disease can refer to pneumonia or an infection of the abdomen, genitourinary system, skin infection, and also related to an intravenous catheter. The greater risk could be due to chemical irritation of the endothelium due to the use of intravenous antibiotics, highlighting that in our patient at the time of diagnosis she had not yet received intravenous antibiotic therapy.[11]

Intravenous antibiotics that have been associated with increased risk are amoxicillin/clavulanate, aminoglycosides, dicloxacillin, cloxacillin, erythromycin, benzylpenicillin, and cefuroxime, possibly due to the presence of microparticles in the infusion. Other intravenous drugs such as potassium chloride and hypertonic solutions may predispose to thrombophlebitis; unlike corticosteroids that reduce this risk.[11]

Ultrasound may be helpful in STP (e.g., if an abscess is present in close proximity to the affected vessel). It can also be diagnostic if a thrombus is revealed in the setting of a positive blood culture. In cases of pelvic or dural vein thrombophlebitis, however, ultrasonography will not provide an adequate study (due to poor penetration). The best test available in these cases is contrast-enhanced computed tomography (CT), which allows assessment of any filling defects within a vessel that may contain a clot, and can also demonstrate any surrounding inflammation. If CT scanning is not available, magnetic resonance imaging (MRI) can also be used to diagnose most cases of STP. MRI combined with venography is the most sensitive non-invasive test for evaluating dural sinuses.[10]

Treatment of STP depends on the source of infection, the organisms involved, the structures affected, and the individual physiology of the patient. The main goals of treatment include removal of the source of infection, such as peripheral or central intravenous catheters, administration of broad-spectrum intravenous antibiotics, possible anticoagulation, and evaluation by a surgical team for possible surgical intervention (in case of persistence of the thrombus, despite the anticoagulation regimen applied, in which thrombolysis in situ is an option to control the infection).[12] The role of anticoagulation is controversial. Some authors recommend anticoagulation to prevent thrombus propagation, while others favor anticoagulation only if there is extension of the thrombus; however, there are no controlled studies to date. Anticoagulation should be discontinued in patients who are thrombocytopenic, with a platelet count of less than 50,000/microL due to a high risk of bleeding.[10]

Mortality from septic thrombophlebitis has drastically decreased over the last century due to the early use of antibiotics and better diagnoses.[10]

In conclusion, we want this clinical case to serve as a reminder, so as not to forget the complications derived from peripheral venous thrombosis, such as septic thrombophlebitis.

SOURCE OF FUNDING

The funding of the work was covered by the authors.

CONFLICT OF INTEREST

The authors deny presenting conflicts of interest in this work

REFERENCES

[1] Heng, Shu Yun et al. “Peripheral Vein Thrombophlebitis in the Upper Extremity: A Systematic Review of a Frequent and Important Problem.” The American journal of medicine vol. 133,4 (2020): 473-484.e3. doi:10.1016/j.amjmed.2019.08.054.

[2] Sherry Scovell, MD, FACS. “Superficial vein thrombosis and phlebitis of the lower extremity veins”. UpToDate. Literature review current through: Nov 2022. This topic last updated: May 31, 2022.

[3] Rahmani, Muhammad Javaid Hameed et al. “Venous thrombosis: not always in the legs.” BMJ case reports vol. 2014 bcr2014207464. 9 Dec. 2014, doi:10.1136/bcr-2014-207464.

[4] Evans, Natalie S, and Elizabeth V Ratchford. “Superficial vein thrombosis.” Vascular medicine (London, England) vol. 23,2 (2018): 187-189. doi:10.1177/1358863X18755928.

[5] Lipe, Demis N., et al. “Septic Thrombophlebitis.” StatPearls, StatPearls Publishing, 5 July 2022.

[6] Tan, Gregory, and Mingwei Ng. “Emergency department point-of-care ultrasound for upper extremity deep venous thrombosis ED POCUS for upper extremity DVT.” International journal of emergency medicine vol. 14,1 66. 4 Nov. 2021, doi:10.1186/s12245-021-00391-4.

[7] Cuddy, Karl et al. “Necrotizing Lip Infection Causing Septic Thrombophlebitis of the Neck: A Rare Variant of Lemierre Syndrome.” Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons vol. 76,1 (2018): 134-139. doi:10.1016/j.joms.2017.05.030

[8] Zhang, Jie et al. “Phlegmasia Cerulea Dolens in the Upper Extremity: A Case Report and Literature Review.” Annals of vascular surgery vol. 76 (2021): 601.e7-601.e11. doi:10.1016/j.avsg.2021.04.042

[9] Blumberg, Garrett et al. “Clinical Mimics: An Emergency Medicine-Focused Review of Cellulitis Mimics.” The Journal of emergency medicine vol. 53,4 (2017): 475-484. doi:10.1016/j.jemermed.2017.06.002.

[10] Lipe, Demis N., et al. “Septic Thrombophlebitis.” StatPearls, StatPearls Publishing, 5 July 2022. PMID: 28613482

[11] Alhassan, Sulaiman et al. “Clinical Presentation and Risk Factors of Venous Thromboembolic Disease.” Critical care nursing quarterly vol. 40,3 (2017): 201-209. doi:10.1097/CNQ.0000000000000159.

[12] Farny B, Vacheron CH, Friggeri A, Allaouchiche B. “Septic Thrombophlebitis with Persistent Bacteremia Treated by Thrombolysis”. Turk J Anaesthesiol Reanim. 2022 Apr;50(2):145-147. doi: 10.5152/TJAR.2021.1125. PMID: 35544255; PMCID: PMC9361394.